Reprinted peer reviewed version with permission from the Journal of Tropical Medicine and International Health, volume 15 no 5 pp645–652 May 2010. For more information on the Carter Center's work to fight river blindness, please visit www.CarterCenter.org

Does onchocerciasis transmission take place in hypoendemic areas? A study in North Region of Cameroon

Moses N Katabarwa[1], Albert Eyamba[2], Mouhamadou Chouaibou[2], Peter Enyong[3], Thomas Kuété[4], Souleymanou Yaya[5], Abdoulaye Yougouda[5], Jean Baldiagaï[5], Kambaba Madi[5], Gervais Ondobo Andze[6], and Frank Richards[1].

1. The Carter Center, Atlanta, USA
2 The Carter Center, Yaoundé, Cameroon
3. Research Foundation for Tropical Diseases and Environment, Buea, Cameroon
4. Department of Parasitology, Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Cameroon
5. Ministry of Public Health, North Region, Cameroon
6. Ministry of Public Health, Yaoundé, Cameroon

Abstract

OBJECTIVE: Community-directed treatment with ivermectin (CDTI) for onchocerciasis control is targeted to meso and hyperendemic areas in Africa. Below the threshold, communities are considered hypoendemic and mass treatment is not recommended. As policy begins to shift from control to elimination, hypoendemic areas' role in maintaining Onchocerca volvulus needs re-examination. The study determined whether independent transmission occurs in a hypoendemic area in the north region of Cameroon.

METHODS: Ten "high risk" communities along the River Mayo Douka system in Ngong Health District, at least 20 km from the nearest CDTI program that has been implemented for over 15 years were studied. 649 adults (≥20 years of age) and 561 children (under 10

years) resident of the communities were examined for nodules and microfilaria. A subsample of 334 adults was examined for onchocercal ocular morbidity. Simulium flies from four collection points were captured over three months yearly for two years, and examined by dissection for larval stages of O. 2

Introduction

Onchocerciasis, also known as river blindness, was one of the world's second leading infectious cause of blindness until a very successful international campaign was launched against it decades ago. The infection is caused by a nematode worm known as Onchocerca volvulus, which lives up to fifteen years in the human host. The infective larval stages of O. volvulus are transmitted to humans through the bite

ivermectin through community-directed treatment with ivermectin (CDTI) in areas where onchocerciasis is considered to be a public health problem: these areas are deemed ‘meso/hyperendemic’ and have a nodule rate of ≥20% and/or a microfilaria prevalence of ≥40%. In those areas, the populations are at greatest risk of developing ocular or skin manifestations, so that ivermectin treatment is a priority. In hypoendemic areas (below meso/hyperendemicity threshold), the risk of morbidity is to a large extent reduced.

Targeting for mass treatment through CDTI was through country by country, large scale Rapid Epidemiological Mapping of Onchocerciasis (REMO) to detect these meso/hyperendemic areas (Ngoumou et al, 1994). REMO was rooted in the fact that the vectors for onchocerciasis have highly specific breeding site requirements and limited flight range, and therefore it was possible with the aid of topographical maps to choose representative communities most likely to be seriously affected by onchocerciasis. The REMO was followed by the Rapid Epidemiological Assessment (REA) that relied on palpation examinations for characteristic onchocercomas (“nodules”) in a sample of 30-50 males aged 20 years and over in the ‘high risk’ or ‘first line’ communities (located on the rivers) drawn from areas likely to have the highest transmission and thus the highest risk for transmission and severe disease (Boatin and Richards, 2006).

What has remained unstudied is the uncertain transmission in hypoendemic areas (nodule rate <20% and microfilaria prevalence of <40 %) and the presumed low onchocerciasis morbidity that led to their exclusion from mass treatment. Richards et al., 2000 assumed that transmission was likely to be ongoing in some of these areas. As policy begins to shift from control of morbidity to complete transmission interruption, the role that hypoendemic areas excluded from the APOC program play in independently sustaining *O. volvulus* needs to be carefully examined. If independent transmission exists in hypoendemic areas, onchocerciasis could be ‘reseeded’ into adjacent meso/hyperendemic areas that presumably have higher vector biting

rates) should the decision be made to halt mass treatment with ivermectin. The aim of the present study was to determine whether incident transmission occurs in a hypoendemic area not targeted for mass treatment by ivermectin in northern Cameroon.

Methods and Materials

Study area: The study took place in North Region of Cameroon in the Ngong Health District, which has a population of about 20,000 people in about 300 km^2 (Figure 1 and 2). "No CDTI" areas shown in Figure 1 may or may not contain hypoendemic areas. Ngong hypoendemic focus was selected based on a review of REMO and REA data conducted in the 1990s which showed that onchocerciasis nodule rates remained occurred in apparently hypoendemic fashion (<20% nodule rate), and nearby meso/hyperendemic areas targeted for mass treatment were at least 20 km away from Ngong focus (Ngoumou et al 1994; Macé et al 1997, APOC's REMO website- http://www.who.int/apoc/cdti/remo/en/index.html). Those meso /hyperendemic areas have been under mass treatment with ivermectin for at least 15 years, with treatments first launched with support from the River Blindness Foundation and subsequently expanded with The Carter Center and APOC assistance.

Study sample: The methods recommended for rapid epidemiological mapping (REMO), and rapid epidemiological assessments (REA) were applied (WHO Report, 1991; WHO Report, 1992; Ngoumou et al, 1994; Abanobi, 1999). There were less than twenty communities in Ngong hypo endemic focus, and ten of them along R. Mayo Douka and its distributaries were selected for the study. These were well established communities with no evidence of significant population mobility that have never been under CDTI. Beyond 10 km on both sides of R. Mayo Douka are uninhabited farmlands and savanna woodlands. The selected communities were "first line" communities from R. Mayo Douka, and supposedly "high risk" for onchocerciasis. Health education about onchocerciasis was given and the purpose of the study explained to local leaders and community members in each community in a general

meeting. After consent was obtained, 42 to 120 adults per community, 20 years of age and above, who had lived in them respectively for at least 10 years were examined. There were no refusals among adults. About 80% of the adults in every selected community were examined. In addition, children (3 to 10 years old) whose parents had assented to their participation were enrolled in the study. A few children who did not participate did not affect the results of the study. In total, 1210 persons (649 adults and 561 children) were examined for onchocercomas by palpation and mf by skin snip. Ocular morbidity related to onchocerciasis was assessed in a subsample of 334 adults in six of the communities, and Simulium flies were collected by human landing capture for dissection in sites located in four of the ten communities.

Nodule palpation: Nodule

– 24 hours in order to allow any mf present to emerge from the skin. Each skin snip was then removed from the well with a needle, and the saline solution was examined unstained under a microscope (40x) for mf of *O. volvulus*. The results were expressed as positive/negative, and as a proportion of the number of persons in the sample.

Ocular morbidity assessment: Although ocular morbidity is not an indicator of transmission,

Selection of the Simulium fly collection sites was based on proximity to the community, favourable river flow, and other ecological conditions necessary for black fly breeding. Four teams of two fly collectors (one team per community) were recruited, consented, trained, and equipped to perform landing captures of Simulium flies. The collectors were at least 18 years of age, and informed that they could opt out of the study if they so wished at any time, without any repercussions. The collectors sat at the 4 selected sites near the river bank and exposed their legs between 0800 – 1200 and 1400 – 1800 hours, three days every two weeks per month from late August to mid-November, 2008 and July to November, 2009 (WHO Report, 1995). Female Simulium flies seeking blood for their eggs would come and settle on the exposed

Ethical Approval: The study was approved by the Emory University Institutional Review Board (eIRB - 11438) and the Ministry of Health of the Government of Cameroon, Yaounde.

Results

Microfilariae (mf) and nodule prevalence: The mean mf prevalence among adults was 2.91%, ranging from 0 to 11.8% in ten communities (Table 1). None of the communities met the 40% mf prevalence criteria for mesoendemicity (and threshold for CDTI). The mean nodule prevalence in the same group was 12.2% (range 0.3% to 27.1%). In contrast to mf results, two of the ten communities had a nodule prevalence of over 20%, which exceeded the 20% threshold that is the currently accepted indicator for CDTI (and the threshold for mesoendemicity). Only three of 516 children (0.47%) under ten years of age had mf detected in their skin snips (community range of 0 to 1.9%). Nodule rates in children, as with adults, were more than anticipated with a mean of 9.2% (range from 1.6% to 17.5%). Four communities exceeded 10% nodule prevalence among children (01 Tw le rean

nature of the REMO map of Africa needs to be reexamined. Treatment areas are not necessarily the only areas where transmission is ongoing, and new investment will be needed to redefine and expand the CDTI program to many of the areas previously left untreated.

Consideration is now being given to stopping CDTI in areas that have been treated with good coverage for over 15 years (WHO Report, 2009; Diawara et al 2009). We suggest that stopping ivermectin in formerly meso/hyperendemic areas that are adjacent to hypoendemic areas like Ngong that have low rate autochthonous transmission could result into "reseeding" of the parasite into those post treatment zones. The result could be prompt disease recrudescence. One option could be application of twice yearly treatment with ivermectin in adjacent areas of low transmission to halt or 'catching up' with the epidemiological trend in nearby and former meso/hyper-endemic areas (Cupp and Cupp, 2005).

Only 294 Simulium flies were collected in 8 months of intermittent field activities during 2008 and 2009. A longer period of study could provide better data on annual biting, transmission and infection rates (Renz, 1987) and we recommend future studies to assess entomological and environmental indicators throughout the year, to include activities in the meso/hyperendemic areas in the vicinity of Ngong, over a period of at least two years if possible. This could also reveal changes in rainfall period, how it may impact the development of larval stages of Simulium damnosum s.l, and the ability to transmit onchocerciasis within or reseed former meso and hyperendemic areas if ivermectin treatment was halted.

Confounding factors. In the study, nodule rates were higher than expected given corresponding skin snip derived mf prevalence, especially in children. This could have been confounded by the presence of ganglia in some communities. Ganglia can form around any joint, and are usually painless and often bare visible as localized swellings. They usually do

We thank the local chiefs, and community members of Ngong onchocerciasis area for their

References:

1. Abanobi OC, (1999). Cross-validation of the rapid epidemiological mapping of onchocerciasis endemicity in Anambra state, Nigeria. Annals of Tropical Medicine & Parasitology, 93, (7) 721- 726

2. Albiez EJ, Buttner DW, Duke BO, (1988) Diagnosis and extirpation of nodules in human onchocerciasis. Trop Med Parasitol. 39 (Suppl 4): 331-346.

3. Boatin BA, Richards FO, Jr. (2006). Control of onchocerciasis. Adv Parasitol. 61:349-94

4. Brieger WR, Awedoba AK, Eneanya CI, Hagan M, Ogbuagu KF, Okello DO (1998). The effects of ivermectin on onchocercal skin disease and severe itching: results of a multicentre trial. Tropical Medicine and International Health. 3(12):951-961.

5. Busson J, Bourée P, and Doyon D (1978) Intérêt de la lymphographie dans 13 cas d'onchocercose. J. Radiol. Electrol. 59 (3) 203-208.

6. Chippaux JP, Boussinesq M, Fobi G et al. (2001). Effect of repeated ivermectin treatments on ocular onchocerciasis: evaluation after six to eight doses. Ophthalmic Epidemiol. 6(4):229-46.

7. Cupp EW, Cupp MS (2005). Short report: impact of ivermectin community-level treatments on elimination of adult Onchocerca volvulus when individuals receive multiple treatments per year. Am J Trop Med Hyg. 73(6):1159-61

8. Davies JB (1995) A rapid staining and clearing technique for detecting filarial larvae in alcohol-preserved vectors. Trans R Soc Trop Med Hyg. 89(3):280.

9. Diawara L, Traoré MO, Badji A, et al. (2009) Feasibility of onchocerciasis elimination with ivermectin treatment in endemic foci in Africa: first evidence from studies in Mali and Senegal. PLoS Negl Trop Dis. 3.

11. Macé JM, Boussinesq M, Ngoumou P, Enyegue Oye J, Koéranga A, Godin C (1997) Country-wide rapid epidemiological mapping of onchocerciasis (REMO) in Cameroon. Ann Trop Med Parasitol 91(4):379-91

12. Ngoumou P, Walsh JF, Mace JM (1994) A rapid mapping technique for the prevalence and distribution of onchocerciasis: a Cameroon case study. Ann Trop Med Parasitol 88 (5):463-74

13. Richards F, Hopkins D, Cupp E (2000) Programmatic goals and approaches to onchocerciasis. Lancet. 356(9240):1523-4.

14. Renz A (1987) Studies on the dynamics and transmission of onchocerciasis in a Sudan-savanna area of North Cameroon III. Infection rates of the Simulium vectors and Onchocerca volvulus transmission potentials. Ann Trop Med Parasitol 81(3):239-52

15. Schulz-Key, H. (1978) A simple technique to assess the total number of Onchocerca volvulus microfilariae in skin snips. Tropenmed Parasitol 29:51-54.

16. Thomson CT, Obsomer V, Kamgno J, Gardon J, Wanji S, Takougang I, Enyong P, Remme JH, Molyneux DH and Boussinesq M (2004). Mapping the distribution of Loa loa in Cameroon in support of the African Programme for Onchocerciasis Control. Filaria Journal 3:7.

17. Thylefors B (2008) The Mectizan Donation Program (MDP). Ann Trop Med Parasitol 102 Suppl 1:39-44

18. Wanji S, Tendongfor N, Nji T, Esum M, Che JN, Nkwescheu A, Alassa F, Kamnang G, Enyong PA, Taylor MJ, Hoerauf A, Taylor DW (2009) Community-directed delivery of

21. WHO Report (1995) Onchocerciasis and its control. Report of a WHO Expert Committee on Onchocerciasis Control. Technical Report Series 852; 104 pp.

22. WHO Report (2009) Elimination of river blindness feasible: WHO study shows that areas in Mali and Senegal require no further mass treatment. News release WHO/25 21 July. TDR Communication, Geneva, Switzerland

23. WHO/APOC website. Rapid epidemiological mapping of onchocerciasis (REMO). http://www.who.int/apoc/cdti/remo/en/index.html

24. Winthrop KL, Proaño R, Oliva O et al.(2006) The reliability of anterior segment lesions as indicators of onchocercal eye disease in Guatemala. Am J Trop Med Hyg. 75 (6):1058-62.

Legend

Figure 1: Figure 1: Rapid Epidemiological Map of Onchocerciasis (REMO) of Cameroon showing: definate CDTI areas (meso and hyperendemic), no CDTI areas (hypoendemic) including Ngong study area, and excluded areas (not endemic for onchocerciasis).

Figure 2: Map of North Region of Cameroon showing the Ngong onchocerciasis hypoendemic focus.

Figure 3: Ngong onchocerciasis hypoendemic focus *S. damnosum s.l* captures and rainfall 2008-2009

Monthly *Simulium* flies collected during 2008.

Monthly *Simulium* flies collected during 2009.

▲ Rainfall (mm) during 2008

■ Rainfall (mm) during 2009

Figure 1

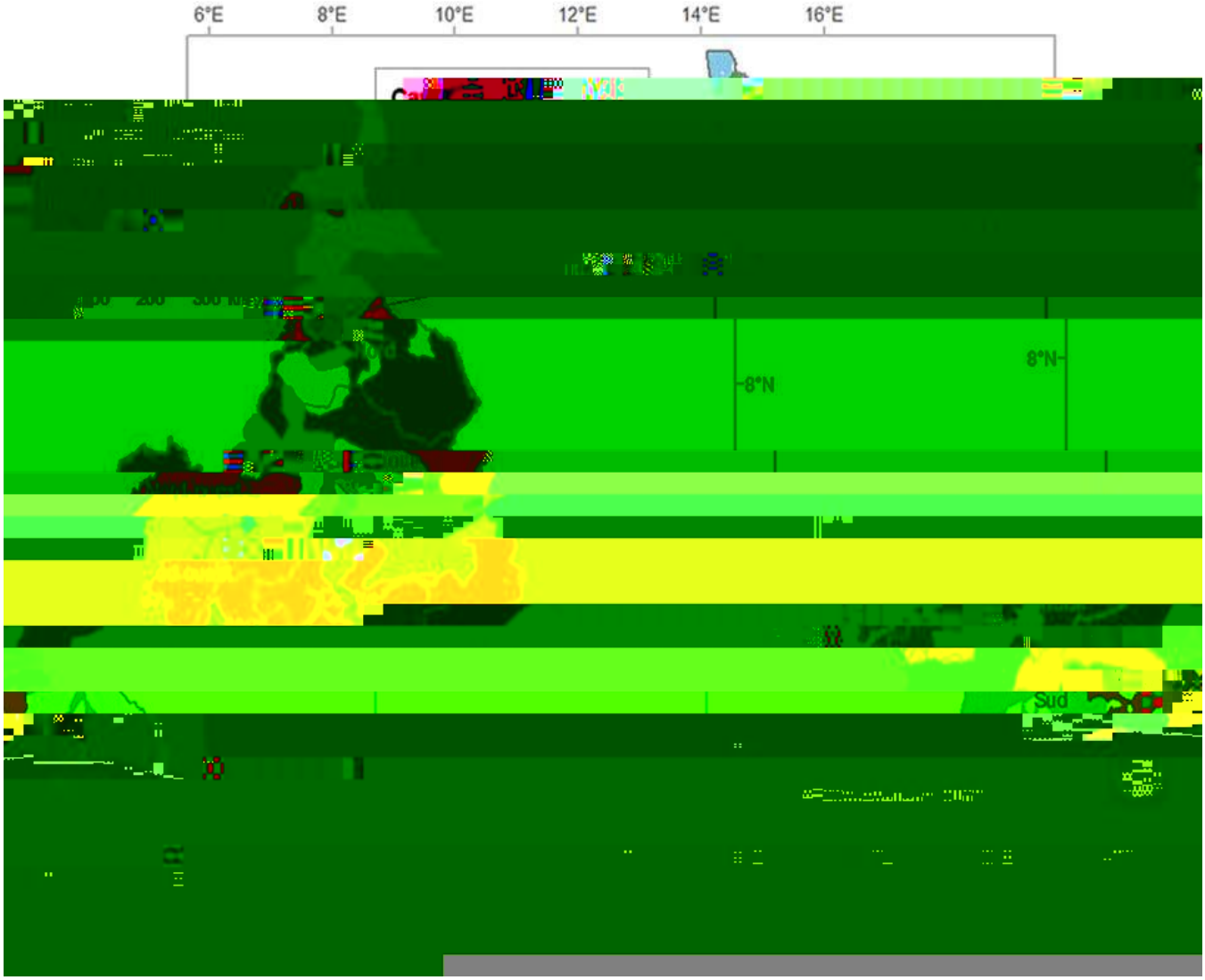
6°E
8°E
10°E
12°E
14°E
16°E
8°N
8°N
Sud

Figure 2

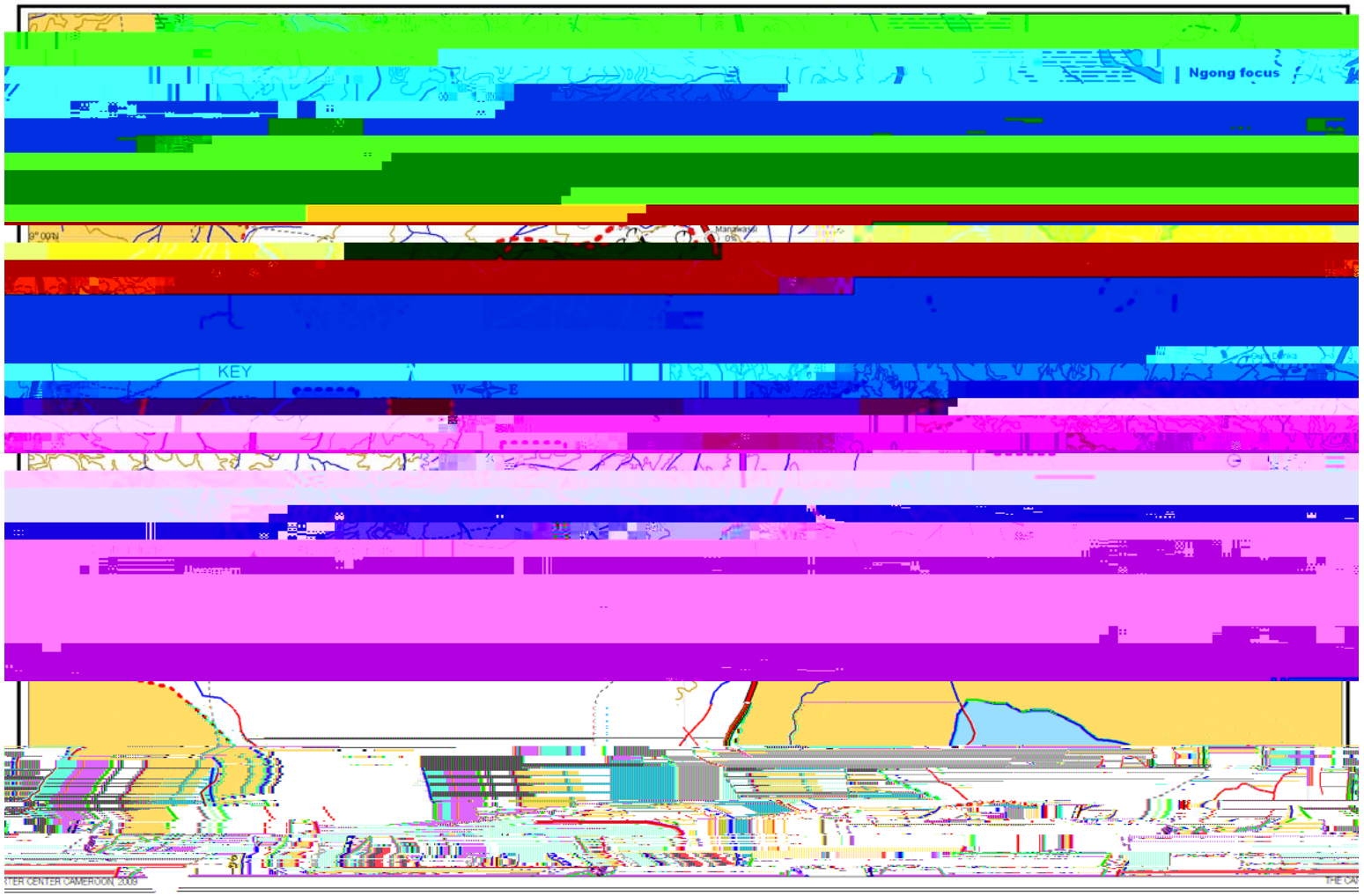

Figure 3

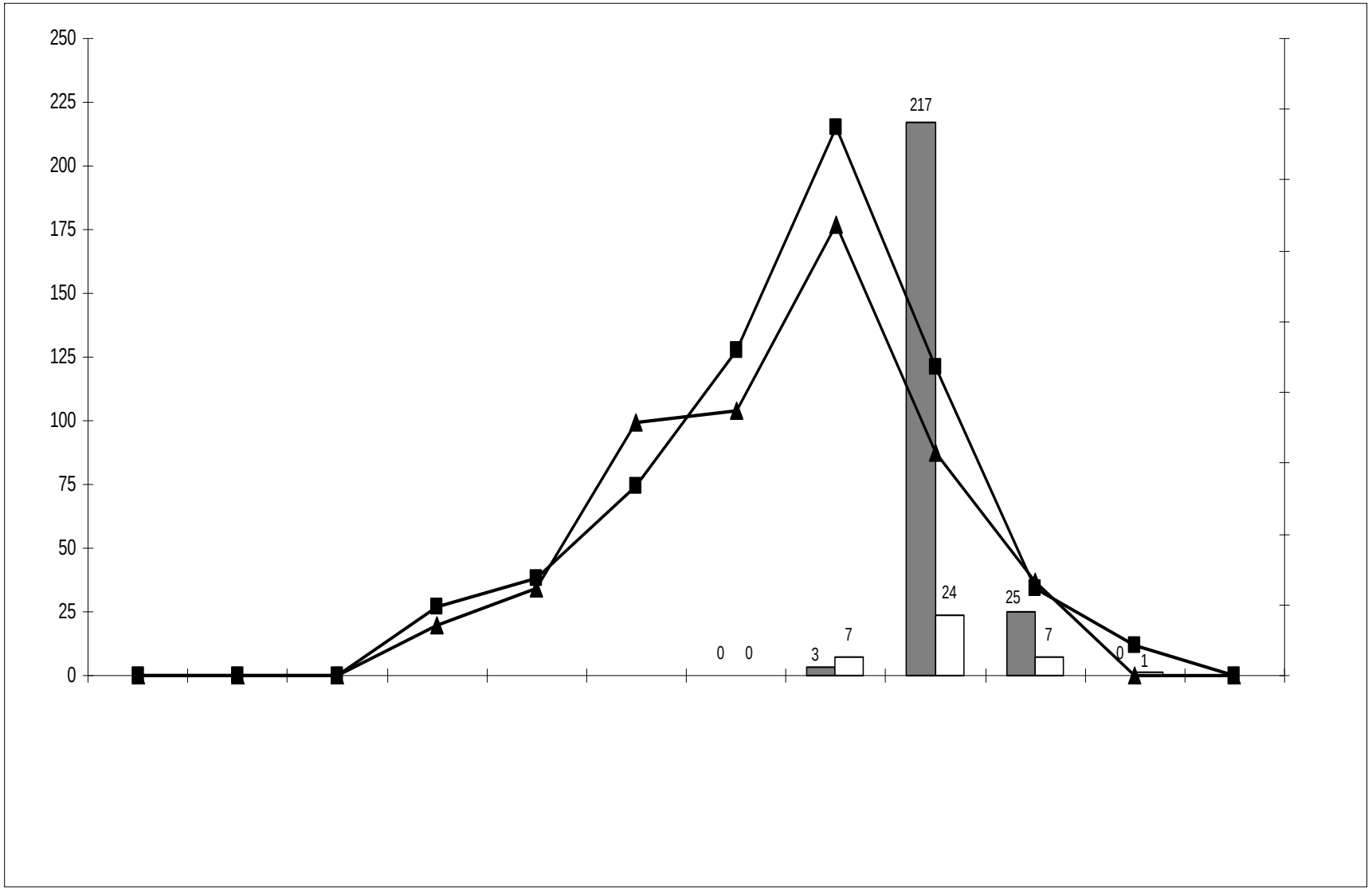

Table 2: Microfilariae and nodule prevalence in 561 children, 3-10 years old.

Community Name	No. of Children	Mean age	No. positive	% mf	No. positive (nodules)	% nodules
Winde Ngong	57	7.56	0	0	10	17.54
Ouro Malloum	67	7.73	1	1.49	5	7.46
Ouro Falli-Panai	52	7.42	1	1.92	4	7.69
Ouro Donka	14	5.57	0	0	1	7.14
Koubadje	79	6.91	1	1.27	5	6.33
Kone	55	6.69	0	0	3	5.45
Douka Gaïnako	63	7.79	0	0	11	17.46
Dellem	62	7.75	0	0	1	1.61
Ouro Mbolta	53	8.05	0	0	6	11.32
Boumedje-Nassarao	59	7.59	0	0	6	10.2
	561		**3**	**0.47**	**52**	**9.2**

Table 3: Ocular lesions specific to onchocerciasis in 334 adults of 20 years old

Community Name	No Assessed	Mean Age	No. of mf in anterior Chamber	% mf present in anterior Chamber	No of Stage A+B specific punctate keratitis	% Stage A+B specific punctate keratitis	No. of Scelerosing keratitis cases	% scelerosing keratitis
Ouro donka	34	32.9	0	0.00	0	0.00	0	0.00
Ouro Falli-Panai	61	34.1	0	0.00	0	0.00	0	0.00
Bounmedje-Nassarao	50	23	0	0.00	0	0.00	1	2.00
Ouro Malloum	66	25.5	1	1.52	0	0.00	0	0.00
Douka Gainako	62	27.4	0	0.00	0	0.00	1	1.61
Kone	61	27.8	0	0.00	1	1.64	0	0.00
Total	334	28.45	1	0.30	1	0.30	2	0.60