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Impact of repeated large scale ivermectin treatments on the transmission of *Loa loa*

J.-P. Chippaux, B. Bouchité, M. Boussinesq, S. Ranque, T. Baldet and M. Demanou *Antenne ORSTOM auprès du Centre Pasteur du Cameroun, B.P. 1274, Yaoundé, Cameroon*

Abstract

We have studied the impact of large-scale treatment with ivermectin on the transmission of loiasis in a forest village in south Cameroon where loiasis was highly endemic, with a prevalence of 30%. After one year of parasitological and entomological surveillance without treatment, all consenting residents aged >5 years received ivermectin 200 μg/kg every 3 months. For ethical reasons, treatment was interrupted after 2 years, but parasitological and entomological surveillance continued for 18 months after the end of treatment. The prevalence of loiasis was reduced to <10% and the mean microfilaraemia decreased by 90% in 2 years. The prevalence and average intensity of infection remained stable during the 18 months after treatment ended. Two vector species were identified, *Chrysops dimidiata* (representing about 90% of the fly population) and *C. silacea*. The infection rate (all stages) in *Chrysops* decreased by 75% and the infective rate (percentage of *Chrysops* harbouring third-stage larvae of *Loa loa* in the head) decreased by 85% in *C. dimidiata* and became zero in *C. silacea*. After the end of treatment, the infection and infective rates increased gradually. Large-scale treatment seemed an efficient method for the control of *L. loa* transmission provided high drug coverage was achieved. Nevertheless, because of the high risk of adverse effects when using the current microfilaricidal drugs, such a strategy remains unacceptable.

Keywords: loiasis, *Loa loa*, *Chrysops dimidiata*, *Chrysops silacea*, chemotherapy, ivermectin, Cameroon

Introduction

Loiasis is limited to the Central African rain forest from Nigeria to the former Zaire (PINDER, 1988). Amongst the methods available for its control, larviciding breeding sites of the vector (*Chrysops*) or trapping adult insects are ineffective or impracticable on a large scale (WILLIAMS & CREWE, 1963; NOIREAU, 1990). The only means of controlling transmission of loiasis is to eliminate the human microfilarial reservoir through large-scale treatment with filaricidal drugs. To our knowledge, the only attempt to use such a strategy was made by DUKE & MOORE (1961) in a rubber estate at Sapele, Nigeria. The attempt was regarded as unsuccessful by the authors.

Because of this disappointing result, together with the difficulty of organizing large-scale treatment with diethylcarbamazine (DEC) over several days and the increasing evidence that this drug may induce encephalopathy in patients with very high *Loa loa* microfilaraemia (FAIN, 1981), no further attempt was made to control the transmission of loiasis with DEC. However, as emphasized by DUKE & MOORE (1961), the general strategy was theoretically promising and justified by the facts that the human population is probably the only reservoir of *Loa*, that the *Chrysops* population density is low, even in highly endemic areas (generally <1000/km^2), and that the flight range of the vectors is short (generally <5 km) (CREWE & O'ROURKE, 1951; BEESLEY & CREWE, 1963; NOIREAU *et al.*, 1990; CHIPPAUX *et al.*, in press).

Over about 10 years, several studies have demonstrated that ivermectin may bring about a marked decrease in *Loa* microfilaraemia (RICHARD-LENOBLE *et al.*, 1988; CARME *et al.*, 1991; CHIPPAUX *et al.*, 1992; MARTIN-PRÉVEL *et al.*, 1993; GARDON *et al.*, 1997). This, together with the fact that ivermectin, in contrast with DEC, is efficient as a single oral dose and can thus be much more easily used, and was considered at the outset of the study to be a safe treatment for loiasis, prompted us to reinvestigate the principle of DUKE & MOORE (1961) and determine whether large-scale treatment with this drug would have an impact on the transmission of loiasis. The present paper reports the results of this investigation.

Address for correspondence: J.-P. Chippaux, CERMES, B.P. 10887, Niamey, Niger; fax +227 75 20 45.

Patients and Methods

Study area and parasitological surveys

The study was conducted in Ngat (3°23′N, 11°34′E), a village in the Central Province of Cameroon, 70 km south of the capital Yaoundé, in an area of degraded forest. The area has been described in detail previously (MOMMERS *et al.*, 1994; GARCIA *et al.*, 1995; CHIPPAUX *et al.*, in press). Briefly, Ngat lies at an altitude of 600–700 m; the climate is equatorial, with 2 rainy and 2 dry seasons; the mean annual rainfall is 1600 mm and the mean annual temperature is 24·1°C. The initial census revealed a total population of 788, of whom about 600 lived permanently in the village in small dwellings on both sides of an earth road 10 km long. The major occupations were subsistence agricultural farming and cultivation of cocoa. The fields, which extend 500–2000 m from the road, can be reached by a system of forest trails perpendicular to the main road. Muddy places fringing the numerous streams and swamps overgrown with raffia constitute very suitable breeding sites for *Chrysops*.

The level of endemicity of loiasis in the village was assessed before the first ivermectin distribution. Capillary blood smears (30 μL) were taken between 10:00 and 15:00 from 667 volunteers aged 6 months or more, stained with Giemsa's stain, and examined under a microscope (MOMMERS *et al.*, 1994; GARCIA *et al.*, 1995). Ngat was highly endemic for loiasis: in the total population, the prevalence of *Loa* microfilaraemia was 30·1%, and the Williams geometric mean *Loa* microfilarial load was 81·4 microfilariae per 30 μL of blood.

Ivermectin efficacy was assessed by parasitological surveys one week after the first distribution (April 1993) and just before both the second (July 1993) and third (October 1993) treatment rounds. The next 2 surveys (in July and October 1993) were carried out on microfilaraemic persons only. Further parasitological surveys were spaced to avoid withdrawal from treatment; they were performed in April 1994, April 1995, and finally in April 1996, and involved the whole population.

Entomological studies were also conducted to determine the dispersal of *Chrysops* in the study area, and to evaluate the annual fluctuation in the density of the fly population and in the *Loa* infection rates.

Treatment schedule

At the outset of the study, the long-term effect of ivermectin on *Loa* microfilaraemia was not documented,

and it was assumed, wrongly (GARDON *et al.*, 1997), that the level of parasitaemia would have increased considerably 6 and 12 months after a single dose. As our objective was to obtain the optimum effect of treatment on transmission, we decided to treat the population at intervals of 3 months over 2 years, from April 1993 to April 1995. It was also planned to limit the first treatment to individuals who had undergone a parasitological examination previously; from the second treatment round, however, ivermectin would be distributed to all the volunteers attending for the treatment, whether they had undergone an initial parasitological examination or not. This strategy was modified because serious reactions, including disorders of consciousness, were recorded after the first dose in 2 patients who had very high *Loa* microfilaraemia (199000/mL and 217000/mL, respectively) (CHIPPAUX *et al.*, 1993). Assuming that the risk of developing such reactions was related to the intensity of infection, and because a single dose of ivermectin brings about a marked decrease in microfilaraemia, even in patients with very high initial values, we decided to limit the subsequent distribution to those individuals who had received a first treatment. New residents, who had settled in the treatment area between April 1993 and July 1994, were thus excluded from the treatment, because some of them were assumed to harbour high infections and to be at risk of serious reactions. However, after having noticed that these new residents constituted an increasing proportion of the population, and thus a significant microfilarial reservoir, we decided, in November 1994 and April 1995, to examine parasitologically those new residents who expressed their wish to receive ivermectin, and to treat them if their microfilaraemia was <10000/mL.

At each treatment round, the drug was administered at a dose of 200 µg/kg of body weight, taking into account the usual exclusion criteria: children <5 years of age, weight <15 kg, pregnancy, first month of lactation, and severe illness. The dose of 200 µg/kg was chosen because RICHARD-LENOBLE *et al.* (1988) demonstrated that it was much more effective on *Loa* microfilaraemia than a dose of 150 µg/kg (the latter being presently the standard dose for the treatment of onchocerciasis). The rounds lasted one week: on each of the first 3 d, the distribution team was installed at a different place, in the house of the village chief or in that of a quarter chief; these 3 distribution points had been selected so that the most remote residents lived within 1 km of a dosing point. During the last 4 d of the week, a mobile team walked along the main road of the village in order to give ivermectin to the individuals who were absent from the distribution point, and to record and treat any reactions to ivermectin. The drug coverage at each distribution round, and the effect of the successive treatments on *Loa* microfilaraemia, have been reported previously (RANQUE *et al.*, 1996).

Assessment of the Loa *infection rate in* Chrysops

From November 1992 to November 1993, catches of *Chrysops* were made every week on 2 consecutive days. After November 1993, it was decided for logistical reasons to limit the entomological study to the periods of high transmission of *L. loa*, i.e., according to the preliminary results, April–May and October–November. Fly catches were thus organized in April–May 1994, 1995, and 1996, and in October–November 1995 and 1996. Each of these catches lasted 15–20 consecutive days. Flies were caught between 06:00 and 18:00 in hand nets by individuals stationed by a wood fire, the smoke of which appeared to attract the flies (DUKE, 1955). The same 6 catching sites, representative of the various places visited by the villagers, were used throughout the study. These sites were located in the centre of the village, i.e., in places where an optimum impact on transmission would be expected. All the flies caught were kept separately in glass tubes closed with a cotton-wool plug. A label on each tube indicated the catching site, day, and hour. At the laboratory, all flies were specifically identified, and a sample was examined for parity, following the method of DUKE (1960), and the presence of *Loa* larvae.

The *Chrysops* population density was evaluated as the mean number of flies per person–day. The head, thorax and abdomen were dissected separately in order to distinguish infected and infective flies.

The infection rate was defined as the proportion of dissected flies containing developing forms of any stage of *L. loa*, and the infective rate corresponded to the proportion of dissected flies with third-stage larvae (L3) in the head or mouthparts.

Results

Drug coverage

Of the 788 inhabitants at the beginning of the study, 32 (3·7%) died, 268 (30·9%) left the village, and 20 (2·3%) refused treatment. Between April 1993 and April 1995, 130 subjects entered the study. The drug coverage achieved at the various treatment rounds ranged between about 46% and 80% of the whole population, and about 74% and 94% of the persons with pre-treatment *Loa* microfilaraemia (Table 1).

Table 1. Ivermectin treatments, Ngat (Cameroon)

Treatment dates	No. of residents	Percentage treated: All residents	Percentage treated: Microfilaraemic residents
April 1993	603	64·0	79·9
July 1993	585	56·4	74·7
October 1993	571	75·8	87·9
January 1994	677	52·7	73·7
April 1994	671	45·9	93·8
July 1994	659	58·4	91·2
October 1994	649	59·3	89·8
January 1995	751	70·4	90·7
April 1995	565	80·4	93·4

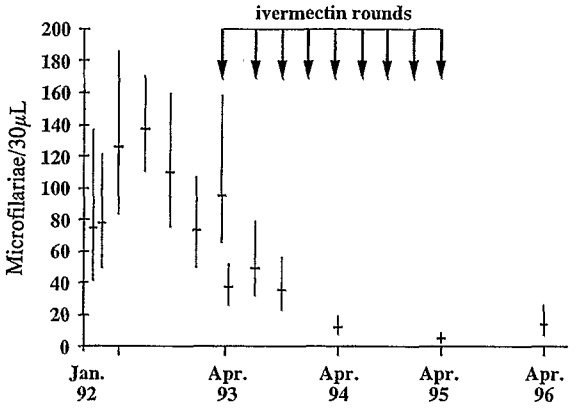

Fig. 1. *Loa loa* microfilaraemia, January 1992–April 1996 (means±SD).

The decrease in microfilaraemia of the subjects who received all 9 doses of ivermectin has been reported by RANQUE *et al.* (1996) and is shown in Fig. 1.

Chrysops *population density*

Population densities of *C. dimidiata* were much higher than those of *C. silacea*. For the former species, the biting rates recorded at the different catching rounds varied from 16·3 to 95·4 bites per person–day, whereas they ranged between 1·2 and 9·0 bites per person–day for the latter (Fig. 2). The highest biting rates of *C. dimidiata* were recorded in April–May 1994 and 1996, and the lowest in October–November 1992, 1995 and

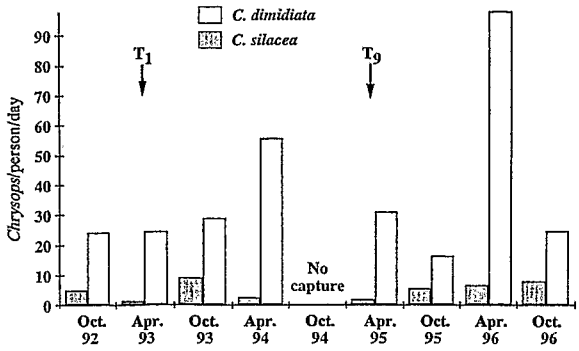

Fig. 2. Density of *Chrysops*, November 1992–November 1996; T_1 and T_9 indicate the first and last rounds of ivermectin treatment.

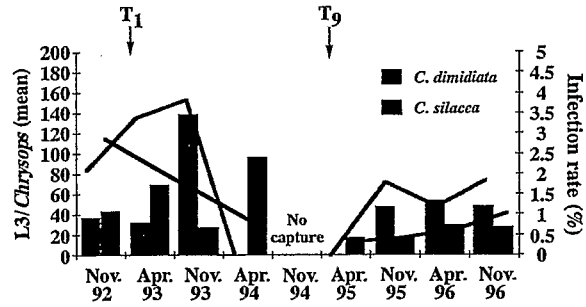

Fig. 3. Third-stage larvae (L3) of *Loa loa* in *Chrysops*; the bars indicate the average number per head of infected flies, and the curves shows the infection rate.

1996 (and, unusually, in April–May 1993). This suggests that the population density for this species is higher at the beginning of the short rainy season than at the end of the main rainy season. In contrast, the population density of *C. silacea* tended to be higher in October–November (biting rates between 4·7 and 9·0 bites per person–day) than in April–May (biting rates between 1·2 and 7·9 bites per person–day).

When both species were considered together, the maximum densities and infection rates, and thus the maximum intensity of transmission, were recorded in April–May and October–November (CHIPPAUX *et al.*, in press). During the whole study, *C. silacea* represented only 4–8% of the human-biting *Chrysops* population in April–May and 16–26% in October–November.

Infection and infective rates of Chrysops

The total numbers of *C. dimidiata* and *C. silacea* dissected were 26947 and 3294, respectively (Table 2). For both species, the parous rates did not differ markedly from one catching round to another: they generally ranged from 24% to 28% for *C. dimidiata* and from 23% to 30% for *C. silacea*.

In April 1993, just before the first ivermectin distribution, the infection rates of *C. dimidiata* and *C. silacea* were 7·4% and 10·3%, respectively, and the infective rates were 3·0% and 4·6%. Six months later, the infection and the infective rates were not significantly different from the pre-treatment values; however, the infective rate tended to increase for *C. silacea* and to decrease for *C. dimidiata*. In April–May 1994, i.e., 3 months after the third ivermectin distribution, the infection and infective rates of *C. dimidiata* (2·8% and 1·2% respectively) were significantly lower ($P<10^{-7}$ and $P=0·0025$, respectively) than the pre- treatment values. At the same time, the infection rate of *C. silacea* had decreased, with a P value (0·053) close to the limit of significance; in addition, none of the infected flies of this species was infective. The infection rates recorded in April–May 1994 and April–May 1995 were not significantly different for each of the 2 species. However, the infective rate of *C. dimidiata* continued to decrease significantly ($P<0·05$).

The last ivermectin treatment was given in April–May 1995; at this time, the infection and infective rates for both species of *Chrysops* were at a minimum. They then tended to increase gradually until November 1996. The increases in the infection and infective rates of *C. dimidiata*, and in the infection rate of *C. silacea*, were not significant between April–May and October–November 1995, but they were significant between April–May 1995 and April–May 1996 ($P<0·05$). In November 1996, i.e., 18 months after the last ivermectin distribution, the infection rates of both species were still lower than their respective initial values: they were about 70% of the rates recorded just before the first treatment in April 1993. The infective rates were 50–54% of the initial values.

Table 2. Infection rate of *Loa loa* in *Chrysops*, Ngat (Cameroon)

	Chrysops silacea				*Chrysops dimidiata*			
	No. of insects			Total no.	No. of insects			Total no.
Dates	Dissected	Infected[a]	With L3 larvae[b]	of L3 larvae[c]	Dissected	Infected[a]	With L3 larvae[b]	of L3 larvae[c]
Nov. 92	47	5 (10·6)	1 (20)	37 (7·4)	240	17 (7·1)	7 (41)	302 (17·8)
Apr. 93	87	9 (10·3)	3 (33)	97 (10·8)	1457	108 (7·4)	31 (29)	2209 (20·5)
Nov. 93	103	10 (9·7)	4 (40)	596 (59·6)	332	19 (5·7)	5 (26)	137 (7·2)
Apr. 94	75	2 (2·7)	0	0	1367	38 (2·8)	11 (29)	1058 (27·8)
Nov. 94		None captured				None captured		
Apr. 95	364	9 (2·5)	0	0	6286	124 (2·0)	23 (19)	388 (3·1)
Nov. 95	932	38 (4·1)	17 (45)	792 (20·8)	2867	60 (2·1)	14 (23)	231 (3·9)
Apr. 96	1039	51 (4·9)	13 (25)	724 (14·2)	12605	375 (3·0)	89 (24)	2504 (6·7)
Nov. 96	647	47 (7·3)	12 (25)	560 (11·9)	1793	94 (5·2)	20 (21)	539 (5·7)

[a]Numbers in parentheses show the number infected as a percentage of those dissected.
[b]Numbers in parentheses show the number with third-stage (L3) larvae as a percentage of those infected with any stage.
[c]Numbers in parentheses are the mean number of third-stage (L3) larvae per infected fly.

Discussion

DEC, albendazole and ivermectin are filaricidal drugs which bring about a marked decrease in *Loa* microfilaraemia, but have little direct effect on the adult stage of the parasite, which is assumed to be the cause of most of the signs of the disease. The current individual treatment of loiasis is thus not satisfactory. It is possible that large scale treatment with a microfilaricidal drug may reduce the microfilaricidal reservoir, and therefore the intensity of transmission of *Loa*, the population of adult worms, and the prevalence or severity of symptoms related to the latter. The only evaluation of the possibility of reducing the transmission of *Loa*

through large scale treatment has been carried out by DUKE & MOORE (1961) in an area of Nigeria where the main vector was *C. silacea*. The objective was to treat, with a 20 d course of DEC, all individuals, among a total population of 5120 persons at risk, who harboured *Loa* microfilariae. However, about 35% of the population did not attend for the pre-treatment blood examination. The authors assumed that the proportion of microfilaraemic persons, and their microfilarial loads, would be similar in the subjects who attended for examination and those who did not. They thus estimated that 35% of the microfilaria carriers had not been treated, and that the treatment brought about a reduction of the infection potential of the whole population at risk to only 30% of the pre-treatment level. After treatment, the infection rate of *C. silacea* was reduced to 50% of the pre-treatment value; in contrast, no reduction was observed in the infection rate of *C. dimidiata*. The authors concluded that these fairly disappointing results were mainly related to the unsatisfactory drug coverage.

The general principles of the present study were similar to those of DUKE & MOORE (1961). However, besides the fact that the drug distribution was repeated every 3 months, we made 2 other alterations. First, we decided to treat the total population of the study area, and not only those subjects who carried *Loa* microfilariae. Doing this, we were certain not to exclude from treatment some microfilaria carriers who had not been detected at the outset of the study because their microfilaraemia was very low. This strategy was also ethically justified because *Ascaris* infection was common in the area; as ivermectin is very effective against this parasite, it was thought that even persons who were not microfilaraemic would take advantage of the treatment. The second alteration concerned the location of the catching sites within the study area, which were chosen so that the distance between them and the nearest untreated community exceeded 5 km, the maximum flight range of *C. silacea* and *C. dimidiata* (see BEESLEY & CREWE, 1963; CHIPPAUX *et al.*, in press). It was hoped that the flies caught would not, therefore, have taken a potentially infective blood meal on individuals living outside the treatment area.

The most surprising observation was the fact that the infection and infective rates in April and November 1993, i.e., after the first and third treatment rounds, were reduced only very slightly, if at all. As the entomological surveys were carried out at the same time as the treatment round, we assumed that, in April 1993, most of the flies had become infected either before ivermectin distribution or before the drug had had an effect on microfilaraemia. In November 1993, the unexpected result was less easily explained. Two possible reasons are: (i) infected flies originated from outside the treated area, and (ii) untreated infected residents (about 15–20% of the microfilaria carriers at this time) and infected visitors constituted an adequate parasite reservoir. The first hypothesis can be rejected as the flight range was less than the distance between the catching zone and untreated communities, and because of the marked decrease in infection rates in April 1994 and April 1995.

The reductions in infection and infective rates, and in the average number of L3 per infected fly, from April 1994, could be attributed to the drug treatment. A direct impact of ivermectin on *Loa* larvae should reduce the percentage of *Chrysops* harbouring L3, which was not observed (Table 2). In April 1994 (fifth treatment round), more than 85% of the entire population, and 95% of microfilaria carriers, received at least one ivermectin dose, which is enough to reduce the parasite load for one year or more (GARDON *et al.*, 1997). The low infection and infective rates remained stable until April 1995, due to the parasite reservoir remaining reduced: the prevalence of microfilaria carriers in April 1995 was 6·7% (RANQUE *et al.*, 1996). Treatment was stopped in April 1995 because of the risk of reactions in areas highly endemic for loiasis (CHIPPAUX *et al.*, 1996), even though those already treated could have continued to receive the drug without risk. In April 1995, a number of immigrants potentially infected with *L. loa* arrived in the village, making it ethically difficult to continue mass treatment. After November 1995, the infection and infective rates increased gradually until the end of the study in November 1996. The geometric mean parasite density did not vary significantly between April 1995 and April 1996 (Fig. 1) but the prevalence of microfilaraemia rose from 6·7% to 14·2%. It is likely that the increased number of microfilaria carriers, mainly recent immigrants who formed a quarter of the village population in April 1996, was sufficient to increase the infectivity rate in *Chrysops*. Thus, it seems that continued high drug coverage is essential to obtain and maintain a significant decrease in the human infection rate.

Conclusion

This study confirmed that the human parasite reservoir can be drastically reduced by large-scale treatment (RANQUE *et al.*, 1996). There was also a notable reduction of the infection rate in *Chrysops*, especially in the number of infective larvae in the heads of the insects. Large-scale treatment therefore seems to be efficient and is a potential control strategy providing that drug coverage exceeds 90% of the microfilaria carriers. Nevertheless, considering the risks of severe adverse effects in patients with high microfilaraemia and treated with ivermectin (CHIPPAUX *et al.*, 1996), large-scale treatment cannot be recommended.

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References

Beesley, W. N. & Crewe, W. (1963). The bionomics of *Chrysops silacea* Austen, 1907—II. The biting rhythm and dispersal in rain-forest. *Annals of Tropical Medicine and Parasitology*, **57**, 191–203.

Carme, B., Ebiliki, B., Mbitsi, A. & Copin, N. (1991). Essai thérapeutique de l'ivermectine au cours de la loase à moyenne et forte microfilarémie. *Annales de la Société Belge de Médecine Tropicale*, **71**, 47–50.

Chippaux, J.-P., Ernould, J.-C., Gardon, J., Gardon-Wendel, N., Chandre, F. & Barberi, N. (1992). Ivermectin treatment of loiasis. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **86**, 289.

Chippaux, J.-P., Garcia, A., Ranque, S., Schneider, D., Boussinesq, M., Cot, S., Le Hesran, J.-Y. & Cot, M. (1993). Adverse reactions following ivermectin treatment in a hyperendemic loiasis area. *American Journal of Tropical Medicine and Hygiene*, **49**, 161.

Chippaux, J.-P., Boussinesq, M., Gardon, J., Gardon-Wendel, N. & Ernould, J.-C. (1996). Severe adverse reaction risks during mass treatment with ivermectin in loiasis-endemic areas. *Parasitology Today*, **12**, 448–450.

Chippaux, J.-P., Bouchité, B., Demanou, M., Morlais, I. & Legoff, G. (in press). Study of the dispersal and the density of loiasis vectors *Chrysops dimidiata* in rain forest of southern Cameroon. *Medical and Veterinary Entomology*.

Crewe, W. & O'Rourke, F. J. (1951). The biting habits of *Chrysops silacea* in the forest at Kumba, British Cameroon. *Annals of Tropical Medicine and Parasitology*, **45**, 38–50.

Duke, B. O. L. (1955). Studies on the biting habits of *Chrysops*—II. The effects of wood fires on the biting density of *Chrysops silacea* in the rain-forest at Kumba, British Cameroon. *Annals of Tropical Medicine and Parasitology*, **49**, 260–273.

Duke, B. O. L. (1960). Studies on the biting habits of *Chrysops*. VII. The biting-cycles of nulliparous and parous *C. silacea* and *C. dimidiata* (Bombe form). *Annals of Tropical Medicine and Parasitology*, **54**, 147–155.

Duke, B. O. L. & Moore, P. J. (1961). A trial of Banocide as a means of controlling the transmission of loiasis on a rubber estate in Nigeria. *Annals of Tropical Medicine and Parasitology*,

55, 263–277.
Fain, A. (1981). Épidémiologie et pathologie de la loase. *Annales de la Société Belge de Médecine Tropicale*, **61**, 277–285.
Garcia, A., Abel, L., Cot, M., Ranque, S., Richard, P., Boussinesq, M. & Chippaux, J.-P. (1995). Longitudinal survey of *Loa loa* filariasis in south Cameroon: long term durability and factors influencing individual microfilarial status. *American Journal of Tropical Medicine and Hygiene*, **52**, 370–375.
Gardon, J., Kamgno, J., Folefack, G., Gardon-Wendel, N., Bouchité, B. & Boussinesq, M. (1997). Marked decrease in *Loa loa* microfilaraemia six and twelve months after a single dose of ivermectin. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **91**, 593–594.
Martin-Prével, Y., Cosnefroy, J.-Y., Tshipamba, P., Ngari, P., Chodakewitz, J. A. & Pinder, M. (1993). Tolerance and efficacy of single high-dose of ivermectin for the treatment of loiasis. *American Journal of Tropical Medicine and Hygiene*, **48**, 186–192.
Mommers, E. C., Dekker, H. S., Richard, P., Garcia, A. & Chippaux, J.-P. (1994). Prevalence of *Loa loa* and *Mansonella perstans* filariasis in southern Cameroon. *Tropical and Geographical Medicine*, **47**, 2–5.
Noireau, F. (1990). Possibilités actuelles de lutte contre la filariose à *Loa loa*. *Annales de la Société Belge de Médecine Tropicale*, **70**, 167–172.
Noireau, F., Nzoulani, A., Sinda, D. & Itoua, A. (1990). *Chrysops silacea* and *C. dimidiata*: fly densities and infection rates with *Loa loa* in the Chaillu mountains, Congo Republic. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **84**, 153–155.
Pinder, M. (1988). *Loa loa*. A neglected filaria. *Parasitology Today*, **4**, 279–284.
Ranque, S., Garcia, A., Boussinesq, M., Gardon, J., Kamgno, J. & Chippaux, J.-P. (1996). Decreased prevalence and intensity of *Loa loa* infection in a community treated with ivermectin every three months for two years. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **90**, 429–430.
Richard-Lenoble, D., Kombila, M., Rupp, E., Papaylou, E. S., Gaxotte, P., Nguiri, C. & Aziz, M. (1988). Ivermectin in loiasis associated with or without concomitant *Onchocerca volvulus* and *Mansonella perstans* infestations. *American Journal of Tropical Medicine and Hygiene*, **39**, 480–483.
Williams, P. & Crewe, W. (1963). Studies on the control of the vectors of loiasis in West Africa. *Annals of Tropical Medicine and Parasitology*, **57**, 300–306.

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