

REVIEW ARTICLES

Onchocerciasis in the Thyolo highlands of Malawi

GM Burnham

Skin snips for 23,373 persons living in the Thyolo highlands showed infection with *Onchocerca volvulus* to be widely but unevenly distributed within the Thyolo highlands. Although 60% of adults in some areas were infected, the intensity of infection was light. Infection with *O. volvulus* is associated with blindness in the Thyolo highlands, though the number of excess blind due to onchocerciasis is probably less than 300. Persons infected were found to weigh significantly less and to have more symptomatic complaints than those not infected.

Introduction

The Thyolo highlands are a densely populated area at the southern end of the Great Rift Valley. Most of the arable land is given over to cultivation of maize by subsistence farmers, but on land above 600 m a considerable amount of tea is grown. Onchocerciasis was first reported in the Thyolo highlands in 1939, but its presence had been noted some years earlier^{1,2}. Reports by Harvey³, Ben Sira et al⁴ and Rampen⁵ suggested that the Thyolo highlands are the only substantial focus of the disease in Malawi although onchocerciasis may be found in other highland areas of southern Malawi as well.

During the past 90 years the population of the Thyolo highlands has increased from 18,000⁶ to

about 500,000. With this population growth has come widespread deforestation which is perhaps responsible for *Simulium damnosum* replacing the less aggressive *S. neavei* previously predominant in the Thyolo highlands^{7,8}. Inhabitants believe the prevalence of *Simulium* flies has increased steadily since the 1950s when Berner & Carr⁹ observed that *S. damnosum* were hardly noticeable. Local residents are also certain that the skin changes of onchocerciasis are also seen more commonly than in earlier years. However, these inhabitants may have difficulty distinguishing between various pruritic skin conditions.

In order to determine prevalence, intensity and distribution of infection with *Onchocerca volvulus* in the Thyolo highlands, this survey was carried out. This survey was also designed to study any association between infection and symptomatic complaints and changes in body weight in a subsample of adults.

Methods

Between 1984 and 1987 two skin snips were taken with a Holth sclerocorneal punch bilaterally from the posterior iliac crest of 23,373 persons aged one and older. The 211 survey sites were selected to give population samples from all ecological zones within the Thyolo highland area. Personal data were recorded and visual acuity measured in persons aged 15 and above using an illiterate E-chart. Efforts were made to sample all persons in each area selected. The sample size included in the survey represents approximately 5% of the highland's population.

Each skin snip was placed in a numbered well of a microtitre plate containing 200 µl of isotonic saline. Plates were covered with cling film for transport to the hospital laboratory. After 4 hours' incubation, 1 drop of 10% formalin was added to each well and microfilariae (mf) subsequently counted. Skin snips were blotted dry and weighed. Microfilarial counts were expressed as mf per mg of skin.

From 119 sample sites representing all parts of the highland area, 5,653 persons were asked if they regularly experience one or more of seven symptoms. These were: generalised body aches or pains, backache, joint pains, itching of the skin, feelings of weakness, dizziness and feelings of being hot or

Malamulo Hospital, P.O. Makwasa
GM Burnham

Address for correspondence:
Dr. Gilbert M. Burnham
Department of International Health
The Johns Hopkins University
615 N. Wolfe Street
Baltimore, Maryland 21205, USA

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2. Onchocerciasis in Malawi. 2. Subjective complaints and decreased weight in persons infected with *Onchocerca volvulus* in the Thyolo highlands. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1991;85:497-500.

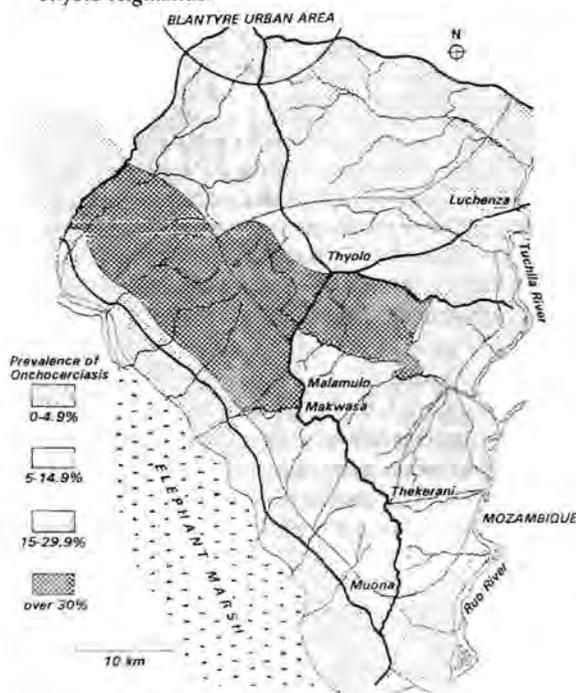
feverish. Positive responses were recorded if these complaints were said to be regular or common occurrences.

Data from the sample were standardised for age and sex using information from the 1977 Malawi National census¹⁰. Rates for blindness and impaired vision were compared using the Mantel Haenszel- χ^2 test¹¹. The relationship between the frequency with which various complaints were reported and rising microfilarial counts was assessed using χ^2 for trend. Mean body weight and body mass index (weight : height²) for those infected and those uninfected with *O. volvulus* living in each of the sampling sites were compared using the *t* test.

Results

PREVALENCE OF MICROFILARIAE IN SKIN SNIPS: For all persons included in the survey prevalence of infection was 15.6%. In persons aged 5 and older, prevalence was 17.9%; and in those 15 and above, microfilariae were present in 22.7%. These prevalence figures are diluted by the inclusion of large numbers of uninfected persons from the margins of the onchocerciasis focus. In some sample sites over 60% of adults had microfilariae present in skin snips. Prevalence of microfilariae by area is set out in Figure 1. Prevalence of infection by age among 6,565 persons sampled who lived within the principal area of the focus is depicted in Figure 2.

Figure 1: Map showing prevalence of microfilariae in skin snips by area among 23,373 persons aged one year and older in the Thyolo Highlands.



INTENSITY OF INFECTION: Overall intensity of infection with *O. volvulus* was low although a few persons had counts of over 400 mf per mg of skin. In no area did intensity of infection exceed a geometric mean of 8 microfilariae per milligram of skin. Areas with highest prevalence of infection generally had the highest microfilarial intensity. Intensity of infection by age in persons from the areas of highest prevalence of infection is set out in Figure 3.

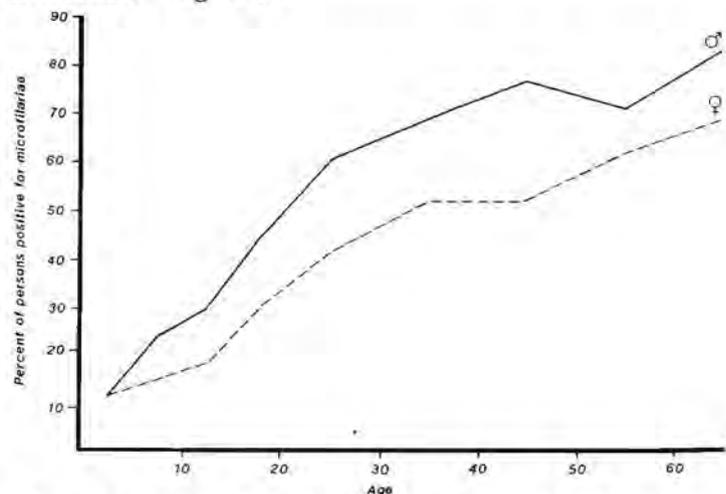


Figure 2. Prevalence of *O. volvulus* infection by age among 6,562 persons living in the principal area of the Thyolo focus.

VISUAL IMPAIRMENT: Visual acuity was recorded for 10,262 persons aged 20 and older. A person was classified as having impaired vision if visual acuity was 6/18 or worse in both eyes but still able to count fingers at 1 m with both eyes. If a person was able to count finger at 1 m with neither eye he was classified as bilaterally blind. Persons unable to count fingers at 1 m with one eye and having a visual acuity of 6/18 or poorer in the companion eye were considered as bilaterally blind.

A visual acuity of 6/18 or poorer was present in 8.56% of persons in the survey. Prevalence of poor vision and bilateral blindness by age is shown in Figure 4. Of persons infected with *O. volvulus*, 9.6% had visual impairment compared with 8.2% or those uninfected ($P=0.054$). Among persons over age 50 with microfilariae in skin snips, visual impairment was no greater than among persons with negative skin snips.

There was no correlation between the extent of visual impairment in a particular area of the Thyolo highlands and the prevalence or intensity of infection in that area.

In all, 235 bilaterally blind were registered during the this survey. Bilateral blindness was present in 2.96% of persons with microfilariae in skin snips, and in 1.97% of those without infection ($P=0.0014$).

PREVALENCE ESTIMATES: It can be estimated that some 327,000 persons live in areas of the Thyolo highlands where prevalence of infection with *O. volvulus* is 10% or greater. Overall, it is estimated that 94,500 persons aged one and above are infected. Of those infected, an estimated 50,500

were compared with those having negative skin snips, there was a significant difference in weights. Men who were normally sighted with positive skin snips weighed 1.3 kg less than men without microfilariae in skin snips ($P=0.015$). Among women with normal vision the difference was 1.6 kg ($P=0.03$).

The presence of microfilariae has an effect on body weight which appears to be independent of the influence of visual impairment. Increasing microfilarial counts did not correlate with a decreasing body weight. Body weights for persons with and without microfilariae in skin snips are set out in Table 2.

Discussion

Onchocerciasis was found by this survey to be unevenly distributed in the Thyolo highlands focus. The majority of adults living in the centre of the focus are probably infected although the intensity of infection is light. Because microfilarial loads tends to be light, taking

only two skin snips tends to miss many persons with low levels of infection¹². It is probable that the number of persons actually infected with *O. volvulus* is considerably higher than revealed during this survey.

Despite the high prevalence of microfilariae in parts of the Thyolo highlands, intensity of infection tends to be low. This probably is a function of the high population density of the Thyolo focus where there are in excess of 265 persons per km² of land. By contrast, many of the areas severely affected by onchocerciasis in the Volta basin of West Africa

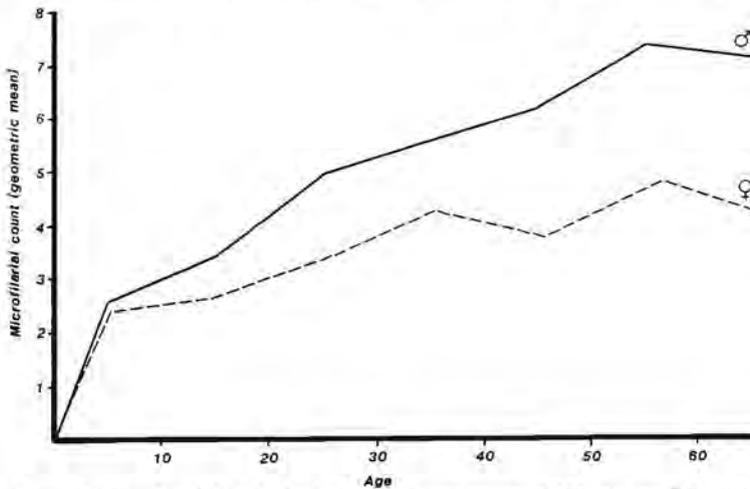


Figure 3. Intensity of *O. volvulus* infection by age among 6,562 persons living in the principal area of the Thyolo focus.

are in economically active age groups. For the entire highland area the estimated prevalence of infection with *O. volvulus* is 18.9% rising to 28.8% in the centre of the focus.

SUBJECTIVE COMPLAINTS: The frequency of subjective complaints among 5,653 persons aged 20 and above are set out in Table 1. Of these subjects, 27% had microfilariae present in skin snips. Complaints of generalised body aches or pains, backache, joint pains, pruritus, dizziness, and poor vision were statistically associated with the presence of microfilariae in skin snips while being weak or feeling hot or feverish were not.

IMPAIRED VISION AND BODY WEIGHT: If vision were normal in one eye, body weight differed little from that of persons normally sighted in both eyes. Persons with impaired vision in both eyes weighed less than those with good vision in one or both eyes. Persons bilaterally blind or who were blind in one eye and had poor vision in the companion eye, weighed consistently less than persons normally sighted. For men the difference in weight between the normally sighted and the bilaterally blind (or blind in one eye with impaired vision in the other) was 4.9 kg (P). Blind women weighed 6.8 kg less than normally sighted women ($P=0.002$).

When body weights of normally sighted persons aged 20 and over infected with *O. volvulus*

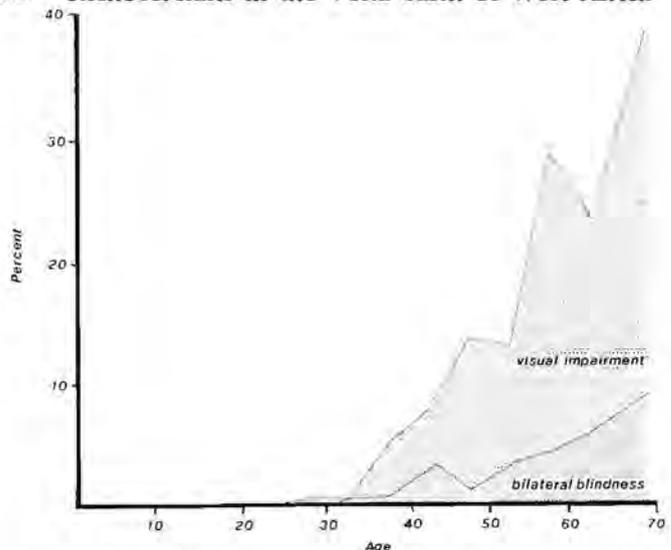


Figure 4. Prevalence of impaired vision and blindness by age among 10,262 persons aged 20 and above from the Thyolo highlands.

Table 1. Comparison of subjective complaints reported by 5,653 persons with and without microfilariae present in skin snips. The relationship between the frequency with which various symptoms were reported and rising microfilarial counts was determined using χ^2 analysis for trend.

Symptom	negative skin snips n=4145		positive skin snips n=1508		P value	trend analysis P value
	no. with Symptom (%)	no. without Symptom	no. with Symptom (%)	no. without Symptom		
body pains	1662 40.1	2482	762 48.1	778	<0.001	<0.001
backache	1630 39.3	2515	709 47.0	796	<0.001	<0.001
joint pains	1615 40.0	2530	651 43.2	856	0.003	<0.001
pruritus	1802 43.5	2343	866 57.4	640	<0.001	<0.001
weakness	8 0.2	4136	15 1.0	1493	-	-
dizziness	73 1.8	4072	92 6.1	1414	<0.001	<0.001
poor vision	462 11.1	3683	241 16.0	1254	<0.001	<0.001
feeling hot or feverish	15 0.4	4128	20 1.3	1485	-	-

have a population density of only 50-100 persons per km² of land.

High prevalence with low intensity of infection is also found where transmission of onchocerciasis is seasonal¹³. Roberts observed that over a five-year period from 1985, Monthly biting rates (MBR *) showed marked seasonal variations from a low MBR of 122 to a high of 9,855¹⁴. Preliminary *Simulium* dissections indicate that most *O. volvulus* transmission in the Thyolo highlands occurs during the rainy months of November through April.

Although onchocerciasis in the Thyolo highlands is associated with decreased body weight and a variety of subjective complaints, it is not a major cause of blindness. Although onchocerciasis was strongly associated with bilateral blindness in this survey, the excess blindness produced by *O. volvulus* is probably less than 300 persons among a population at risk of some 327,000. However, the numbers of blind (irrespective of cause) enumerated in this survey is of concern since they considerably exceed the blindness estimates of Budden¹⁵.

The association observed in the Thyolo highlands between complaints of backache, body and joint pains and the presence of microfilariae in skin snips indicates the findings of Lamp¹⁶ and Pearson¹⁷ are not phenomena restricted to Nigeria and may be properly regarded as clinical features of onchocerciasis.

As expected, itching was more commonly seen among persons with microfilariae present in skin snips. The extent of itching reported by persons who had no microfilariae in skin snips is remark-

able. Undoubtedly there are multiple causes of itching in the Thyolo highlands other than onchocerciasis. However, some persons complaining of pruritus and who were lightly infected were most certainly misclassified as uninfected because of the diagnostic insensitivity of two skin snips where intensity of infection is low.

Subjective complaints of poor vision correlated strongly with the presence of microfilariae in skin snips, but objective evidence of impaired visual acuity in persons with *O. volvulus* was only marginally significant. Subjects could have been aware that in some way their vision was not normal, but still had normal visual acuity as tested with an illiterate E chart. Ordinary visual acuity testing would detect impairment of central visual acuity but could miss more subtle visual changes. Both loss of peripheral vision and night blindness have been associated with the posterior segment lesions of onchocerciasis^{18,19}.

Analysis by trend of these findings showed that complaints of musculoskeletal pains, poor vision, pruritus and dizziness increased as microfilarial counts rose. This could suggest that generalised body complaints would be observed more frequently in areas where community microfilarial loads were high. On the other hand, both generalised body complaints and higher microfilarial counts were found in older persons, which would confound trend analysis.

The finding that persons with microfilariae in skin snips weigh less on the average than those with negative skin snips confirms the earlier observations of Rolland and Bray²⁰. The Malawi data demonstrate that this decreased body weight of persons with positive skin snips is independent of changes in visual acuity. Reduced body weight in persons with onchocerciasis may be due to mech-

* MBR = $\frac{\text{No. of flies caught in 12 hrs} \times \text{No. of days in month}}{\text{number of catching days}}$

Table 2. Body weight in 10,335 persons age 20 and over, with and without microfilariae present in skin snips.

Body weight (in kg)	skin snips	
	microfilariae	no microfilariae
men, normal vision	54.76	56.06
men, reduced vision*	51.27	53.27
men, bilaterally blind	49.87	51.69
women, normal vision	50.16	51.73
women, reduced vision*	47.73	47.70
women, bilaterally blind	42.67	44.96

anisms similar to those operative in other chronic diseases.

If onchocerciasis were responsible for these various subjective complaints and loss in body weight, could infection have an economic impact as well? Productivity might be impaired both by actual pathophysiological effects of the disease as well as time spent away from labour seeking medical attention for onchocerciasis-related medical complaints. The majority of persons likely to suffer from onchocerciasis-related symptoms are economically active and providing for multiple dependents. Onchocerciasis in the head of a household could have a substantial economic effect on the entire family.

Most African countries with endemic onchocerciasis survive on a subsistence economy with only a few commodities earning foreign exchange. *Per capita* food production in many countries endemic for onchocerciasis continues to fall. In these circumstances, even a modest loss of productivity as a consequence of onchocerciasis would be of national significance. Measuring the productivity of a community in a subsistence economy is difficult. Measuring days lost from productive labour due to illness or other causes among those infected with onchocerciasis and those uninfected might be a more satisfactory approach. Even with this approach results could be blurred by effects arising from undetected light infections or residual effects from a previous infection.

Are control methods indicated for the Thyolo highlands? In the past control depending on larvaciding streams where *Simulium* flies bred. The vast Onchocerciasis Control Project of West Africa was established with the purpose of eliminating the fly breeding for a period of approximately 15 years. At the end of this time it was predicted that onchocerciasis would have died out in its human hosts, fly control could stop, and although flies would reappear, there would be no *O. volvulus* to transmit. Parts of the 11 nation project area have now completed 15 years of *Simulium* control, but various

unforeseen factors now make it difficult to decide when it is safe to bring larvaciding to a close.

In the Thyolo highlands complete suppression of fly breeding is probably not possible, but some principal breeding sites could be controlled with larvaciding and by the removal of plants trailing in streams on which *Simulium* flies breed. Although this would probably have to be continued for many years before any change in prevalence rates of infection would be apparent, it is possible that annoyance from biting flies could be reduced in some areas.

The discovery of ivermectin has opened a new possibility for control of onchocerciasis. This drug kills microfilariae after a single annual dose. Although the drug does not destroy the adult worms, treatment given on an annual basis suppresses microfilariae which are responsible for the symptoms of onchocerciasis. Given on a community-wide basis this drug leads to a marked reduction in skin microfilarial counts and ocular involvement²¹. There is also some evidence that given regularly, ivermectin can interrupt transmission of infection²².

Ivermectin is presently being distributed in 27 of the 33 countries where onchocerciasis is endemic. The drug was well tolerated with no serious side effect noted when distributed on a community-wide basis in the Thyolo highlands as part of a WHO-sponsored phase IV trial from 1988-1991. Mass distribution of ivermectin in the Thyolo highlands holds promise both of preventing development of blindness as well controlling the extensive skin lesions which are present as a result of onchocerciasis. If as the data presented here suggests, onchocerciasis has an effect on productivity, mass treatment with ivermectin may be of benefit to the economy of the community as well.

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Folic acid and neural tube defects

Diet has had a suggested aetiological role in neural tube defects (spina bifida and anencephaly) for many years. Folic acid was suggested as having a role in preventing neural tube defects in 1964. Two studies giving folic acid and other vitamins showed a reduced risk of neural tube defects. These studies unfortunately were open to selection bias and could not say whether folic acid or some other vitamin were the beneficial agent. A study to resolve this issue was denied ethical approval. This decision to withhold ethical approval has subsequently been seen as inappropriate. The present international study involving 33 centres was eventually given ethical approval but took eight years to complete. Folic acid (4 mg), other vitamins (A, D, B₁, B₂, B₆, C, nicotinamide) and placebo was given in randomised, double-blind fashion to women who had had a previous neural tube defect before conception. Informed consent followed strict guidelines and data was reviewed every 6 months. One percent of the pregnancies in the folic acid supplemented group had neural tube defects whereas 3.5% had defects in the unsupplemented group. This gives a relative risk of 0.28. The study thus clearly established that folic acid supplements should be given before conception to women who have had an affected pregnancy.

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