Bull. Org. mond. Santé } 1967, 37, 195-212
Bull. Wld Hlth Org. }

Onchocerciasis in Kenya 9, 11 and 18 Years after Elimination of the Vector

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Elimination of the onchocerciasis vector Simulium neavei *through larvicidal operations in focal areas of Kenya in 1946, 1953, and 1955 achieved complete interruption of transmission. Since no treatment was administered to the infected population, the areas provided an opportunity for studying the natural course of the infection in man in the absence of reinfection, with particular emphasis on its average duration and the effect of duration of exposure to the infection. In a follow-up survey conducted in 1964 in four focal areas, approximately 2000 people were examined parasitologically and clinically; slightly over half this group were also given a thorough ophthalmological examination. The results showed that, 11 years after interruption of transmission,* live Onchocerca volvulus *adults were present in nodules and microfilariae were present in the skin; after 18 years, however, microfilariae were no longer found in the skin. Assuming that in hyperendemic areas parasites are acquired until shortly before interruption of transmission, it can thus be postulated that* O. volvulus *worms lose their reproductive potentiality after 16 years or possibly earlier. A comparison of recent microfilarial rates with adjusted rates found in earlier surveys seems to indicate that the onchocercal infection, after interruption of transmission, follows a straight regression line, theoretically reaching zero after about 13-17 years.*

Onchocerciasis is unquestionably a long-standing infection in man. Yet it is a disease on which there is a lack of information that is of primary importance from the point of view of control. For example, the life-span of the adult worm is still largely a matter for speculation, and the natural course followed by the disease in man in the absence of super-infection is far from being entirely understood.

Areas in which the transmission of onchocercal infection has been interrupted through elimination of the vector provide ideal conditions for the study of such problems. A unique opportunity for investigation exists in Kenya where, for the first time, continuous interruption of transmission has been achieved through the eradication of *Simulium neavei* Roubaud, the only vector species in the country. Formerly, there were six known onchocercal areas in Kenya. Vector eradication was completed in Kodera in March 1946; in Riana in February 1946; in Kuja in 1952; in Ngoina in January 1953; and in the Kakamega-Kaimosi areas in January 1955. Since then, repeated entomological surveys in all former foci have confirmed the complete elimination of *S. neavei*.

After a preliminary study in late 1963 of the former endemic onchocerciasis areas, a comprehensive follow-up survey was conducted in four areas during April and May 1964 by the Division of Insect-Borne Diseases, Ministry of Health, Kenya, with the assistance of WHO.

* This study was supported, in part, by the World Health Organization.

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PURPOSE OF INVESTIGATION

The objective of the follow-up survey in Kenya was to gain fuller knowledge of the epidemiology of onchocerciasis and of the life-span of *Onchocerca volvulus*. Confirmation of the interruption of transmission in the focal areas was not sought, since previous entomological surveys had provided sufficient evidence of the absence of the vector.

As the time of definitive interruption of transmission was known, it appeared possible to estimate the time required for the infection to die out naturally and, on the basis of prevalence data, to observe the trend followed by the declining infection in a community. Such information would be of practical importance for control operations in areas where vector elimination cannot be undertaken or where reintroduction of the vector is likely to occur—i.e., wherever control measures must be continued as long as the infection remains transmissible in the human population of a given area.

It was also hoped that the study of prevalence rates and of the frequency of clinical manifestations in different age groups in areas with different levels of endemicity would lead to better understanding of the influence of the duration and degree of exposure to the risk of infection on the intensity of the infection and on the severity of clinical manifestations, particularly eye lesions.

EPIDEMIOLOGY OF ONCHOCERCIASIS IN KENYA

General description

In Kenya, as noted above, onchocerciasis was originally endemic in six fairly well-defined areas of different size, all in Nyanza Province. Although the disease was first reported by Dry in 1921, it can be assumed that the infection had been a threat to the population for many generations before, as the local people were known to suspect blackflies to be the cause of blindness. It was not until the late 1930s, however, that serious attention was paid to the disease.

Simulium neavei was found to be the only vector in Kenya. Based on the high susceptibility of the aquatic stage of *S. neavei* to insecticides, the first control project was initiated in 1946 in the Kodera focus by Garnham & McMahon, resulting in the elimination of the vector from the area. The later discovery that the immature forms of *S. neavei* live in phoretic association with freshwater crabs of the genus *Potamonautes* facilitated the delimitation of the focal areas, as well as the assessment of control operations. Subsequently, large-scale larvicidal measures against *S. neavei* were applied in 1952 in the southern part of the province, and in 1954 in the remaining areas in the northern part where onchocerciasis was known to occur. As a result, complete elimination of the vector from the treated focal areas was achieved.

Kenya is now free from *S. neavei* except for a very small focus in two river valleys in the foothills of Mount Elgon, close to the Uganda border. The fly density in this focus is extremely low and no cases of onchocerciasis have so far been reported.

In order to confirm the absence of the vector, and in view of the persistence of the small isolated pocket of infestation near Mount Elgon, detailed entomological investigations to detect adult *S. neavei*, as well as larval and pupal forms, have been carried out twice yearly for at least 8 years in each of the previously treated areas.

With the exception of two small drug trials—in 1953 in the Kaimosi-Kakamega focus on slightly more than 100 onchocerciasis cases, and in 1957 in the Kodera focus on 102 parasitologically confirmed cases—no mass drug administration took place in any of the foci and no significant individual treatment was given by medical institutions.

The original level of endemicity in the various focal areas was difficult to determine from information recorded during the past 25 years. Previous entomological data were too few and too variable to be of help in determining the endemicity of the focal areas. Furthermore, data obtained from surveys of different investigators were not strictly comparable, since sampling techniques and the age composition of the samples differed. Surveys had been repeated at various places in the infected areas with extremely variable results. The different sites on the body chosen for performing biopsies in different surveys were another complication in the assessment of the level of endemicity. In a survey in Kodera, Nelson & Grounds (1958) compared the positivity of biopsy specimens taken from the forearm with that of specimens taken from other parts of the body; it was found that the use of skin snips from the thigh and chest disclosed approximately twice as many cases as the use of skin snips from the forearm.

Among the former foci of onchocerciasis, those most suitable for a follow-up survey appeared to be Kodera, Ngoina, and Kakamega-Kaimosi. The foci of Riana and Kuja were excluded: the former because it was considered to be too small to provide significant data and the latter because it was unsuitable owing to considerable population movement. Detailed epidemiological description of the focal areas will be limited to those selected for the 1964 survey.

Kodera

Kodera was formerly called the " Valley of the Blind " by the population of the area. The focus

TABLE 1
INFECTION RATE OF ONCHOCERCIASIS IN KODERA, 1938-57

Period	Year	Number examined	Percentage of people with positive biopsies			Percentage of people with negative biopsies showing nodules
			Children under 10 years	Adults	Total	
Prior to vector elimination	1938	406 [a]	25.7	66.8	64.1	22.8
	1940	605 [a]			51.0	
	1941	1 196 [a, b]			48.4	23.0
	1946	93 [a]	32.0			
After vector elimination	1950	209 [a]	9.5	35.5		
	1953	352 [a, b]	5.0	50.3		
	1957	311 [c]	0	33.5 [d]		

[a] One biopsy only (forearm).
[b] Two biopsies (one thigh, one chest).
[c] In Kitare valley only.
[d] Persons 16 years of age and older (161) examined.

extended over an area of approximately 65 square miles (170 km^2) and in 1940 the population at risk was estimated to be 4000. The density of *S. neavei* was found to be very high (McMahon, 1940). Eradication of the vector, by application of DDT to the rivers, was completed by March 1946 (Garnham & McMahon, 1947).

The first survey of the human population was carried out in 1938 by Harris (1939); other surveys were made in 1940 by McMahon, in 1941 by Buckley (1949), and in 1946 by Garnham & McMahon (1947). In the period following vector elimination, parasitological surveys were undertaken in 1950, 1953, and 1957. The results are summarized in Table 1. No onchocerciasis was detected in children born after eradication of the vector.

Bearing in mind the fact that infection rates found prior to 1957 were based on biopsy specimens taken from the forearm, a site that discloses only about half the infected cases, it might safely be assumed that nearly 100% of the adult population was infected prior to vector elimination. The slight variations in the over-all parasite rates may well be explained by differences in the sampling and selection of survey areas. In the 1957 survey no parasites were found in children below the age of 10 and the results also showed a considerable decrease in the adult parasite rate. Unfortunately, no precise data are available regarding the clinical manifestations of the infection.

The Kodera focus can be considered as having been hyperendemic prior to vector elimination.

Ngoina

The Ngoina focus comprises an area of 1145 square miles (2900 km^2) with a population of approximately 20 000.

S. neavei was first found here by Dry in 1921. The only survey of Ngoina prior to eradication of the vector was carried out in 1941 by Buckley (1949), who examined 834 persons. An over-all infection rate of 28.8% was found, based on single biopsy specimens taken from the forearm. The fly density was moderate.

Eradication of the vector was completed by January 1953. Follow-up entomological surveys, the last one in 1961, were all negative. No follow-up surveys in the human population have been carried out since vector eradication. After elimination of the vector, the forested valleys were converted into farm land and plantations.

It is reasonable to assume that this area was formerly of moderate endemicity.

Kaimosi

This focus covers an area of 200 square miles (520 km^2) with a population estimated at 40 000. It is adjacent to the Kakamega focus.

Onchocerciasis in this area was first reported in 1941 by Buckley (1949), who found, in 142 people examined, an infection rate of over 70% by taking a single biopsy specimen from the forearm; 25.1% of the people examined had onchocercomata.

The vector density was high (up to 200 *S. neavei* per man-hour). Elimination of the vector was first attempted in 1947, but complete eradication was not achieved. The eradication programme was resumed in 1954 and finally completed in January 1955. In 1956 two adult *S. neavei* were captured in dense forest in Kaimosi, and the forest rivers were re-treated in March 1956. Apart from this finding, all entomological searches have been negative.

Although information on the Kaimosi focus is limited, it is assumed that onchocerciasis was hyper-endemic.

Kakamega

Kakamega was the largest onchocercal focus in Kenya, extending over 1500 square miles (4900 km²) and having a population of about 200 000.

It was in Kakamega that the presence of female *Simulium* flies was first noted in 1911 near the Yala river by Neave (1912). Roubaud described and named the species in 1915. The disease was first discovered here in 1938 by Jobson & Timms. In 1941 Buckley (1949) found an infection rate of 35% in 331 persons examined by a single forearm biopsy; in a survey conducted in 1953 Buckley (unpublished information) found an infection rate of 46%. Also in 1953, Laurie & Jordan (unpublished information) found 9% infected out of 450 examined by the same method. Entomological observations revealed a moderate fly density, the average being 15.6 per man-hour.

Vector control operations in Kakamega were combined with those in Kaimosi; thus, eradication was first attempted between 1947 and 1949 and was successfully completed in January 1955. Follow-up entomological surveys have been carried out at 6-monthly intervals until now, all yielding negative results. There was no follow-up survey of the human population in this area. A single therapeutic trial was conducted in 1953, in which 106 persons were treated with diethylcarbamazine.

From the survey results it may be inferred that the area was originally of medium endemicity; however, in such a large area considerable variation in the intensity of infection would be inevitable, depending upon the nearness of shaded streams.

Conclusion

Although little information is available on the original epidemiological situation of onchocerciasis in the former foci in Kenya, it seems reasonable to assume that the Kodera and the Kaimosi foci presented hyperendemic conditions, with an adult infection rate of nearly 100%, while in the other foci onchocerciasis was of moderate endemicity.

The interruption of transmission through the elimination of the vector species *S. neavei* has been satisfactorily proved by routine entomological surveys over many years following control measures. It has also been confirmed by the findings of the recent follow-up survey. As will be shown later, none of the children and adolescents born after vector elimination showed signs of the infection.

SURVEY ARRANGEMENTS AND METHODS

Each of the follow-up survey teams consisted of an epidemiologist, an ophthalmologist, an entomological field officer, two microscopists, two nurses, and a clerk. A mobile laboratory and a mobile ophthalmological examination unit were available.

In each of the four areas approximately 500 people were selected at random for clinical, parasitological, and ophthalmological examination (Table 2). The number of persons in each age group to be included in the survey had been calculated on the basis of census data, with a total of 500 for each focus. Persons were included in the sequence of their arrival until the calculated number was reached. The entire survey covered a total of 2103 persons.

For each person examined, an Individual Investigation Form (see the Annex) was filled out, on which, in addition to the examination results, were recorded name, age, sex, and length of residence in and periods of absence (if any) from focal areas. With the exception of two persons from Kodera, who moved into the area at a later date, all had been living in the endemic areas since birth. Thus, the duration of exposure to the risk of infection could generally be calculated from the age of the individual.

The skin of each person was carefully examined for onchocercal changes and nodules (onchocercomata). At least two skin biopsy specimens were taken from each person: one above the greater trochanter of the femur, and the other from the upper part of the lateral chest wall on the same side. Biopsy specimens were also taken from the skin adjacent to any onchocercomata discovered, and in selected cases with eye lesions further specimens

TABLE 2
DISTRIBUTION OF POPULATION EXAMINED BY FOCAL AREA, AGE-GROUP, AND SEX

Focal area	Type of examination	Sex [a]	Age-group (years) 0-9	10-14	15-19	20-24	25-29	30-39	40+	Total
Kodera	Parasitological and clinical [b]	M	43	23	46	12	13	36	106	279
		F	36	19	26	20	32	36	52	221
		Total	79	42	72	32	45	72	158	500
	Ophthalmological		22	14	53	22	29	47	131	318
Ngoina	Parasitological and clinical [b]	M	65	52	28	15	22	31	137	350
		F	47	27	11	5	20	35	53	198
		Total	112	79	39	20	42	66	190	548
	Ophthalmological		10	14	19	10	21	39	165	278
Kaimosi	Parasitological and clinical [b]	M	54	59	37	5	18	24	86	283
		F	63	33	14	16	17	24	52	219
		Total	117	92	51	21	36 [c]	48	138	503 [c]
	Ophthalmological		27	31	36	13	23	43	122	295
Kakamega	Parasitological and clinical [b]	M	52	57	17	9	11	34	112	292
		F	56	32	25	7	28	48	64	260
		Total	108	89	42	16	39	82	176	552
	Ophthalmological		49	44	18	7	16	43	108	285
All areas combined	Parasitological and clinical [b]	M	214	191	128	41	64	125	441	1 204
		F	202	111	76	48	97	143	221	898
		Total	416	302	204	89	162 [c]	268	662	2 103 [c]
		% of total examined [d]	20 (16-23)	14 (8-18)	10 (7-14)	4 (3-6)	8 (7-9)	13 (10-15)	31 (27-34)	100
	Ophthalmological	Total	108	103	126	52	89	172	526	1 176

[a] Sex ratio, male/female; Kodera 55.7 %, Ngoina 64 %, Kaimosi 56 %, Kakamega 53 %, Total 57 %.
[b] Other than ophthalmological.
[c] Including 1 person whose sex was not recorded.
[d] Figures in parentheses give the proportion range in the different focal areas.

were taken from the skin of the outer canthus of the eye and from the ankle. Biopsy specimens were examined in saline under the low power of the microscope for the presence of *O. volvulus* microfilariae. If microfilariae were found, a count was made, and the size of the biopsy specimens was recorded.

The visual acuity of each person was measured. However, only 1176 (56%) persons underwent a full ophthalmological examination (see Table 3); most of these were selected at random (persons with even serial numbers), but a smaller number consisted of those with odd serial numbers who either showed positive skin biopsies or who requested a complete

TABLE 3
PERSONS GIVEN OPHTHALMOLOGICAL EXAMINATIONS

Subjects	Even serial number (random selection)		Odd serial number		Total	
	Examined	Not examined	Examined	Not examined	Examined	Not examined
Onchocerciasis cases	260	5	70	16	330	21
Non-onchocerciasis cases	738	47	108	859	846	906
Total	998	52	178	875	1 176	927

examination (the latter group were examined in order to retain the goodwill of the population).

The eye examination included external inspection in daylight, biomicroscopy with the 16× magnification of a Karl Zeiss slit lamp, and funduscopy with a Keeler ophthalmoscope after mydriasis with 2% homatropine and 10% phenylephrine. In selected cases additional examinations were performed. At the end of the examination, 2% pilocarpine hydrochloride was instilled.

RESULTS

Parasitological results

The only direct evidence of the presence of onchocerciasis that can easily be obtained in a field survey is the demonstration of microfilariae, either in the skin (by biopsy) or in the anterior chamber of the eye (by ophthalmological examination). Nodules are only an indirect proof of infection, unless they are extirpated and the existence of adult worms is confirmed histopathologically. Since nodules can persist when the worms inside are already dead, a nodule is nothing more than a strong indication that the nodule carrier is or has at some time been infected.

For reasons of convenience in the tabulation and analysis of data, the term " onchocerciasis cases " refers to all persons having either microfilariae (detected in biopsies or in the anterior chamber of the eye) or nodules (or both these signs).

Table 4 gives the absolute number and proportion of people harbouring microfilariae and/or nodules by age-groups in the different focal areas. In Kodera no microfilariae were detected, but nodules were found in 61 persons. Nodules were seen in only one person (1.4%) in the 15-19-year age-group and in 2 persons (6.3%) in the 20-24-year age-group; none were found in the 25-29-year age-group. Of those aged 30-39 years, 9.7% were nodule carriers; the figure for those aged 40 years and over was 32.3%.

In Kaimosi, the other originally highly endemic area, the youngest age-group in which microfilariae were found was 10-14 years (the rate was 6.5%); no nodules were detected among them. From the age of 20 years onward the rate of onchocerciasis increased progressively. The over-all prevalence of microfilaria carriers in Kaimosi was 26.4% (58% in persons over 40 years of age) and the rate of persons with nodules was 20.3% (54.4% in persons over 40 years of age). This was the only focal area in which the number of persons with microfilariae exceeded those with nodules; in spite of this fact, it was also the area with the largest number of nodule carriers. Of all onchocerciasis cases 77% had microfilariae, but only 59% had nodules. Kaimosi was also the only area where nodules were more often than not associated with microfilariae, except for the age-groups below 40 years, although the number of persons under 40 years of age was small.

In the areas of originally low endemicity, no microfilariae or nodules were found in children up to the age of 14. In Ngoina, the microfilaria rate, which was 2.6% in the 15-19-year age-group, was more or less constant at about 10% after that age, with a slight increase to 13.7% in persons over 40 years of age. Only a few cases with nodules were found in persons aged 25-39 years, but the proportion increased to 20% in those aged 40 years and over. In Kakamega no microfilariae were found in those aged less than 30 years, while 1 person with nodules was detected in each of the age-groups 15-19 and 25-29 years. The over-all rate of onchocerciasis cases was 12.8% (29.1% in persons over 40 years of age) in Ngoina and 8.5% (22.1% in persons over 40 years of age) in Kakamega. In both areas the

TABLE 4 DISTRIBUTION OF PERSONS WITH MICROFILARIAE [a] AND/OR NODULES BY FOCUS, AGE-GROUP [b] AND SEX

Original endemicity	Focal area	Duration of interruption of transmission (years)	Sex	10-14 years [c]	15-19 years				20-24 years				25-29 years				30-39 years				40+ years				Total			
				Microfilariae only	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases	Microfilariae only	Microfilariae and nodules	Nodules only	Onchocerciasis cases
Absolute figures																												
High	Kodera	18	M	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	4	4	0	0	35	35	0	0	40	40
			F	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	3	3	0	0	16	16	0	0	21	21
			Total	0	0	0	1	1	0	0	2	2	0	0	0	0	0	0	7	7	0	0	51	51	0	0	61	61
	Kaimosi	9	M	5	4	0	2	6	1	0	1	2	4	2 (1)	3	9	9	3	4	16	20 (5)	30 (8)	16	66	43	35	26	104
			F	1	2	0	0	2	4 (1)	1	0	5	3	1	2	6	9 (2)	4 (1)	4	17	9	21 (3)	8	38	28	27	14	69
			Total	6	6	0	2	8	5	1	1	7	7	3	5	15	18	7	8	33	29	51	24	104	71	62	40	173
Low	Ngoina	11	M	0	1	0	0	1	1	0	0	1	2 (1)	0	1	3	2	0	2	4	15 (1)	5	23	43	21	5	26	52
			F	0	0	0	0	0	1	0	0	1	1	0	0	1	4	0	0	4	2	2	8	12	8	2	8	18
			Total	0	1	0	0	1	2	0	0	2	3	0	1	4	6	0	2	8	17	7	31	55	29	7	34	70
	Kakamega	9	M	0	0	0	0	0	0	0	0	0	0	0	1	1	2	0	2	4	4	4 (1)	16	24	6	4	19	29
			F	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0	1	2	2	4	9	15	3	4	11	18
			Total	0	0	0	1	1	0	0	0	0	0	0	1	1	3	0	3	6	6	8	25	39	9	8	30	47
Percentage of persons examined																												
High	Kodera	18	Total				1.4	1.4			6.3	6.3							9.7	9.7			32.3	32.3			12.2	12.2
	Kaimosi	9	Total	6.5	11.8		3.9	15.7	23.8	4.8	4.8	33.3	19.5	8.3	13.9	41.7	37.5	14.6	16.7	68.7	21.0	37.0	17.4	75.3	14.1	12.3	8.0	34.3
Low	Ngoina	11	Total		2.6			2.6	10.0			10.0	7.1		2.4	9.5	9.1		3.0	12.1	9.0	3.7	16.3	29.1	5.3	1.3	6.2	12.8
	Kakamega	9	Total				2.4	2.4							2.6	2.6	3.6		3.6	7.3	3.4	4.5	14.2	22.1	1.6	1.5	5.4	8.5

[a] Microfilariae present either in skin biopsies or in the anterior chamber of the eye (the numbers of persons with microfilaria in the anterior chamber of the eye are given in parentheses). [b] No onchocerciasis cases were found in the age-group 0-9 years. [c] No nodules were observed in the age-group 10-14 years.

TABLE 5
POSITIVITY OF BIOPSIES AT ROUTINE SITES (CHEST AND THIGH)

Age-group (years)	Kaimosi			Ngoina			Kakamega		
	Positive both sites	Thigh positive, chest negative	Thigh negative, chest positive	Positive both sites	Thigh positive, chest negative	Thigh negative, chest positive	Positive both sites	Thigh positive, chest negative	Thigh negative, chest positive
10-14	1	5							
15-19	4	2		1					
20-24	4	2		1	1				
25-29	6	2	2	1		2			
30-39	14	10	1	3	3			2	1
40+	60	17	2	8	12	4	6	5	3
Total	89	38	5	14	16	6	6	7	4

number of persons with nodules but without microfilariae exceeded by far the number with both nodules and microfilariae.

The prevalence of onchocerciasis was found to be consistently higher among males than among females in each of the four focal areas. On the basis of the combined evidence the difference was found to be statistically significant. However, the results of the detailed findings of the survey are recorded for both sexes combined, as the numbers on which the comparisons are based would otherwise be too small. This procedure is considered to be proper for the types of comparison made in this paper, taking into account the sex composition of the study population.

Of the total of 334 positive biopsies (in 186 persons), 220 were fixed and stained with haemalum and eosin for the purpose of further microscopic examination. In 188 of these, microfilariae of *O. volvulus* were 'identified. No microfilariae of *Dipetalonema perstans* were found. Nelson & Grounds (1958) reported finding microfilariae of *D. perstans* in both peripheral blood and stained specimens obtained in the Kaimosi forest.

The numbers of positive biopsies and the routine body sites from which they were taken are listed in Table 5. In Kaimosi, an area in which onchocerciasis was originally hyperendemic, positive biopsies at both routine sites were the most common finding, except for the age-group 10-14 years. In the areas where the disease was formerly of low endemicity, the majority of the microfilaria carriers had a positive biopsy at one site only. Biopsy materials taken from the thigh consistently yielded more positive results than those taken from the chest. If the thigh alone had been examined the proportion of cases missed in Kaimosi, Ngoina, and Kakamega would have been 4%, 17% and 24%, respectively, whereas if the chest alone had been examined the figures would have been 29%, 44%, and 41% respectively. Thus, although the finding of positive results appears to be more likely with biopsy specimens from the thigh than with those from the chest, in the area studied, a considerable proportion of cases might be missed if both sites were not examined.

In 67 cases biopsies were also performed on material from the head and/or near a nodule. All but two of these persons showed microfilariae in biopsy specimens taken at the routine sites. Of 63 people from whom biopsy specimens were taken near nodules, microfilariae were detected in 42 (67%), while of 20 people from whom specimens were taken from the head microfilariae were found in 11 (55%).

The microfilarial density was measured in all cases having positive biopsies. As the area of each skin snip was known, the density figures were adjusted to the most common area of 2 mm^2. The results are presented in Table 6. In Kaimosi approximately half of the cases had densities of 6 or more microfilariae per 2 mm^2; a few showed densities of over 50 per 2 mm^2. In Ngoina and Kakamega the microfilarial density ranged, in most cases, from 1 to 5 per 2 mm^2. Among persons with microfilariae, no clear evidence was found of any relationship between microfilarial density and age, probably because

TABLE 6

DISTRIBUTION OF MICROFILARIAL DENSITY BY FOCAL AREA AND AGE-GROUP

Microfilarial density per 2 mm² of skin area	Number of people with positive biopsies															
	Kaimosi							Ngoina						Kakamega		
	10-14 years	15-19 years	20-24 years	25-29 years	30-39 years	40+ years	Total	15-19	20-24 years	25-29 years	30-39 years	40+ years	Total	30-39 years	40+ years	Total
1-5	4	5	3	5	22	49	88	1	2	3	6	23	35	2	12	14
6-10	1	1	1	4	1	15	23					1	1		2	2
11-20	1		1	1	1	8	12							1		1
21-50			1		1	5	7									
51-100						3	3									

of the small number of observations in each group. Persons with a high microfilarial density were usually those in whom microfilariae were also found in the anterior chamber of the eye. With rare exceptions, biopsy specimens from the thigh showed higher counts than those from the chest.

Histological examination of nodules removed from 10 persons in Kamosi, Ngoina, and Kakamega revealed the presence of live worms and microfilariae in 5 persons. Of 6 onchocercomata examined from Kodera, none showed microfilariae, and all the adult worms were dead. An onchocercal core was detected in 3 of 5 giant nodules or lipomata that were excised for histological examination.

In nodule carriers, the common finding was 1-2 nodules. In the Kaimosi focus only, a few persons over 40 years of age had 3-5; rarely, a person with more than 5 nodules was found. Regions of the body on which nodules were found are listed in Table 7. The abdominal and lumbar region was the most commonly affected area (68% of all nodule carriers). The next most frequently affected parts were the thorax and lower limbs; nodules were found only rarely on the head and upper limbs.

Of the 349 nodules detected 83% were small, 13% were medium, and only 4% were large. Their consistency (which was recorded as soft, firm, or hard) varied according to their size. Small nodules were usually firm or hard, while larger nodules were more frequently soft (Table 8). Of all the nodules found in Kaimosi, 10% were either medium or large; for Kakamega the figure was 8%, while for Kodera and Ngoina the figures were 30% and 24%, respectively. The differences, which were statistically significant, may indicate that with increasing duration of interruption of transmission the medium and large nodules, which are also frequently soft, tend to remain longest.

Finally, it should be noted that in none of the four areas were microfilariae or nodules detected in those born since the elimination of the vector.

Clinical results

As skin lesions of possible onchocercal etiology atrophy, thickening and depigmentation of the skin may occur. Table 9 shows the frequency with which such lesions were found in the four focal areas. Atrophy, mainly over the buttocks and lower limbs, was the most frequently observed skin lesion, and was found more often in onchocerciasis cases than in others. Thickening and depigmentation occurred much more rarely and were usually associated with atrophic signs. Although the frequency of skin lesions varied somewhat in the different focal areas (in persons with and without microfilariae), no evidence that they might be associated with the level of endemicity was found. In view of the small number of persons with microfilariae observed in the lower age-groups, no conclusions can be drawn on the relationship between age and the occurrence of skin lesions. However, it might be said that, in general, the frequency of skin lesions was much higher in persons over the age of 40 than in the younger age-groups. Although this was true of persons with and without microfilariae, skin lesions were found to be less frequent in persons without microfilariae.

TABLE 7

OCCURRENCE OF NODULES BY SITE, AGE-GROUP, AND FOCAL AREA

Original endemicity	Focus	Duration of interruption of transmission (years)	Site of nodules	Number of people with nodules in the following age-groups [a]					
				15-19 years	20-24 years	25-29 years	30-39 years	40+ years	Total
High	Kodera	18	Head and neck	1 (1)				5 (1)	6 (2)
			Thorax					12 (6)	12 (6)
			Upper limbs					2 (1)	2 (1)
			Abdominal and lumbar region		2 (2)		7 (6)	34 (28)	43 (36)
			Lower limbs				1	8 (6)	9 (6)
	Kaimosi	9	Head and neck					2	2
			Thorax			1 (1)	1 (1)	14 (6)	16 (8)
			Upper limbs					2	2
			Abdominal and lumbar region	3 (3)	2 (2)	5 (5)	13 (13)	60 (46)	83 (69)
			Lower limbs			1 (1)	1 (1)	14 (7)	16 (9)
Low	Ngoina	11	Head and neck					3 (3)	3 (3)
			Thorax			1 (1)	1 (1)	10 (9)	12 (11)
			Abdominal and lumbar region				1	23 (22)	24 (22)
			Lower limbs					3 (3)	3 (3)
	Kakamega	9	Thorax	1 (1)				2 (1)	3 (2)
			Abdominal and lumbar region			1 (1)	3 (3)	28 (26)	32 (30)
			Lower limbs					5 (4)	5 (4)

[a] No nodules were found in the age-group 0-14 years. Figures in parentheses are the number of persons having nodules only at the site indicated.

TABLE 8

SIZE AND CONSISTENCY OF NODULES [a]

Focal area	No. of nodules	Small			Medium			Large		
		Soft (%)	Firm (%)	Hard (%)	Soft (%)	Firm (%)	Hard (%)	Soft (%)	Firm (%)	Hard (%)
Kodera	84	12	36	21	15	5	2	7	1	—
Ngoina	52	17	50	10	10	6	—	4	4	—
Kaimosi	174	15	50	25	3	4	1	1	1	—
Kakamega	39	—	77	13	2	5	—	1	—	—
Total	349	13	50	20	7	5	1	3	1	—
		83			13			4		

[a] As percentages of the number of nodules detected.

TABLE 9

SKIN CHANGES AND GLANDULAR ENLARGEMENTS BY AGE-GROUP AND FOCAL AREA

Original endemicity	Focal area	Duration of interruption of transmission (years)	Age-group (years)	Number examined		Skin changes (% of people examined)								Glandular enlargements (% of people examined)			
						Atrophy		Thickening		Depigmentation		Combined		Mild		Marked	
				OP [a]	NO [b]	OP	NO	OP	NO	OP	NO	OP	NO	OP	NO	OP	NO
			0-14	0	121										18		
			15-19	1	71		3						3	100	37		
			20-24	2	30	100		50		50		100		100	33		
	Kodera	18	25-29	0	45		12						12		51		
			30-39	7	65	57	15	28	2			57	15	100	40		
			40 +	51	107	94	55	74	26	39	13	94	55	82	62	12	3
High			Total	61	439	89	17.3	66	66	34	3	89	17.3	85	37	10	0.7
			0-9	0	117		1				3		3.7		2		
			10-14	6	86		1		1		5		7		3		1
			15-19	8	43	12	2				5	12	7	25	14		
	Kaimosi	9	20-24	7	14	14	7			14		14	7	14	14		
			25-29	15	21	20			5		5	20	9.5	13	38		
			30-39	33	15	33	13	6		15	30	42.5	40	33	27	9	
			40 +	104	34	62	27	38	12	40	15	75	41	42	3	18	9
			Total	173	330	46	5	24	2	27	6	55.5	11	34	10	12	10
			0-9	0	112										6		
			10-14	1	79										23		
			15-19	1	38		26						26	100	39		5
	Ngoina	11	20-24	2	18										68		5
			25-29	4	38						26		26	50	31		3
			30-39	8	58	24	10		2	12	2	37	14	50	35	12	7
			40 +	55	135	55	20	11	4	9	2	54.5	20	49	49	45	17
Low			Total	70	478	46	7	9	1	9	1	47	7.7	48	32	37	6
			0-9	0	108		1						1		5		1
			10-14	0	89										3		
			15-19	1	41	100						100		100	15		2
			20-24	0	16										38		
	Kakamega	9	25-29	1	38		8				3		10.5		34		3
			30-39	6	76	33	7		4			33	10.5	17	33	33	7
			40 +	39	137	84	28	28	11	10	29	85	39	49	35	36	11
			Total	47	505	76	9	23	4	9	1	76.5	13	45	21	34	5

[a] OP = persons with microfilariae and/or nodules. [b] NO = persons without microfilariae or nodules.

Glandular enlargements, when found, were mostly of a mild form. Marked enlargements were seen more frequently in onchocerciasis cases (all being over the age of 30 years) than in others. Typical hanging groin was diagnosed in 12 persons, all of whom were over the age of 40 and half of whom were onchocerciasis cases.

Ophthalmological findings

The total number of persons found with ophthalmological lesions was very small, and consequently a comparison of infected with uninfected persons was not possible. For this reason, it was considered unnecessary to separate such data, particularly since the persons not chosen for ophthalmological examination by random methods represented only about 15% of the total examined. Originally, such separation was made for several different eye lesions, but no significant difference from the combined data was found.

Microfilariae in the anterior chamber of the eye. In 24 of the 1176 persons who were examined ophthalmologically, microfilariae were found in the anterior chamber of the eye. Of these 24 persons, 21 came from the Kaimosi focus, 2 from Ngoina, and 1 from Kakamega. The age distribution of these persons is shown in Table 4; the youngest was 23 years of age, but the majority were over the age of 40 years. All of the 24 cases had positive skin biopsies, commonly of high microfilarial density. In one person, who yielded negative biopsies at routine sites, microfilariae were found at the ankle only after repeated skin snips had been taken.

Eye lesions of possible onchocercal origin. For the purpose of this survey, all the findings listed in section 4 of the Individual Investigation Form (see the Annex) were considered to be of possible onchocercal origin, based on the findings of a large-scale ophthalmological investigation undertaken in the endemic areas of onchocerciasis in Guatemala and West Africa (Monjusiau et al., 1965).

Of the 1176 persons who underwent a full ophthalmological examination, punctate keratitis was discovered in 390; this was the most frequently found lesion, and the great majority of lesions were bilateral. The number of nummular lesions per

TABLE 10
FREQUENCY OF BLINDNESS, BY FOCAL AREA AND AGE-GROUP

Original endemicity	Focal area	Age-group (years)	Number examined		Number of people with			
					Blindness [a] in both eyes		Blindness [a] in one eye, impaired vision in the other	
			OP [b]	NO [c]	OP	NO	OP	NO
High	Kodera	0-14		92		1 (1.1 %)		
		15-19	1	70				1 (1.4 %)
		20-29	2	70				
		30-39	7	65		1 (1.5 %)		2 (3.1 %)
		40+	50	103	3 (6 %)	4 (3.9 %)	1 (2 %)	3 (2.9 %)
	Kaimosi	0-39	68	218				
		40+	99	34	4 (4 %)		1 (1 %)	
Low	Ngoina	0-39	14	270				
		40+	47	117				
	Kakamega	0-39	8	284				
		40+	37	133		2 (1.5 %)		

[a] Visual acuity of 3/60 or less.
[b] OP = persons with microfilariae and/or nodules.
[c] NO = persons without microfilariae or nodules.

cornea rarely exceeded 5. There was no apparent difference in the prevalence of punctate keratitis in the four focal areas or between the infected and non-infected groups. Sclerosing keratitis was found in 69 persons, often in combination with other onchocercal eye lesions. Nearly half of these persons were from Kodera.

Chronic iritis was found in 26 persons; in most of them, the lesion was manifested by posterior synechiae only. Keratic precipitates, if present, were usually pigmented; in only 3 persons was active cyclitis present. Chorioretinitis (9 cases) and optic atrophy (9 cases) were rarely seen. In 13 persons secondary glaucoma could be diagnosed. These lesions occurred predominantly in people over 40 years of age. No difference could be observed in their frequency in the infected and apparently non-infected population.

Visual acuity. With the exception of young children, the visual acuity of nearly all persons covered in the follow-up survey was measured. Blindness was defined as being visual acuity less than 3/60. From Table 10 it can be seen that the frequency of blindness in one or both eyes, in persons aged over 40 years, was significantly higher in areas of former high endemicity than in the other areas. Accepting blindness to be of onchocercal origin whenever the impairment of vision was associated with an eye lesion of possible onchocercal etiology, it was found that onchocerciasis was the most frequent single cause of blindness. The next most frequent causes of blindness were senile cataract and corneal leucomata due to keratitis in infancy or trauma. There were 2 cases with primary optic atrophy, both without any evidence of onchocercal infection.

DISCUSSION

The follow-up survey confirmed not only the complete interruption of transmission of onchocerciasis in the formerly endemic foci that were investigated, but also the estimate that was made of their original level of endemicity. From the results of the parasitological examinations and the remaining permanent stigmata of onchocercal infection, it is evident that the areas of Kodera and Kaimosi must have been of high endemicity. In Ngoina and Kakamega the prevalence of microfilariae and nodules, as well as of clinical onchocercal signs, was significantly lower than in the other two foci, thereby justifying their original classification of low endemicity.

Estimation of life-span of O. volvulus

Since it is known when complete interruption of transmission of onchocerciasis in Kenya was achieved, some indication of the life-span of *O. volvulus* may be obtained from observations made on large population groups. Estimates of the life-span of *O. volvulus* are based on the assumptions that all persons in a given focal area were exposed to the infection until the time of elimination of the vector, and that in hyperendemic areas parasites must have been acquired until shortly before interruption of transmission.

The finding of live worms in nodules removed from persons from Ngoina demonstrates that *O. volvulus* worms can live for more than 11 years (the duration of interrupted transmission in this focus). Furthermore, microfilariae were found in the skin of persons in this focus, which means that worms are still capable of producing microfilariae after 11 years —or at least can do so for 9-10 years, assuming that the average age of a microfilaria is 1-2 years.

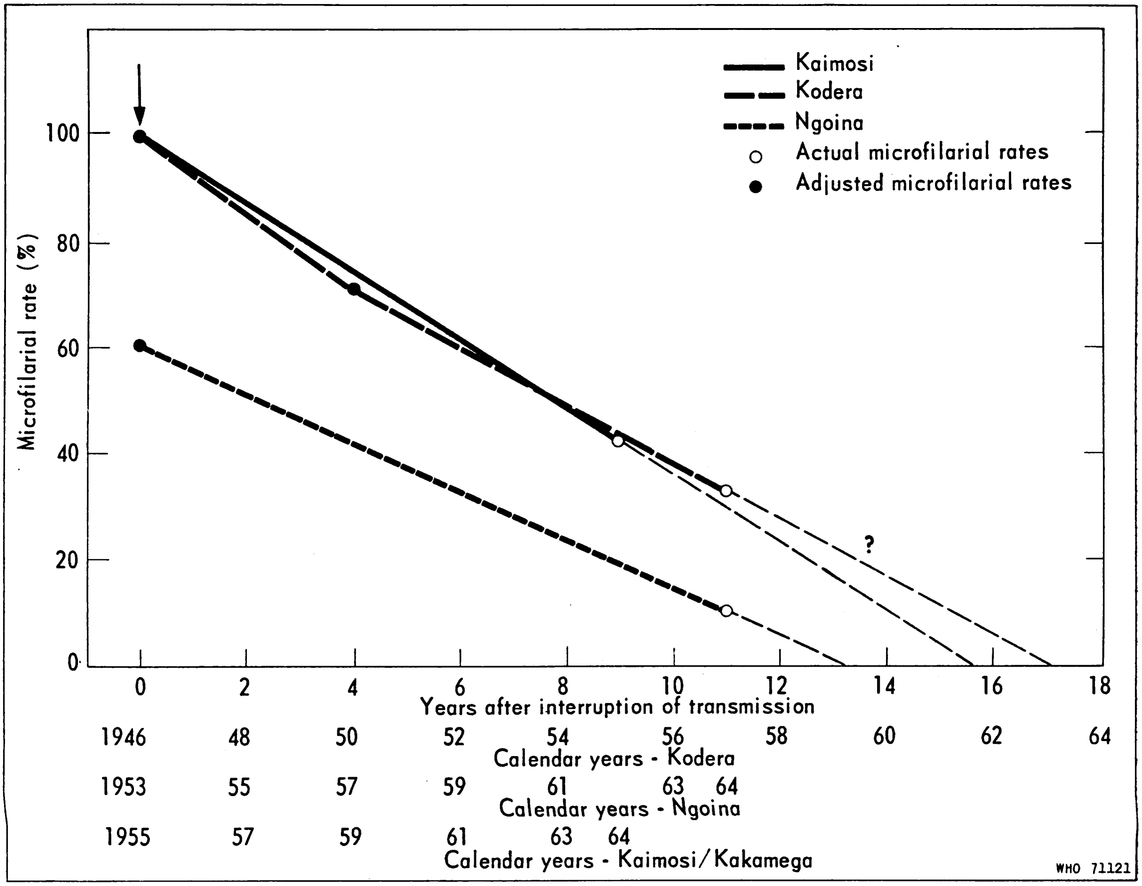
In Kodera, where interruption of transmission had been achieved 18 years previously, all worms examined from 6 extirpated nodules were dead. Since the number of nodules examined was rather small, it can only be stated that in the persons examined no adult worm survived for 18 years. However, because microfilariae were not found in any of the persons—numbering over 500—examined in Kodera, it is almost certain that *O. volvulus* worms lose their reproductive potential after 16 years, or possibly earlier.

Normal trend of disappearance of the infection

At the time of interruption of transmission, infected persons harbour living parasites of all ages—from fairly young, recently acquired worms to others that are close to their natural death. With the cessation of transmission one would expect the gradual reduction in the worm load to result first in a reduction in the microfilarial density, without an immediate effect on the microfilarial rate itself (which is a qualitative rather than a quantitative measure of the infection). Eventually, the microfilarial rate also declines, but the trend of this disappearance of the infection is as yet unknown.

The present survey can throw only partial light on the normal trend of disappearance of the parasite from a community. Changes in the average microfilarial density over the years could not be measured, owing to the absence of comparable data from previous surveys. There remains the possibility of

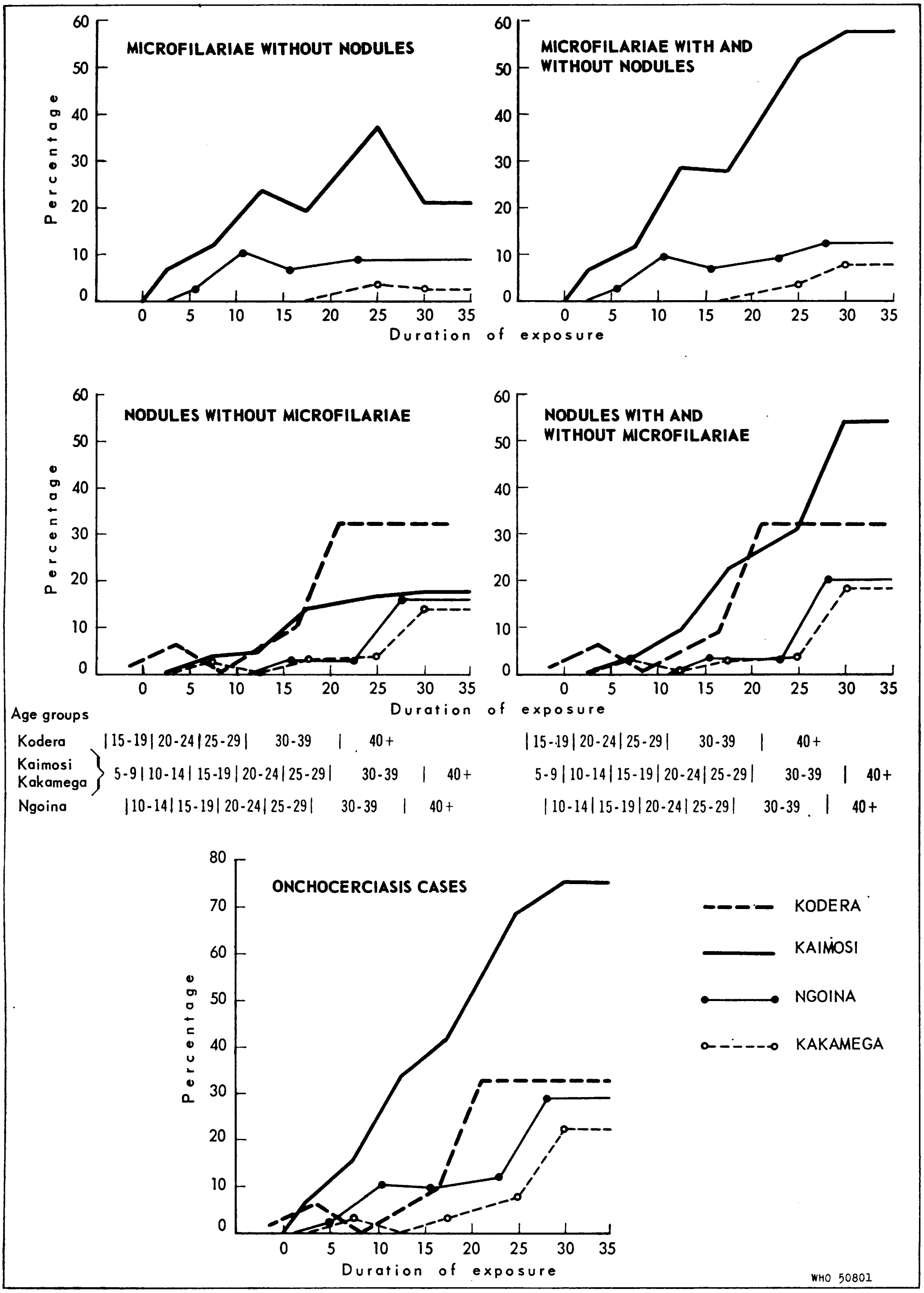
FIG. 1. TREND OF MICROFILARIAL RATE AFTER INTERRUPTION OF TRANSMISSION, KENYA, 1946-64



assessing parasite rates, although here, too, the inadequacy of data from former surveys must be taken into account.

Comparable data on the microfilarial rates of adults are available only for Kodera, Kaimosi, and Ngoina. In Kakamega, data obtained prior to vector elimination were too few and inconsistent to be of use. Estimates of the original microfilarial rates were based on one skin snip only; to simplify analysis, estimates have been made of the rates that would have been found if two skin snips instead of one had been taken. Furthermore, since the original rates probably excluded younger children, the fraction of the population born 5 years before interruption or later has been excluded from the 1964 rates. No large-scale onchocerciasis surveys were carried out during the years immediately following interruption of transmission; hence, no factual information exists on early changes in microfilarial rates. To give an impression of the trend of reduction of the microfilarial rates, the few available data were plotted on normal graph paper (Fig. 1). The purely speculative nature of a graphic presentation based on data from only three periods is fully recognized, particularly since the data for the first two periods are adjusted figures and, as such, subject to certain variability. Since the curve produced by the data for Kodera is a nearly-straight line, straight lines have also been drawn for the survey data for Kaimosi and Ngoina. Assuming that the curves continue with the same degree of decline to the end, they would reach the zero line after 13-17 years. Further follow-up surveys in the three focal areas in which the infection is still present, particularly Kaimosi, would provide more accurate knowledge of the final trend of disappearance of the infection.

FIG. 2. PREVALENCE OF ONCHOCERCIASIS AND FREQUENCY OF MICROFILARIAE AND/OR NODULES AS A FUNCTION OF DURATION TO EXPOSURE, BY AGE-GROUPS AND FOCAL AREAS



Effect of duration of exposure to the infection

The effect of the duration of exposure to the risk of onchocerciasis on the prevalence of the infection (as measured by the presence of microfilariae and/or nodules) is expressed in Fig. 2, using data from Table 4. As expected, the prevalence of the infection increases with the duration of exposure. The prevalence curve starts earlier and rises more rapidly in areas of high endemicity than in those of low endemicity. In persons exposed to transmission for less than 10 years, microfilariae were more frequently found without nodules, whereas in those exposed for 15 years or more, both microfilariae and nodules were more commonly present. However, no statistically significant difference could be observed in microfilarial density in relation to duration of exposure.

In the Kaimosi area 6 onchocerciasis cases were discovered whose exposure to the infection varied from less than 1 year to 4 years and who still had microfilariae in the skin 10 years after vector elimination. No nodules could be found on these persons in spite of a very thorough examination.

The information provided by the follow-up survey from Kenya is of very limited use in assessing the effects of the duration of onchocercal infection on the clinical manifestations. In fact, the actual duration of the infection is not known for any of the persons examined; it can only be estimated on the basis of the duration of exposure to the infection. Moreover, a large proportion of the presumably noninfected adult population, particularly those in the former hyperendemic foci, must have been infected previously, but their infection has meanwhile either died out or been reduced to such a low intensity that it could not be detected. Finally, the findings of the 1964 survey reveal only the situation with respect to old and long-lasting infections.

Skin changes and glandular enlargements were found with nearly equal frequency in areas of high and low endemicity. In all focal areas most persons with possible onchocercal skin lesions were aged 40 years or over, indicating that skin changes and marked glandular enlargements, such as hanging groin, are not developed before the infection has been harboured for 10 years or more.

The same difficulties of assessment apply to the ophthalmological survey results. Most of the eye lesions of possible onchocercal origin were found in those aged 40 years or over, although there was no marked difference between the infected and the noninfected groups. Since there is no relevant ophthalmological information from the time prior to interruption of transmission, any analysis of the effect of cessation of reinfection on the development of onchocercal eye lesions is purely speculative.

The situation in Kodera shows that, 18 years following complete vector eradication, the most frequent single cause of blindness continues to be onchocerciasis. Taking into consideration the case-histories of the blind persons encountered in the follow-up surveys, it can be stated that the onset of blindness occurred long after vector eradication in at least half of them. This means that further cases of onchocercal eye pathology and blindness may still be expected in Kaimosi, Ngoina, and Kakamega, where live worms still exist.

ACKNOWLEDGEMENTS

The authors extend their thanks to the Headquarters staff of the Ministry of Health, Kenya, and more particularly to Dr J. C. Likimani, Director; Dr N. R. E. Fendall, former Director; Dr J. G. Grounds; and Dr R. B. Heisch, former Director, Division of Insect-Borne Diseases, for their assistance in planning the programme. They also thank Dr P. Jordan, Director, East African Medical Research Unit, Mwanza, for the loan of the Karl Zeiss slit lamp.

Thanks are also due to the Medical Officers of Health of the three Districts of Kenya involved in the survey for their generosity and understanding in providing, often at very short notice, the field staff, nurses, and transport required for work in the field, and for assisting such work in many other ways.

Finally, the success of this field study would have been impossible without the loyal and efficient service of the field staff of the Division of Insect-Borne Diseases, under the able direction of Mr Alphonse Kipkirui. All worked long hours, often under most arduous conditions, to complete the survey before the onset of the heavy rains.

RÉSUMÉ

Au Kenya, la transmission de l'onchocercose a été interrompue par suite de l'éradication du vecteur, *Simulium neavei*, des foyers d'infection entre 1946 et 1955. Ce pays se prête donc particulièrement à l'étude de la durée de vie du parasite, *Onchocerca volvulus*, et de l'évolution naturelle de la maladie chez l'homme en l'absence de réinfection.

Quatre anciens foyers d'onchocercose ont été choisis en vue de cette enquête menée en avril et mai 1964. Dans deux d'entre eux, la maladie avait sévi sous forme hyperendémique (le taux d'infection étant de près de 100%); dans les deux autres, elle n'avait revêtu qu'un caractère d'endémicité modéré. Les équipes d'enquêteurs comprenaient notamment un épidémiologiste, un ophtalmologiste et un entomologiste. Dans chacun des secteurs, 500 personnes environ, désignées au hasard, ont subi un examen clinique, parasitologique et ophtalmologique. On a recherché les signes cutanés de l'affection, prélevé au moins deux biopsies cutanées par personne et mesuré systématiquement l'acuité visuelle. Un examen ophtalmologique complet a été en outre pratiqué chez 1176 (56%) des participants à l'enquête.

Ont été considérés comme cas d'onchocercose les sujets chez lesquels on décelait des microfilaires à l'examen biopsique ou ophtalmologique, ou qui étaient porteurs de nodules. Dans les deux secteurs primitivement très atteints, on a dénombré respectivement 12,2% et 34,3% de cas; dans les deux autres, les pourcentages atteignaient 12,8% et 8,5%. La prévalence de l'affection était nettement plus élevée dans le sexe masculin. Elle s'accroissait régulièrement en fonction de l'âge et était maximale chez les sujets âgés de plus de 40 ans. Des microfilaires ou des nodules n'ont jamais été observés chez les enfants nés après l'éradication du vecteur.

En fait de lésions cutanées, surtout fréquentes chez les sujets âgés de plus de 40 ans, on a noté principalement de l'atrophie, beaucoup plus rarement de l'épaississement de la peau et de la dépigmentation. Sur 1176 personnes examinées, 24 présentaient des microfilaires dans la chambre antérieure de l'œil. On a diagnostiqué 390 cas de kératite ponctuée, et 7 cas de cécité bilatérale ont été observés chez des porteurs de microfilaires ou de nodules. Huit sujets non parasités souffraient également de cette infirmité.

L'analyse détaillée des résultats de l'enquête montre que, 11 ans après l'interruption de la transmission, des parasites adultes vivants étaient encore présents dans les nodules, cependant que les biopsies décelaient des microfilaires dans la peau. *O. volvulus* est donc capable d'engendrer encore des microfilaires après 9-10 ans au moins, si l'on admet que la durée moyenne de vie de ces dernières est de 1 à 2 ans. Dans les foyers où la transmission avait cessé depuis 18 ans, toutes les filaires découvertes dans les nodules étaient mortes. L'absence, après ce laps de temps, de microfilaires chez les personnes examinées donne à penser qu'*O. volvulus* cesse de se reproduire après 16 ans d'existence, ou peut-être plus tôt.

Comparant les données récentes et les observations antérieures relatives aux indices microfilariens, les auteurs suggèrent que le déclin de l'infection, succédant à l'interruption de la transmission, s'effectue suivant une ligne de régression droite, le zéro théorique étant atteint après 13 à 17 ans environ.

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Annex

FORM USED IN FOLLOW-UP SURVEY, KENYA, 1964
INDIVIDUAL INVESTIGATION FORM

Place of Examination .... Date ....

Serial Number ....

NAME:.. Sex:.............................. Age:.................. Estimated/Actual

Resident in area since: Birth Duration of absence from area: ....

or: ____________

Location:.............................. Sub-location: ....

Name of Sub/or Headman .... Name of householder ....

---

1. SKIN LESIONS

1.1 Nodules

Site	Number	Size	Consistency
....	....	....	....
....	....	....	....
....	....	....	....

1.2 Appearance of skin ....

1.3 Glandular enlargements ....

---

2. PARASITOLOGICAL EXAMINATION

Biopsies:

Site	Result	Microfilarial count	Conf. staining
Thigh	....	....	....
Chest	....	....	....
Near nodule	....	....	....

---

3. VISUAL ACUITY

Right eye .... Left eye ....

If blind, since when ....

---

4. OPHTHALMOLOGICAL EXAMINATION Examined: Yes/No

Lesion	Right eye	Left eye
Punctate keratitis (fluffy opacity)	....	....
Sclerosing keratitis	....	....
Microfilariae in anterior chamber	....	....
Chronic iritis	....	....
Chorioretinitis (focal)	....	....
Optic atrophy	....	....
Glaucoma (secondary)	....	....
Cataract (complicated)	....	....
Luxation or sub-luxation lens	....	....
Onchocerciasis cases: Degenerative chorioretinitis	....	....

Remarks (cause of blindness, treatment, etc.): ....

....