REVIEW

Prevalences of *Loa loa* microfilaraemia throughout the area endemic for the infection

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Several cases of encephalopathy recorded in Cameroon since 1991 were in patients with very high, coincident, *Loa loa* microfilaraemias who had been treated with ivermectin for onchocerciasis. There was thus an urgent need to identify those areas where loiasis is hyperendemic, and where specific monitoring procedures should be developed if large-scale ivermectin treatment of onchocerciasis is to be implemented. In the present review, the available data on *Loa* endemicity are detailed and maps showing the prevalence of *Loa* microfilaraemia throughout the area endemic for the infection are presented. By superimposing these maps on those which show where onchocerciasis is meso- or hyper-endemic, it is now possible to identify several areas, in south-eastern Nigeria, southern and central Cameroon, the south of the Central African Republic, Equatorial Guinea, Gabon, and the north and west of the Democratic Republic of the Congo (ex-Zaire), where ivermectin treatment, although indicated, is most likely to lead to adverse reactions because of *L. loa* infections. Additional surveys, to delineate the areas highly infected with *L. loa* more accurately, are required.

Loiasis has for long been regarded as a moreor-less benign filariasis, and this, combined with the fact that its distribution area is limited to Central Africa, has meant that it has been relatively little studied. However, three reasons have recently led to a renewal of interest in loiasis. Firstly, it has been noted that in some regions it is the second or third most common reason for medical consultation, after malaria and pulmonary diseases (Boulesteix and Carme, 1986; Pinder, 1988). Secondly, it has been found that, as for Onchocerca volvulus, a single oral dose of ivermectin brings about a dramatic decrease in the load of Loa loa microfilariae, and even an improvement in some clinical signs related to the infection (Richard-Lenoble et al., 1988; Carme

et al., 1991; Paris et al., 1991; Chippaux et al., 1992; Martin-Prevel et al., 1993; Hovette et al., 1994; Gardon et al., 1997). Thirdly, since 1991, several cases of encephalopathy have been recorded in Cameroon in patients with very high, coincident, L. loa microfilaraemia who had been given ivermectin treatment for onchocerciasis (Chippaux et al., 1996; Boussinesq et al., 1997). The latter reason is all the more important because ivermectin-distribution programmes against onchocerciasis are currently being developed in many African countries, including some where loiasis is co-endemic. The objective of the present review is to update the previous reviews on the global distribution of loiasis (Rodhain and Rodhain-Rebourg, 1973; Sasa, 1976; Hawking, 1977), and to summarize the available data on the levels of endemicity

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Fonas Documentaire ORSTOM Cote: 8*11482 Ex: 1 recorded in the various endemic areas, in order to identify those areas where serious reactions might occur during large-scale, ivermectin treatment of onchocerciasis.

MATERIALS AND METHODS

The main sources of information were published papers and a number of theses reporting detailed epidemiological data on the prevalence of *L. loa* infection. In addition, data collected in four different areas of Cameroon (unpubl. obs.), especially in the Lékié division of Central province (where most cases of *Loa* encephalopathy after ivermectin treatment have been recorded) are reported here for the first time.

The age ranges of the subjects varied widely from one survey to another. To draw maps showing the prevalence of microfilaraemia in all the areas surveyed, it was necessary to standardize the available data. As all the subjects examined in many surveys were at least 5 years of age, the prevalence of Loa microfilaraemia in those aged ≥5 years was taken as the 'standard prevalence'. The previously unpublished data from Cameroon, on 3524 subjects aged \geq 5 years from 18 villages of the Lékié division (an area of degraded forest) and 3386 subjects of the same age from 17 villages of the Mbam division (an area of forest-savanna mosaic), were used to calculate the ratios of the prevalence in individuals aged \geq 5 years and that in subjects aged $\geq x$ years for each community. As, for a given value of x, the ratios were similar in both divisions and whatever the level of the prevalence in individuals aged ≥ 5 years, it was felt reasonable to apply them to all epidemiological situations. When the subjects in a previous survey also included children aged < 5 years of age, standard prevalence was calculated from the results by assuming that prevalence increased linearly between 0 and 5 years of age.

Three types of data were available: (1) prevalences at the village level; (2) prevalences obtained by combining the results of several neighbouring communities; and (3) prevalences for even wider areas, often defined by

the main town of the region. The latter data are especially common in old publications. These three types of data were combined on the maps, but different symbols were used so that they can readily be distinguished. In order to make the maps more legible, the results for several villages which are very close to one another and which were found to have similar endemicity were combined even when each village was surveyed separately; in each of such cases, the number of villages combined is given on the maps, so that a minimum of information is lost.

RESULTS

The result are summarised in three maps (Figs 1-3).

Angola

Loiasis is present in the north-western part of Angola, in Cabinda, Cuenza Norte, Zaire, Uige, and Luanda provinces (Casaca, 1967). No detailed data have been published on the prevalence of infection, but Hawking (1977) stated that 10% of the population probably harbour *Loa* microfilariae (mff) in Cabinda and Cuanza Norte, which are the most densely forested provinces. In contrast, no carriers of *Loa* mff were found by Pires *et al.* (1959) in the Lunda Norte province, in the north-east of the country.

Benin

The endemic area in Benin seems limited to the south-east and the level of endemicity is probably low even there. Among the 194 subjects of all ages examined in Ganvié by Pampiglione and Ricciardi (1971), only two carriers of *Loa* mff were detected. Loiasis has also been found in Pobé, where some individuals harboured > 2000 mff/ml blood (Klion *et al.*, 1991).

Cameroon

The level of endemicity in South Cameroon increases from west to east. Languillon (1957) reported prevalences of 19.0%, 20.0%, 27.0% and 31.5% in adults from the Kribi, Ebolowa,



Fig. 1. Prevalence of loiasis throughout the area endemic for the infection. The prevalences shown correspond to regions (squares), single villages (small circles), and groups of villages (large circles, with a number indicating the number of villages combined). Endemicity, expressed as the prevalence of *Loa* microfilaraemia in the population aged ≥ 5 years (Pmf), is shown as: \bigcirc or \square for Pmf = 0%; \bigcirc or \square for 0% < Pmf < 5%; \bigcirc or \square for $5\% \leq Pmf < 10\%$; \bigcirc or \square for $10\% \leq Pmf < 20\%$; and \bigcirc or \square for Pmf $\geq 20\%$. The limits of the areas shown in greater detail in Figs 2 and 3 are indicated. (+), Areas where *Loa* infection is present, but with unknown prevalence; (×), some of the important towns in the area; (•), village whose prevalence is indicated on Fig. 2 or Fig. 3; DRC, Democratic Republic of the Congo (ex-Zaire)

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Fig. 2. Prevalence of loiasis in Cameroon. The prevalences shown correspond to regions (squares), single villages (small circles), and groups of villages (large circles, with a number indicating the number of villages combined). Endemicity, expressed as the prevalence of *Loa* microfilaraemia in the population aged ≥ 5 years (Pmf), is shown as: $\bigcirc \text{ or } \square$ for Pmf = 0%; $\bigcirc \text{ or } \square$ for 0% < Pmf < 5%; $\bigcirc \text{ or } \square$ for $5\% \leq \text{Pmf} < 10\%$; $\bigcirc \text{ or } \square$ for $10\% \leq \text{Pmf} < 20\%$; and $\bigcirc \text{ or } \blacksquare$ for Pmf $\geq 20\%$. The limits of the areas shown in greater detail in insets A and B are indicated. (\times), Some of the important towns in the area; (•), village whose prevalence is indicated on inset A or B.



Fig. 3. Prevalence of loiasis in Congo, Equatorial Guinea, Gabon, and the Mayumbe area of the Democratic Republic of the Congo (DRC; ex-Zaire). The prevalences shown correspond to regions (squares), single villages (small circles), and groups of villages (large circles, with a number indicating the number of villages combined). Endemicity, expressed as the prevalence of *Loa* microfilaraemia in the population aged ≥ 5 years (Pmf), is shown as: \bigcirc or \square for Pmf = 0%; \bigcirc or \square for 0% < Pmf < 5%; \bigcirc or \square for 5% \leq Pmf < 10%; \bigcirc or \square for 10% \leq Pmf < 20%; and \bigcirc or \square for Pmf $\geq 20\%$. (\times), Some of the important towns in the area.

Sangmelima, and Yokadouma areas, respectively. Between 2% and 18% of subjects of all ages in nine villages in the Djoum area were found to be carriers (J. Gardon, unpubl. obs.).

Loiasis is also highly endemic in the Central province, especially in the forested areas south of the Sanaga River; a 30% prevalence was recorded in Ngat, near Mbalmayo (Mommers et al., 1994). In the Lékié division, Ripert et al. (1977) and J. Gardon (unpubl. obs.) examined seven and 79 communities, respectively (Fig. 2, inset A). On the whole, the prevalences were higher in the districts of Evodoula and Elig-Mfomo (where prevalence reached as high as 38% and was generally > 25%, and >10% of the adult population harboured >10 000 mff/ml blood) than in Obala and Sa'a. Ten of the 8546 subjects from the Lékié division who were aged ≥ 15 years harboured $>150\ 000\ mff/ml$; the existence of such high loads may explain why the incidence of serious reactions to ivermectin treatment is particularly high in this area. The level of endemicity is lower in the northern part of the Central province than in the southern. In the Mbam area, for example, which is a zone of forest-savanna mosaic, the prevalence rarely exceeds 20% (M. Boussinesq, unpubl. obs.) whereas much higher values were recorded in the Ntui (Ernould, 1993) and Ngoumé areas (B. Bouchité, unpubl. obs.), where the population density is low and where the forest is relatively dense.

In the Littoral province, Languillon (1957) recorded a 17% prevalence in adults from the Edéa area, Ripert *et al.* (1980) found prevalences ranging between 5.2% and 21.7% in the total population of eight contiguous communities located near Douala in the Wouri estuary; and Wang Moukatte (1983) recorded an overall prevalence of 9.6% in 345 subjects of all ages from seven areas of the Nkam Valley.

Extensive studies on the transmission of loiasis were conducted by Kershaw (1951) and Kershaw *et al.* (1953) in 11 villages, in the South-West and North-West provinces, which were in the rain-forest, on the forest fringe, or in the mountain grasslands. Brengues *et al.* (1975) and J. Kamgno (unpubl. obs.) surveyed 12 and 38 villages, respectively, in the West province, and Le Bras and Traoré-Lamizana (1978) investigated four communities in the Fontem and Nguti districts (North-West province). Together, these studies showed that the prevalence of Loa microfilaraemia was >20% in the forested areas of the South-West province and the southern part of the North-West province (Fig. 2, inset A). Conversely, Loa microfilaraemias were relatively rare in the West province and the eastern part of the North-West province, prevalences generally being no higher than 10%. Kershaw (1955) indicated that infection with Loa was virtually absent in the Limbe division and around the mouth of the Mungo River, near Tiko.

In the East province, Languillon (1957) recorded a 31.5% prevalence in the adults of the densely forested Yokadouma area, and Haumont *et al.* (1992) found prevalences between 9.6% and 13.5% in the total population of Colomines and two neighbouring villages, located in a savanna area in the Kadei Valley.

The level of endemicity is generally very low in the Adamaoua, North and Far-North provinces, which are covered by savanna. Although Languillon (1957) failed to find a single Loa microfilaraemia in the Meiganga, Ngaoundéré, Bénoué and Diamaré regions, Anderson et al. (1974) demonstrated that loiasis was present, albeit with low prevalence, in some areas of the North province. Boussinesq et al. (1994) recorded high prevalences (>20% of the population aged ≥ 5 years) in three of 13 villages examined in the Faro-Déo area (Fig. 2, inset B) but the microfilarial loads they recorded were very low, and not a single Chrysops was collected in the study communities. Of 762 adults examined by Lochouarn (1990) in the Yagoua area, four (none of whom had ever travelled out of the Far-North province) had Loa microfilaraemias.

Central African Republic (CAR)

Very few data are available on the endemicity in the CAR (Fig. 1). Ouzilleau (1913) recorded a 16% prevalence in 1500 subjects aged ≥ 10 years in the Mbomou division (Ouango, Bangassou and Rafai areas), in the south of the country. In the same province, Testa *et al.* (1994) recorded a 11.2% prevalence in 812 individuals aged ≥ 10 years.

No Loa mff were found in any of the 100 subjects examined by Brumpt *et al.* (1972) in two villages in the north of the country, near the boundary with Chad.

Chad

Loiasis is very rare in Chad (Fig. 1). It seems to be absent in the Mongo and Ndjamena areas (Buck *et al.*, 1970; Shabelnick and Chechugo, 1970) but Bouilliez (1916) recorded a 2.2% prevalence in the area of Sahr, and Buck *et al.* (1970) found several patients with *Loa* mff in Boum Khébir, Ouli Bangala and Ouarai (giving prevalences in the total populations of 0.4%, 1.2% and 8.4%, respectively). Although Buck *et al.* (1970) did not catch any *C. silacea* or *C. dimidiata* they did collect one specimen of *C. longicornis*, in Ouli Bangala.

Congo (Republic of Congo)

The most detailed data available on loiasis in Congo relate to the Lekoumou region, in the Chaillu forest area, where Noireau *et al.* (1989, 1990) and Noireau and Pichon (1992) examined six villages (Fig. 3). In three of the communities, the prevalence of *Loa* microfilaraemia in the total Bantu population exceeded 20% and was higher than in the local Pygmies, although the median microfilarial loads were similar in the two ethnic groups (800–3100 mff/ml in the Bantu v. 150–2250 mff/ml in the Pygmies).

Based on information collected in health centres in Brazzaville and the Pool region, Carme *et al.* (1986) reported prevalences of 15%-20% in two villages north-west of Brazzaville (Mayama and M'Paya Kibouende) and only of <1% in N'tombo Manyanga.

Data on the other areas of Congo are scarce. Carme *et al.* (1986) reported a 13.3% prevalence in 60 adults from M'vouti (in the east of Kouilou region) and a 2.3% prevalence in 86 adults from Impfondo district (Likouala region), in the swampy forested area of northeastern Congo (Fig. 1).

Democratic Republic of the Congo (ex-Zaire)

Loa mi-The highest prevalences of crofilaraemia in the Democratic Republic of the Congo (DRC) appear to be in the Mavumbe area, in the most western part of the Bas-Zaire province (Fig. 3). Amongst the 32 villages surveyed in this area by Fain et al. (1974), six showed prevalences (in adults) above 30%, and 14 others had prevalences between 25% and 30%. The arithmetic mean microfilarial load in the microfilaraemic patients exceeded 8000 mff/ml in 15 of the 32 villages surveyed. The less affected villages (i.e. those with prevalences <15%) were located in the southern and less densely forested part of the region. These results were in accordance with those obtained in the Inga area by Maertens et al. (1971). Fain et al. (1974) also reported that, of the 547 microfilaraemic patients who each provided two blood samples, one during the day and one during the night, 16 were found to be microfilaraemic only at night.

Information on *Loa* in the rest of the Bas-Zaire province is scarce. Fain (1969) indicated that 'loiasis is endemic along the Congo-Zaire River and its affluents, between Matadi and Kasangulu, near Kinshasa. However, the levels of endemicity in this area seem much more variable than in the Mayumbe area'.

In Bandundu province, Fain (1947) surveyed 65 communities located south-west, south, and south-east of the town of Bandundu. He found only 11 carriers of *Loa* mff among the 2510 adults examined and assumed that these 11 might have been infected outside the study area because (1) no *Chrysops* were found in the study area and (2) several local cases of *Loa* infection had been recorded in patients coming from the Kikwit region.

Prevalence in the northern part of the Equateur province was evaluated by Dujardin *et al.* (1982). Although the overall prevalence in the nine villages they examined in the Lua Valley was < 5%, a 30.7% prevalence was recorded in one village in the Bosobolo forest block. The arithmetic mean microfilarial load

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in all the microfilaraemic subjects encountered was 1920 mff/ml.

In the south-western part of Equateur province, Chardome and Peel (1949) found prevalences of 11% in the population of Mbandaka and of 8% in prisoners from the whole of Equateur province, and also examined > 8000 subjects in 72 communities located in the vicinity and south of Mbandaka. Fain (1969), reporting the results of the Mbandaka survey, said that 'the prevalences ranged between 2% and 10% in most of the villages, prevalences between 11% and 20% were rarer, and prevalences > 30% were exceptional'. Fain et al. (1969) examined adults in 10 villages of the Boende area, and found Loa infection in only seven of them, with prevalences generally < 5%.

In the Haut-Zaire province, Fain (1969) stated that the most affected area was the Uélé district, where levels of endemicity were probably similar to those recorded in the Mayumbe area. Fain (1969) reported that loiasis was also endemic in the Kisangani and Kibali-Ituri districts, whereas the infection seemed to be absent in the Haut-Ituri district. Low (1927) examined many cases of loiasis from the Niangara and Isiro areas, in the northern part of the province. Two studies, both on Pygmies, have also been performed in the eastern part of the province: Price et al. (1963) reported prevalences of 0% and 1.2% in patients examined in two dispensaries near Bunia; and Pampiglione et al. (1979) surveyed 11 camps in the Mambasa area and found prevalences of <15% in four of them and of >70% (up to 97%) in the others. [The latter prevalences are extraordinarily high; in endemic areas in general only one in three subjects infected with Loa has a detectable microfilaraemia (Pinder, 1988).] Few relevant data are available from the western part of the Haut-Zaire province; according to Browne (1960), loiasis exists in the villages located on the banks of the Congo-Zaire River, to the east and west of the Lomami River.

There is little information on loiasis in Kivu province. Peel *et al.* (1952) reported a 3.2% prevalence in the total population of Bukavu and took this low value to indicate that *Loa*

was not transmitted locally in this part of the province. In contrast, Fain (1969) assumed that loiasis was endemic in the South-Kivu and Maniema regions, the endemicity in the Maniema region area later being confirmed by Gryseels *et al.* (1985), who recorded a 10.9% prevalence in the combined, total populations of two villages.

Loiasis is probably extremely rare in the south of the DRC. Fain (1969) indicated that neither *Loa* infection nor the *Chrysops* vectors have been found in the Katanga (ex-Shaba) province. He also assumed that loiasis was probably absent in most of the Kasai Occidental province (because the *Chrysops* vectors had never been found in this area) while indicating that the infection might exist in the forested northern part of the province, where the conditions probably favour the survival of *Chrysops* spp.

Equatorial Guinea

When Vila Montlleo (1990) examined 829 subjects aged ≥ 10 years from eight villages in the Niefang district of Equatorial Guinea (Fig. 3), he found *Loa* mff in 27% of them and an arithmetic mean microfilarial load in the microfilaraemic patients of 1020 mff/ml blood.

Gabon

Loiasis in Gabon has been extensively investigated, systematic surveys showing that Loa infections occur throughout the country (Fig. 3). In the east, in Haut-Ogooué province, Languillat et al. (1978) examined 12 villages, Van Hoegaerden et al. (1987) investigated another six and Richard-Lenoble et al. (1980) studied patients in Mounana hospital. The level of endemicity observed was high in the whole region, but the highest prevalences (20% in subjects aged ≥ 9 years) were recorded in the villages located east of Okondja; in these communities, the arithmetic mean microfilarial density in the microfilaraemic patients aged ≥ 9 years was 3260 mff/ml (Van Hoegaerden et al., 1987), and the maximum load recorded was 86 200 mff/ml.

The endemicity in the Ogooué-Lolo province was documented by Languillat *et al.* (1978), who examined nine villages, and by Richard-Lenoble *et al.* (1985). The prevalences were high in the whole province, > 40% of the adults in some villages harbouring *Loa* mff. Languillat *et al.* (1978) showed that, on the whole, the levels of endemicity were higher in the Ogooué-Lolo province than in the Haut-Ogooué, and attributed this difference to the fact that Ogooué-Lolo is densely forested whereas Haut-Ogooué is partly covered by the savanna of the Batéké Plateau.

Galliard (1932) and Richard-Lenoble et al. (1980, 1985) investigated Loa infection in the Ngounié and Nyanga provinces. The prevalences were generally lower in the study communities of the Ngounié Valley itself (Lébamba, Fougamou, Sindara) than in those located in the mountainous and forested areas north-east (Mimongo) and south-west of the valley (between Tchibanga and Ndendé); in the latter areas, > 20% of the total population were carrying Loa mff. The levels of endemicity in the Nyanga province were generally lower than those recorded in the Ngounié province. Prevalences of 3.4% and 6.3% were found in the Tchibanga savanna (Galliard, 1932) and in the Moabi area (Richard-Lenoble et al., 1985), respectively. However, prevalence seems to vary greatly from village to village in this province, since Richard-Lenoble et al. (1985) found that 23% of the population of Tchibanga were microfilaraemic for Loa.

Loa microfilaraemias in the Ogooué-Maritime and Moyen-Ogooué provinces have not been investigated very much. The results of Galliard (1932), who recorded an overall prevalence of 8.4% in several villages located in the forested plain of Ogooué-Maritime, indicate that the level of endemicity is probably low in this province. Loiasis is probably relatively frequent in Moyen-Ogooué, where a prevalence of 22% was recorded in 247 subjects living 'between Ndjolé and Booué' (Richard-Lenoble *et al.*, 1985).

The data presented by Richard-Lenoble *et al.* (1980) indicate that loiasis is highly endemic in the Estuaire province. An overall

prevalence of 18% was recorded in those who attended the health centres of Libreville, 18.9% of the total population of Ntoum showed *Loa* mff, and 27.3% of young adults in the timber yards near Pointe-Denis had detectable *Loa* microfilaraemias.

In the north-east quadrant of Gabon (i.e. the provinces of Ogooué-Ivindo and Woleu-Ntem), Ringenbach and Guyomarc'h (1914) reported a 19.6% prevalence in 949 subjects of all ages living 'between Ivindo River and Atlantic Ocean' and Richard-Lenoble *et al.* (1985) recorded prevalences of 28.2% in the Makokou area and of 23.9% in Woleu-Ntem province; these observations indicate that loiasis is highly endemic in this part of the country.

Nigeria

The most affected areas of Nigeria are south of latitude 6°N (i.e. in the area around the Niger delta and between the delta and the boundary with Cameroon; Fig. 1). Kershaw (1951) recorded a 22.2% prevalence in the total population of the Sapele rubber plantation, in the western part of the delta, and Duke and Moore (1961) recorded a 12.9% prevalence in the same area, with a geometric mean microfilarial density of 600 mff/ml in the microfilaraemic patients. The endemicity in the eastern part of the delta was studied by Udonsi (1986) and Arene and Atu (1986). Udonsi (1986) examined persons of all ages in four villages of a forest and mangrove area (Ahoada, Degema, Opobo and Okrika-Eleme) and found a prevalence of > 30% in three of the villages. In contrast, Arene and Atu (1986) examined 1674 subjects from the Bori area and failed to find a single Loa microfilaraemia. The endemicity in Imo state (i.e. north-west of the delta) was investigated by Udonsi (1988); prevalences between 10% and 15% were recorded in three of the seven villages surveyed; in the four others, the prevalences were < 10%.

Few relevant data are available from the most south-eastern part of Nigeria, but Hinz (1968) showed that loiasis was one of the main causes of consultation in Cross River and Akwa Ibom states. Emeribe and Chuks Ejezie (1989) found a prevalence of only 1.3% in 480 blood donors in Calabar, and one may assume that such a low prevalence is due to the fact that the individuals examined lived almost permanently in this town.

The level of endemicity between the Niger delta and the boundary with Benin is relatively low (Hinz, 1968). Cowper and Woodward (1961) detected only 38 carriers of Loa mff (0.7%) among the 5150 patients they examined at the University College Hospital in Ibadan. In the same town, Ngu and Folami (Cowper, 1967) reported a 4.9% prevalence amongst 1340 hospitalized patients and Akinboye and Ogunrinade (1987) reported that 3.5% of local blood donors had Loa microfilaraemias. Low prevalences were also recorded in the vicinity of Ibadan: Cowper and Woodward (1960) found only four individuals with Loa mff amongst 100 employees of the Moor plantation, and Gilles (1964) reported a 4.1% prevalence in Akufo, a village close to Ibadan.

Extensive surveys, principally of schoolchildren, were performed by Ogunba (1971, 1972) in south-western Nigeria. Between 0% and 10.2% of the children examined in 20 villages in the Ijebu division (between Ibadan and Lagos) had Loa microfilaraemias; prevalences in adults in the three villages in which > 30adults could be examined were 6.0%, 10.1% 14.8%. Ogunba (1972) and examined >10000 children and 1380 adults from sites throughout the whole of what was Western state, and gave separate results for the villages in forest, savanna and mangrove areas. When one extrapolates the data recorded in the adults, it appears that the prevalences in the whole populations did not exceed 5% in the savanna areas, and ranged between 5% and 10% in the forest areas.

Two surveys have been carried out in areas located north of 8°N. Ufomadu *et al.* (1991) examined 10 villages in the Jarawa River Valley, in Plateau state; patients with *Loa* mff were recorded in four of the communities, including one where the prevalence in subjects aged ≥ 13 years reached 12.4%. Akogun (1992) examined nine contiguous villages in Mutum Biyu district (Gongola state), and recorded prevalences between 0.9% and 5.2% in the total populations, although he failed to find *Chrysops* in his study area.

Rwanda

Fain (1969) indicated that, despite the existence of the potential vector *C. distinctipennis*, he never found any cases of *Loa* infection during systematic surveys in Rwanda. He suggested that this absence was because (1) *C. distinctipennis* was mainly zoophilic, and (2) the relatively low temperatures in Rwanda (a mountainous country) hampered the development of *Loa* in local *Chrysops*.

Sudan

Cruickshank (1936) and Woodman and Bokhari (1941) were the first to demonstrate that loiasis is endemic in south-western Sudan, between latitudes 4° and 6°N, and west of longitude 30°E. Some 15% of the population in this area had Loa mff and the periodicity of the local Loa mff was not diurnal (Woodman and Bokhari, 1941). The role of the various potential vectors of Loa in transmitting the parasite in Sudan has been controversial (Woodman and Bokhari, 1941; Woodman, 1949, 1958; Lewis, 1953; Kirk, 1957). However, C. silacea is probably the main vector, because the area endemic for loiasis is limited to the distribution area of this species (Lewis, 1953).

Uganda

Most of the arguments for the existence of loiasis in Uganda are based on examinations of patients presenting with a specific ocular syndrome, called 'Kampala eye worm', which consists of nodules in the bulbar conjunctiva, oedema of the evelids, and occasionally proptosis. Cases of Kampala eye worm have been reported from many parts of Uganda, particularly Kampala, Mbale, Tororo and Masaka areas (Nnochiri, 1972; Poltera, 1973; Hawking, 1977). Baird et al. (1988) examined eight patients with this condition, including five from Uganda, and found that Mansonella perstans was the cause in five of them, a 'Wuchereria bancrofti-like worm' was the cause in another, and an unidentifiable worm the cause in the other two. However, the findings

of Poltera (1973) indicate that L. loa can also cause the condition. Arguments for the existence of loiasis in Uganda were given by Price (1961), who recorded seven cases of Loa infection out of > 100 subjects examined in Toro district, and indicated that two cases of loiasis were found on examination of autopsy material collected in patients from Lengo and Mengo districts. Ongom (1974) reported two cases of loiasis in Uganda, although these were both immigrants from southern Sudan. Infected patients in Uganda low microfilaraemias (E. Nnochiri, had unpubl. obs.) and Poltera (1973) suggested that this was because of the relatively low temperatures in Uganda (which may decrease the number of mff in the peripheral blood) or because of nocturnal periodicity of the Loa mff in the country.

Other Countries

Several authors have reported cases of Loa infection in countries west of Benin. Gordon ct al. (1950) presented a map which indicated such cases, and Hawking (1977) stated that Loa 'probably occurs' in Guinea, Liberia, and Ghana. The point is, however, controversial. Rodhain and Rodhain-Rebourg (1973) simply acknowledged that the western limit of the distribution area of Loa is difficult to define, although they concluded that Loa does not exist in the forest block which extends from Guinea to Ghana. They based this conclusion on the facts that: (1) no autochtonous case of Loa infection has been recorded during surveys in this area, which involved several thousand subjects in total (Thiroux, 1912; Poindexter, 1950; Pfister, 1954; Burch and Greenville, 1955; Thomas, 1958), and (2) C. silacea and C. dimidiata do not exist in this block (except in Ghana), and the only potential vectors in the area are C. distinctipennis and C. longicornis, whose vectorial capacities are low. Rodhain and Rodhain-Rebourg (1973) assumed that some of the cases of loiasis reported in West Africa corresponded to misdiagnosis of patients with heavy W. bancrofti infections and the others may have acquired their infections while working in countries east of Benin.

In Zambia, Buckley (1946) indicated that *Loa* mff were found in the blood of six subjects from Mankoya, Balovale and Senanga.

DISCUSSION

The main objective of this review was to identify the areas where large-scale distributions of ivermectin, for onchocerciasis control, should include careful monitoring procedures because of the risk of occurrence of Loa encephalopathy post-treatment. At the individual level, this risk is related to the intensity of infection with L. loa, and Chippaux et al. (1996) have estimated that the threshold value above which this risk exists is about 30 000 Loa mff/ml. Within each community, the proportion showing such considerable loads is related to the mean microfilarial density in the community. As very few published surveys on loiasis have included measurement of the microfilarial load in the community, it is currently impossible to identify the areas at risk on the basis of this indicator. However, assuming that there is a relationship between the intensity and the prevalence of infection, an alternative method to delineate the regions at risk would be to use prevalence. Despite the lack of detailed studies describing the pattern of any relationship, we propose that all the areas where the prevalence of Loa microfilaraemia exceeds 20% should be regarded as at-risk if mass distribution of ivermectin is to be implemented. Prevalences of this magnitude appear to occur in Nigeria (south of latitude 6°N), in the Central province of Cameroon, in continental Equatorial Guinea, in most of the provinces of Gabon (except Nyanga and Ogooué-Maritime), in the Lekoumou region of Congo, and in the Mayumbe area in the DRC. Although little information is available from the Mbomou division in the CAR or the Haut-Zaire province and the northern part of Equateur province in the DRC, the levels of endemicity may be also very high in these areas.

In principle, mass treatment with ivermectin should be limited to the areas where onchocerciasis is meso- or hyper-endemic. Consequently, it should be possible to identify the areas at risk of ivermectin-induced encephalopathy by superimposing the distribution maps of onchocerciasis and loiasis. The distribution of onchocerciasis in Central Africa has already been reviewed (Crosskey, 1981; Boussinesq, 1991; Fain, 1991) and maps of the distribution, including levels of endemicity, should soon be available for all the African countries where the disease is endemic, the products of a rapid assessment method in which the prevalence of nodules is measured in adult males (Taylor et al., 1992; Ngoumou et al., 1994; Macé et al., 1997). In contrast, much more information has to be collected before similar maps can be produced for loiasis, and before the areas at risk of ivermectin-induced encephalopathy can be delineated in detail. However, the available data do indicate that such areas appear to be restricted to several regions: some areas of Cameroon (Sanaga, Dja and Ntem Valleys), the CAR (Mbomou, Lobaye and Sangha-Mbaéré divisions), Equatorial Guinea, Gabon (Fougamou-Sindara, Lebamba and Makokou areas and the Ogooué Valley, especially near Lastourville), Nigeria (the forested parts of the Cross River, Abia, Imo, and Delta states), and some areas of the DRC [Haut-Zaire province (especially the Kisangani area, the Ituri Valley, and the left bank of Uélé River) and parts of the Equateur and Bas-Zaire provinces (especially the Mayumbe area)]. The total population of all these areas at risk probably exceeds 1 million. Additional surveys should

be carried out urgently in order to determine whether the high prevalences of loiasis recorded in these regions are associated with high microfilarial loads. These should be completed before the implementation of mass treatment with ivermectin. The high Loa microfilaraemias recorded in the Sanaga Valley in Cameroon probably exist in other areas. They have been detected in the Mayumbe region, where many cases of Loa encephalopathy occurred after treatment with diethylcarbamazine (Fain, 1978). As two probable cases of serious reactions to ivermectin treatment have recently been reported in the CAR (André, 1996), attention should perhaps be focused on the areas endemic for loiasis in that country. At present, the only means of determining the intensity of Loa infection in an individual or a community is the classical one of microscopical examination of standardized blood smears. As this method is too time-consuming to be used routinely, an alternative means of assessing Loa microfilaraemias, at both the individual and community level, is required. Until such a method has been developed, the classical method must be applied to samples of the communities located in those areas where loiasis is suspected to be highly endemic.

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