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POPULATION DYNAMICS OF *LOA LOA* AND *MANSONELLA PERSTANS* INFECTIONS IN INDIVIDUALS LIVING IN AN ENDEMIC AREA OF THE CONGO

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Abstract. A followup of *Loa loa* and *Mansonella perstans* microfilaremia was carried out in an adult population living in a highly endemic area of the Congo. Infection rates and parasite loads were found to be stable in the general population, both in the short-term (two months) and long-term (3–4 years) followup. The microfilarial status of most of the subjects examined did not change between tests. At the individual level, the microfilarial densities of *L. loa* and *M. perstans* also remained remarkably constant over time. This results in a qualitative and quantitative stability of the parasitic material available for the vectors.

Epidemiologic studies on filariasis cases with microfilaremia are most often cross-sectional, and the microfilarial status of an individual is determined from a single parasitologic examination carried out during the period of maximum distribution of microfilariae in the peripheral blood. However, to make a diagnosis of filarial infection, repeated blood sampling is recommended, given the variable degree of detection of microfilariae in low-density carriers. Indeed, the detection of microfilariae is inconsistent from one day to another in approximately 15% of the population infected with *Mansonella perstans* and *Loa loa*.[1] In regions endemic for these parasites, all subjects may be carriers of *M. perstans* microfilariae, whereas the prevalence rate of *L. loa* carriers does not exceed 40%.[2–4] It has been suggested that the absence of *L. loa* microfilariae in a high proportion of the population may be due to genetically controlled resistance.[5] However, it has not been possible to clearly demonstrate this supposition since the dynamics of production of microfilariae in human hosts harboring several female worms is unknown.[6] To confirm the short- and long-term durability of microfilarial status and to study the variability of the parasitic load in humans over time, we undertook a qualitative and quantitative followup of microfilaremias in a stable population living in a region highly endemic for *L. loa* and *M. perstans*.

MATERIALS AND METHODS

The survey was conducted on an adult Bantu lage of Missama (Lekoumou region), Congo. After an initial blood examination carried out on the 192 subjects in February 1985, 171 (mean ± SD age 48.5 ± 8.1 years, M:F sex ratio = 0.41) were re-examined two months later for the short-term followup of microfilaremia. The long-term followup, including the examination of a blood sample, was carried out on 66 of the 192 subjects in January 1988. Eighteen additional subjects were examined in March 1989. More than 100 subjects moved out of the area and were not included in the long-term study. No subject had received diethylcarbamazine between the examinations.

Capillary blood samples (40 μl) were taken between 10:00 AM and 2:00 PM, stained with Giemsa, and the microfilariae were identified and counted. Parasitemia was expressed as microfilariae/40 μl of blood. The transformation log (x + 1) was carried out on individual microfilarial densities. Modified geometric means (Williams' mean) with standard deviations for parasitic species and period of sample were calculated for the whole population.

RESULTS

Short-term trend of microfilaremia

The prevalences of *L. loa* and *M. perstans* microfilaremic subjects and the microfilarial densities in the overall study population in February and April 1985 are shown in Table 1. Although the rates of infection increased, they did not vary

TABLE 1

Trend in Loa loa *and* Mansonella perstans *microfilaremias over a 2-month period, showing the prevalence of microfilaria carriers and the Williams' mean of microfilarial densities per 40 mm³ of blood with standard deviations, for the overall population studied**

		L. loa			*M. perstans*		
	No. examined	No. of microfilarial carriers (%)	Microfilarial density	SD	No. of microfilarial carriers (%)	Microfilarial density	SD
February 1985	171	47 (27.5)	3.3	9.0	52 (30.4)	1.8	3.0
April 1985	171	51 (29.8)	3.2	8.3	59 (34.5)	2.0	3.2

* For *L. loa*, $\varepsilon = 1.07$ and *t*-test value = 0.32. For *M. perstans*, $\varepsilon = 1.15$ and *t*-test value = 1.78. None of the comparisons were statistically significant.

The microfilarial load of the overall population also remained remarkably stable for both parasite species.

Table 2 shows the short-term durability of the study subjects, with 157 (91.8%) of 171 maintaining their *L. loa* status and 134 (78.4%) maintaining their *M. perstans* status. The *L. loa* status seemed to be more stable than that of *M. perstans* ($P < 0.0001$; by Fisher's exact test).

Figures 1 and 2 show that there is a significant relationship between individual microfilarial densities of both filaria species calculated in February and April of the same year ($R = 0.94$, $P < 0.001$ for *L. loa* and $R = 0.87$, $P < 0.001$ for *M. perstans*). The coefficients of the regression lines for transformed data did not differ significantly from the values expected for a relationship of type $y = ax + b$ (with a tending to 1 and b tending to 0). This indicates that the microfilarial densities were remarkably stable during the initial study period (total stability would be expressed by $y = x$). Thus, $a = 0.92 \pm 0.20$ and $b = 0.11 \pm 0.20$ for *L. loa* and $a = 0.81 \pm 0.16$ and $b = 0.19 \pm 0.18$ for *M. perstans*.

Long-term trend of microfilaremia

The percentages of subjects with microfilaria and their parasite densities remained stable in the population at the long-term followup, i.e., 3–4 years (Table 3).

The long-term stability of the microfilaremic status was demonstrated in most patients, with 77 (91.7%) of 84 subjects maintaining their *L. loa* status and 58 (69.0%) maintaining their *M. perstans* status (Table 4). As in the short-term followup, the stability of *L. loa* was significantly higher than that of *M. perstans* ($P < 0.0001$, by Fisher's exact test).

Because of the small number of subjects followed-up, there were no significant differences between sex and age relating to the gain or loss of infection (by sex, $P = 0.5$ for *L. loa* and 0.3 for *M. perstans;* by age, $P = 0.5$ for *L. loa* and 0.15 for *M. perstans*).

Over a period of several years (Figures 3 and 4), loiasis and mansonellosis showed stable individual microfilarial densities ($R = 0.79$, $P < 0.0001$ for *L. loa* and $R = 0.72$, $P < 0.01$ for *M. perstans*). The coefficients of the regression lines for transformed data did not differ significantly from values expected for a relationship of the type $y = ax + b$, with a tending to 1 and b tending to 0 ($a = 0.75 \pm 0.22$ and $b = 0.34 \pm 0.42$ for *L. loa* and $a = 0.65 \pm 0.28$ and $b = 0.16 \pm 0.20$ for *M. perstans*). Thus, at long-term followup, the individual microfilarial densities were stable.

DISCUSSION

The virtual impossibility of taking blood samples at fixed times is one of the major difficulties encountered in studies on filariases with periodic microfilaremia. Thus, at the earliest and latest sampling times, usually 10:00 AM and 3:00 PM, the level of *L. loa* microfilaremia is reduced by approximately 30% of its maximum value.[7] Such 24-hr variation suggests that correction factors should be introduced to take into account the time of sampling. However, the demonstrated

TABLE 2

Trend in the microfilaremic (mf) status of 171 subjects over a 2-month period

	February 1985	April 1985		*P**
		mf−	mf+	
Loa loa	mf−	115	9	1.8×10^{-25}
	mf+	5	42	
Mansonella perstans	mf−	97	22	5.6×10^{-11}
	mf+	15	37	

* By Fisher's exact test.

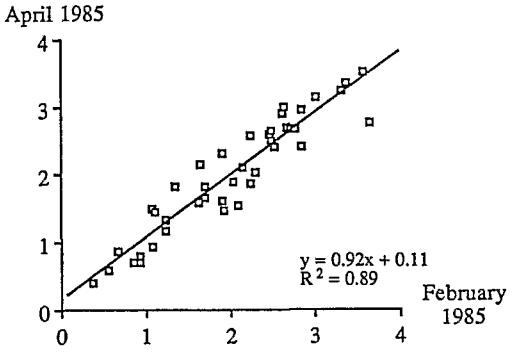

FIGURE 1. Trend in the *Loa loa* microfilarial densities, expressed as log (x + 1), in the blood of 42 microfilaria-positive subjects before and after a 60-day interval.

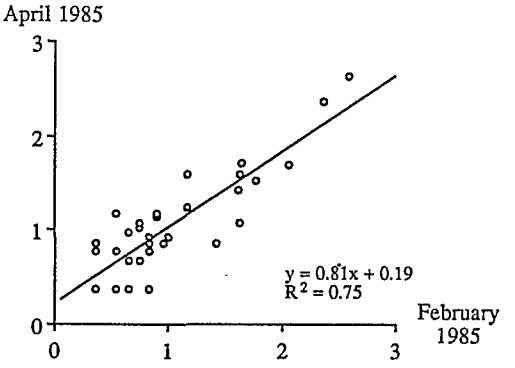

FIGURE 2. Trend in the *Mansonella perstans* microfilarial densities, expressed as log (x + 1), in the blood of 37 microfilaria-positive subjects before and after a 60-day interval.

absence of marked variation in quantitative microfilaremias over time, both in the short-term and long-term, allows us to assume that such a bias is of little importance. The durability of the microfilarial status demonstrated in this study both at short- and long-term confirms previous observations carried out after an interval of one year.[6] For loiasis, this durability suggests that the demonstration of microfilaremia is genetically controlled and, consequently, varies according to the individual. Changes in status are less frequent for *L. loa* (< 10% of the subjects) than for *M. perstans* (> 20% of the subjects). This difference may be related to the lower microfilaremia observed in patients with mansonellosis. Thus, the median microfilarial density (DMf 50) is of the order of 50 microfilariae/20 μl for *L. loa* and 5 microfilariae/20 μl for *M. perstans* in the population residing in the study area.[4] In both infections, changes in status were observed only in low-density carriers. An examination of a larger volume of blood detecting low levels of microfilaremia would have been expected to reveal fewer changes in status.[8]

The constancy over time of the average microfilarial load calculated for the whole study population demonstrates the remarkable quantitative stability of parasitic material available for the vectors. This overall stability is the consequence of the lack of variation of the loads at individual level. These data corroborate and explain the results of cross-sectional studies that showed that the DMf 50 remained stable in the various age groups of an adult population.[4] In studies on *Wuchereria bancrofti* filariasis in the Polynesian archipelago, Rosen also showed that microfilaremia remained stable in infected subjects retested three years after the initial examination.[9]

The dynamics of production of microfilariae in a host presenting stable peripheral microfilaremia is not well documented. However, such hosts represent a considerable proportion of the human population living in transmission areas.

TABLE 3

Trend in Loa loa *and* Mansonella perstans *microfilaremia over a 3–4-year period, showing the prevalence of microfilaria carriers and Williams' mean of microfilarial densities per 40 mm³ of blood with standard deviations, for the overall population studied**

		L. loa			*M. perstans*		
	No. examined	No. of microfilarial carriers (%)	Microfilarial density	SD	No. of microfilarial carriers (%)	Microfilarial density	SD
1985	84	31 (36.9)	3.7	8.6	34 (40.5)	1.9	2.8
1988/1989	84	32 (38.1)	3.8	8.4	38 (45.2)	1.7	2.1

* For *L. loa*, $\varepsilon = 0.37$ and t-test value = 1.11. For *M. perstans*, $\varepsilon = 0.78$ and t-test value = 1.28. None of the comparisons were statistically significant.

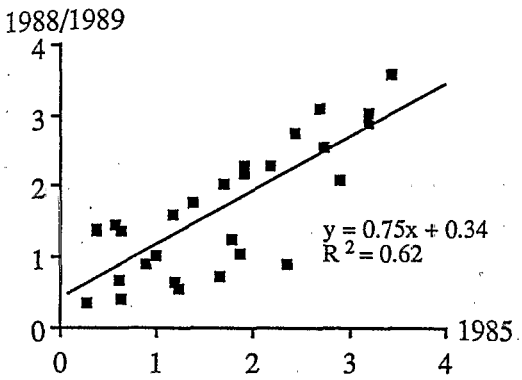

FIGURE 3. Trend in the *Loa loa* microfilarial densities, expressed as log (x + 1), in the blood of 28 microfilaria-positive subjects before and after a 3–4-year interval.

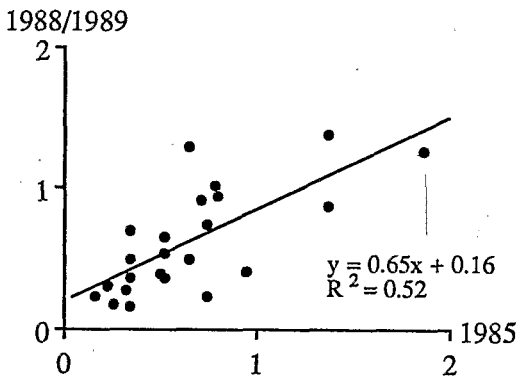

FIGURE 4. Trend in the *Mansonella perstans* microfilarial densities, expressed as log (x + 1), in the blood of 23 microfilaria-positive subjects before and after a 3–4-year interval.

No obvious relationship between the number of gravid females and the rate of microfilaremia has been established for *L. loa* in the simian host, as has been generally observed in other filarial infections.[6, 10, 11] During the period of stable microfilaremia, the fecundity of the female *L. loa* is high, and production has been estimated at approximately 10,000 microfilariae/day.[6] The factors that regulate the periodic release of microfilariae and contribute to the stability of parasitemia may be inherent both in the gravid females and in the host.[6, 10] Indeed, as described for other filarial infections, the definitive host may, as an immune defense reaction, reject increasing numbers of *L. loa* and *M. perstans* L3 infective larvae while being repeatedly inoculated.[12] This gradual decrease in the survival rate of filariae, which leads to a slow increase in the population of adult worms, might compensate for the decrease in fecundity and mortality of old females, thus causing a balance in the load of female worms. Other factors that may contribute to the stability of microfilaremia in individuals parasitized with *L. loa* and *M. perstans* are 1) the longevity of the adult filaria and the microfilaria,[13–15] 2) the regularity of transmission of both filariases in the study region,[16] and 3) the possibility that the acquisition of new worms and the fertilization of females in individuals who are already carriers may be facilitated, for example, by the impregnation of host tissue by sexual attractants of parasitic origin.[17]

Finally, the release of microfilariae by gravid females may merely compensate for their slow natural elimination. The demonstration of the considerable stability of the parasitic load in a population exposed for decades to repeated invasions of L3 larvae underlines the importance of continuous followup of parasitologic indices in a program for filariasis control.

TABLE 4

Trend in the microfilaremic status (mf) of 84 subjects over a 3–4-year period

	1985	1988/1989 mf−	1988/1989 mf+	P*
Loa loa	mf−	49	4	8.5×10^{-15}
	mf+	3	28	
Mansonella perstans	mf−	35	15	6.8×10^{-4}
	mf+	11	23	

* By Fisher's exact test.

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