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Leishmaniasis in Cameroon and neighboring countries: An overview of current status and control challenges

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ABSTRACT

Leishmaniasis causes the ninth largest disease burden among infectious diseases but remains a very neglected tropical disease. Although the disease is endemic in Cameroon and some neighboring countries, data on its epidemiology are very scanty. The present review summarizes the available information on leishmaniasis in the central region of Africa. According to available records, Cameroon, Chad and Nigeria have been identified as endemic foci of both cutaneous (CL) and visceral leishmaniasis (VL). In addition, the phlebotomine vectors of leishmaniasis have been reported in these three countries and also in Congo and the Central African Republic. Although Gabon, Central African Republic, Equatorial Guinea and Congo are all situated next to the above leishmaniasis-endemic countries and are characterized by similar landscapes and vegetation, they lack published reports of autochthonous cases of leishmaniasis. Considering that many cases of the disease might remain unreported, it might not be an overstatement to recommend that research should be carried out in Gabon, Equatorial Guinea, Central African Republic and Congo to identify cases of leishmaniasis (CL and/or VL), the parasite and vector species, and the mammalian reservoir host. This review updates data on leishmaniasis and its insect vector in the geographical region of Central Africa. Such updates are basic requirement for the development of successful control programmes in individual countries and the whole region. In order to address the shortcomings identified in the present review, the authors recommend training of more scientists in leishmaniasis epidemiology in the region that should be accompanied by necessary funding. This training must be multidisciplinary and include development of laboratory and field skills for studies of the parasite, the vector, the reservoir, the vegetation and the soil in potential endemic foci. In addition, prospective studies involving geographers and other experts should develop a disease risk map of the Central Africa region.

1. Introduction

Leishmaniasis is a neglected vector-borne disease (Telda et al., 2018) caused by obligate intracellular protozoans of the genus *Leishmania* that affect the mammalian reticuloendothelial system (Poulaki et al., 2021). Parasites are mainly transmitted by the bites of female phlebotomine sand flies of the genera *Phlebotomus* and *Lutzomyia*, in the Old and New Worlds, respectively (Dondji, 2001; Dawit et al., 2013). Although there is no strong evidence of sand flies of the genus *Sergentomyia* transmitting human leishmaniasis, *Leishmania tropica*, an agent of cutaneous leishmaniasis, has been detected in *Sergentomyia* sand flies from a cutaneous leishmaniasis focus in Ghana (Nzelu et al., 2014). Previous studies have indicated a potential role of *Sergentomyia* sand flies transmitting leishmaniasis (Mutinga et al., 1994). Using ecological, parasitological and molecular evidence, Senghor et al. (2016) provided some evidence on the possible transmission of *L. infantum*, the causative agent of visceral leishmaniasis in Senegal, by *Sergentomyia* sand flies (*Se. dubia* and *Se. schwetzi*). The potential role of *Sergentomyia* sand flies is supported by detection of human blood meal (Tateng et al., 2018) and *Leishmania* DNA and/or parasites (Maia and Depaquit, 2016) in several species of this genus. Consequently, *Sergentomyia* sand flies continue to be considered as a potential vector of leishmaniasis. In addition, biting midges in the genus *Culicoides* are now incriminated in *Leishmania* transmission (Slama et al., 2014; Rebêlo et al., 2016; Becvar et al., 2021). In humans, the disease can also be transmitted occasionally through non-vector routes including blood transfusion, congenital, laboratory (Patel & Shah, 2008),

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and needle sharing by intravenous drug users (Cruz et al., 2002).

More than 20 different species of *Leishmania* are known to cause disease in humans with varying degrees of pathology (Yemeli et al., 2021; McNolty et al., 2021). There are three major clinical forms of the disease: cutaneous, mucocutaneous and visceral (Patel & Shah, 2008). Cutaneous leishmaniasis (CL) is a less severe but the most prevalent form of the disease with usually self-healing ulcers. On the contrary, visceral leishmaniasis (VL) is the most severe form of the disease resulting in 100% mortality of infected patients if not treated (Dondji et al., 2005). Leishmaniasis is reported in 98 countries worldwide with an estimated 700,000–1.2 million new cases annually, and more than 350 million people at risk of acquiring the disease (Telda et al., 2018; Palma et al., 2021). The incidence of CL is *c.*1 million while that of VL is 50,000–90,000. About 20,000–40,000 deaths are attributable to the disease each year (Telda et al., 2018). Leishmaniasis is estimated to cause the ninth largest disease burden among infectious diseases. However, the disease is largely ignored in discussions of tropical disease priorities, hence it is listed among the most neglected diseases (Alvar et al., 2012). In countries of the sub-Saharan Africa, for example, the disability and the number of CL cases are largely underestimated probably because the disease is understudied. The passive epidemiological surveillance system that prevails in these countries leads to the patchy data from the region (Sunyoto et al., 2018). The therapeutic tools against leishmaniasis are very limited (Almeida & Santos, 2011). Many researchers have focused their studies for the development of an appropriate *Leishmania* vaccine; nevertheless, a small fraction of them has been found as a promising approach for prevention of leishmaniasis (Moafi et al., 2019). It should be noted that naturally acquired immunity is protective especially against CL (Dondji, 1999). However, cross-protection between *Leishmania* species is problematic due to potential cross-reactive antibody-dependent disease enhancement. A number of studies have examined exposure to *Leishmania major*, agent of CL for protection against *L. infantum*, agent of the fatal VL. However, reports have recorded disease exacerbation when mice are primed with self-healing dose of *L. major* and challenged with *L. infantum* (Nation et al., 2012; McNolty et al., 2021).

Data on leishmaniasis in the central Africa region are scarce. Recently, Demba et al. (2021) published a systematic review on visceral leishmaniasis in the region. However, this review did not include the cutaneous form of the disease and Nigeria, an important endemic country near Cameroon. The first cases of leishmaniasis reported in Cameroon were in 1930s (Hervé, 1937), and today both CL and VL have been reported in many regions of the country (Dondji, 2001; Dondji et al., 2001; Ngouateu et al., 2012; Tangie et al., 2017).

In the present paper, we provide a review of the available data on leishmaniasis in Cameroon and neighboring countries, and an overview of control challenges with potential avenues to address the knowledge gaps in this geographical area. The literature search was conducted mainly in the Google Scholar, Medline and PubMed databases including the following terms: leishmaniasis, sand fly, *Phlebotomus* and *Leishmania*. These terms were each time associated with Central Africa, Cameroon, Gabon, Nigeria, Chad, Central African Republic, Congo, Equatorial Guinea. Languages used for the search were English and French.

2. *Leishmania* spp. life-cycle

The life-cycle of *Leishmania* spp. (Fig. 1) is simple and involves two stages without sexual reproduction in both the mammalian host and the insect vector. However, studies have shown evidence for hybridization of *Leishmania* species in sand flies and sexual reproduction of the parasite in

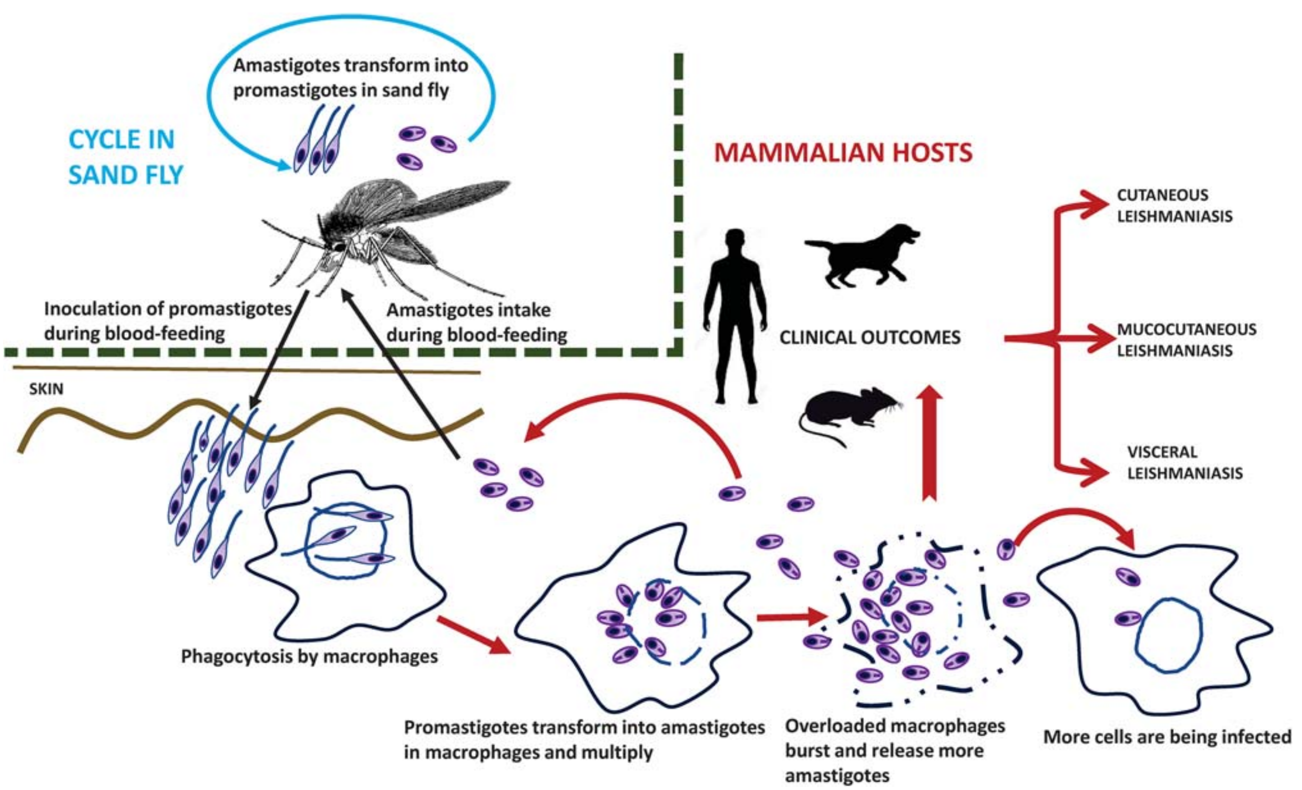

Fig. 1. *Leishmania* life-cycle.

the insect vector (Rogers et al., 2014). In the two-stage cycle, the amastigote (ovoid, non-motile, intracellular stage), resides inside the reticuloendothelial cells such as macrophages of the vertebrate host, and the promastigote (elongated, flagellated, motile, extracellular stage), replicates in the gut of the sand fly. When the vertebrate host is bitten by the infected female sand fly, the vector transfers the promastigotes (Patel & Shah, 2008). Upon entry, the promastigote loses its flagellum and multiplies within the cell potentially overloading it. In most cases, overloaded infected cells lyse, releasing amastigotes that will infect additional cells. During blood-feeding on infected vertebrates, female sand flies ingest amastigotes within macrophages from blood or skin that will transform into promastigotes (Despommier et al., 2017).

3. History of leishmaniasis in Cameroon

Cameroon is a country situated in the Gulf of Guinea between 1–13°N and 8–17°E. The country has a surface area of 475,650 km^2 and a population density of 40.8 inhabitants/km^2 (Kamga et al., 2012).

Localities where visceral leishmaniasis (VL) has been reported are: Yaoundé (Center Region), Kousseri, Gawar (Far North Region) (Deniau et al., 1986; Kaptué et al., 1992; Dondji et al., 2001). Places with reported cutaneous leishmaniasis (CL) cases include Mokolo, Logone Birni, Mora, Waza, Gawar, Goulfey (Far North Region), Garoua (North Region), Fontem (South-West Region) (Dondji et al., 2001), Kumbo (North-West Region) (Tangie et al., 2017). Phlebotomine sand flies have been collected in Bafia, Yaoundé (Center Region), Douala (Littoral Region), Garoua, Mokolo, Logone Birni, Kousseri (Far North Region) (Dondji et al., 2000; Dondji, 2001). Currently, in Cameroon, Mokolo is considered as a major focus of CL while Kousseri is a VL focus (Dondji, 2001).

The first cases of leishmaniasis (overall 326) were recorded in Garoua and its surroundings in the 1930s (Hervé, 1937). Rageau (1951) mentioned that the vector was likely *Phlebotomus roubaudi*. It should be noted that *Ph. roubaudi* was later reclassified as *Ph. duboscqi* (Abonnenc, 1958). Later, Rageau & Adam (1953) collected sand flies in Evoudoula (Center Region). Nevertheless, in Mokolo, a current important focus of CL, the first cases were reported in the early 1970s (Djibrilla et al., 1979; Dondji, 2001). Djibrilla et al. (1979) undertook a prospective study between December 1975 and January 1976 and reported 58 cases of CL in Mokolo.

In 1979, a suspicious case of VL was described in Gawar (Desjeux, 1991). In 1986, Deniau et al. (1986) provided the first parasitological confirmation of VL (kala-azar) in a young girl in the south part of the country but who previously lived in Kousseri (Far North Region). In 1992, Kaptué et al. (1992) confirmed 13 cases of VL amongst which 11 from Kousseri (Far North Region), two from Yaoundé (Center Region), and one from Fontem (South-West Region). One of the patients in the latter study was co-infected with HIV. In the late 1990s, Dondji et al. (2001) conducted a sero-epidemiological survey among schoolchildren in Kousseri and reported a 4% seroprevalence of VL in the area.

Despite reports of CL cases in Cameroon, it was until late 1990s that the first identification of one of the causative agents (*L. major*) of the disease was carried out by Dondji et al. (1998). The parasite strain isolated from a patient in the Mokolo focus of the Far North Region was inoculated into mice in the field, and following culture in the laboratory, it was characterized using the isoenzyme profile as *L. major* zymodeme MON-26 (Dondji et al., 1998).

In 1996, a study was carried out to evaluate leishmanin skin test positivity among school children in the Mokolo focus and registered a high skin positivity rate of 90.5% among children tested, with the diameter of the induration varying between 5 and 28 mm (Dondji, 1997, 1999). Positivity to the leishmanin skin test reflects exposure to the parasite and development of cell-mediated immunity (Carstens-Kass et al., 2021). The high positivity rate recorded by this study further confirms the endemicity of the disease in the focus and a higher prevalence of CL in the school-aged group as recorded in clinical studies (Dondji, 1999; Ngouateu et al., 2012).

Ngouateu et al. (2012) reported the first cases of CL associated with HIV infection in the country (in Mokolo). This study recorded 146 cases of cutaneous leishmaniasis amongst 32,466 (0.4%) persons surveyed. In CL patients, seven (4.8%) subjects were co-infected with HIV. Subsequently, Ngouateu et al. (2015) presented cellular and immunological bases of CL exacerbation in HIV co-infected patients. These authors showed that HIV-positive patients with CL develop decreased IFN-γ-associated T-cell responses. They also mentioned that the inability to recruit enough numbers of CD4$^+$ T cells with a Th1 profile is responsible for higher lesion numbers, larger lesions and delayed healing in patients co-infected with *L. major* and HIV (Ngouateu et al., 2015).

Using three different polymerase chain reaction tests for detection of *L. major*, and fluorescence *in situ* hybridization to visualize parasites, Hamad et al. (2015) observed *L. major* amastigotes and promastigotes in fecal samples of gorillas from the Dja National Reserve (South Region). This report supports carriage of human pathogenic *Leishmania* by gorillas.

In 2017, one deathly case of CL associated with HIV was reported by Tangie et al. (2017) in the southern part of the country (in Kumbo, North-West Region). It would have been interesting to know the species of *Leishmania* in this patient, but the authors described the clinical symptoms and parasitological diagnosis without species identification of the parasite.

Tateng et al. (2018) published the first detection of *Leishmania donovani*, a known VL causative agent, in sand flies collected from the known Mokolo CL focus. The authors justified the report of *L. donovani* in a CL focus by the recent migration of population due to political unrest in the Sahel region from Kousseri, a VL focus (Tateng et al., 2018).

Yemeli et al. (2021) have recently published a review on leishmaniasis in Cameroon to show the situation of the disease in the country and what is done so far.

Cases of canine leishmaniasis have been reported by the Ministry of Livestock and Husbandry in the North Region without any parasitological confirmation (Same Ekobo, 1999). Reports of leishmaniasis in Cameroon are summarized in Table 1. The country has 10 administrative regions; six of these are known as potential foci of leishmaniasis. Figure 2 shows the regions where CL and/or VL cases have been already described or where the presence of the vector has been reported and Table 2 recapitulates the status of leishmaniasis in Cameroon and neighboring countries.

Fig. 2. Cameroon regions with indication of reported leishmaniasis cases and/or where sand flies have been collected. Reports available on: sand flies (circles); cutaneous leishmaniasis (triangles); and visceral leishmaniasis (stars).

Table 1
Chronology of main events of leishmaniasis investigations in Cameroon

Year	Locality	Region	Research outcome	Reference
1937	Garoua	North	First cases ($n = 326$) of CL reported	Hervé (1937)
1951	–	–	First study of sand flies in Cameroon	Rageau (1951)
1953	Evoudoula	Center	Study of sand flies	Rageau & Adam (1953)
1975	Mokolo	Far North	58 cases of CL reported in the locality	Djibrilla et al. (1979)
1979	Gawar	Far North	A suspected case of VL mentioned	Desjeux (1991)
1983	Kousseri	Far North	A parasitologically confirmed case of VL reported	Desjeux (1991)
1986	Yaoundé	Center	First case of VL in a girl who stayed in Kousseri	Deniau et al. (1986)
1992	Yaoundé	Center	13 cases of VL described	Kaptué et al. (1992)
1998	Mokolo	Far North	First isolation and identification of the causative agent (*L. major*)	Dondji et al. (1998)
2000	Mokolo	Far North	Presentation of species composition of sand fly fauna	Dondji et al. (2000)
2001	Kousseri and other localities	Far North	Sero-epidemiological survey on VL	Dondji et al. (2001)
		Far North	Updating the data on Cameroon sand flies	
2012	Mokolo	Far North	First report on CL associated with HIV. Overall, 146 cases of CL including 7 HIV cases reported	Ngouateu et al. (2012)
2015	Dja National Reserve	South	Identification of *L. major* in stool samples from *Gorilla gorilla*. Out of 91 gorillas, 12 (13.2%) showed the presence of the parasite in the feces while 4 revealed the presence of the vector	Hamad et al. (2015)
2015	Mokolo	Far North	Description of the immunological basis of worsened CL outcome on *Leishmania*/HIV co-infection	Ngouateu et al. (2015)
2017	Kumbo	North-West	One deathly case of CL associated with HIV reported in Kumbo	Tangie et al. (2017)
2018	Mokolo	Far North	Isolation of *L. donovani*, a VL causative agent, from sand flies	Tateng et al. (2018)
2019	Mokolo	Far North	Inventory and taxonomy of phlebotomine sand flies of the Mokolo, with description of new *Sergentomyia* taxa	Tateng et al. (2019)
2021	–	–	Publication of a review on leishmaniasis in Cameroon	Yemeli et al. (2021)

Abbreviations: CL, cutaneous leishmaniasis; HIV, human immunodeficiency virus; VL, visceral leishmaniasis.

Table 2
Status of endemicity of leishmaniasis in Cameroon and neighboring countries

Country	Status of endemicity		Year of the first reported cases		Year of recently reported cases	
	CL	VL	CL	VL	CL	VL
Cameroon	EC	PRC	1937	1992	2017	1992
Central African Republic	PRC	PRC	–	1949	–	–
Chad	EC	EC	1966	1968	2012	2004
Nigeria	EC	PRC	1924	–	–	2019
Gabon	NACR	–	–	1920	–	–
Equatorial Guinea	NACR	NACR	–	–	–	–
Congo	NACR	NACR	–	–	–	–

Abbreviations: CL, cutaneous leishmaniasis; EC, endemic country; ICR, imported cases reported; NACR, no autochthonous case reported; NICR, no imported cases reported; PRC, previously reported cases; VL, visceral leishmaniasis; –, no data.

4. Phlebotomine sand flies in Cameroon

Entomological investigations have been carried out in Cameroon and recorded a number of phlebotomine sand fly species. In Mokolo (Far North Region), these are *Phlebotomus duboscqi* (with an important epidemiological role in leishmaniasis), *Ph. rodhaini*, *Sergentomya africana*, *Se. bedfordi*, *Se. clydei*, *Se. schwetzi* and *Grassomyia squamipleuris* (Dondji et al., 2000). In addition, *Se. adami*, *Se. adleri*, *Grassomyia. affinis vorax*, *Se. antennata*, *Se. christophersi*, *Se. cincta*, *Se. distincta*, *Se. dubia*, *Se. herollandi*, *Se. logoonsis*, *Se. magna*, *Grassomyia ghesquierei* and *G. squamipleuris* were recorded recently in the Mokolo focus of CL (Tateng et al., 2019). These authors described two new taxa of phlebotomine sand fly, namely *Se. thomsoni mandarai* and *Se. coronula*, adding more to the worldwide diversity (Tateng et al., 2019). However, phlebotomine sand fly species were previously collected in other parts of Cameroon, namely in Yaoundé, Center Region (*Se. africana*), Bafia, Center Region (*Se. africana*, *Se. schetzi* and *Se. grenieri*), Evodoula, Center Region (*P. duboscqi*, *Se. schoutedeni* and *Se. simillima*); Kousseri (*Ph. duboscqi*, *Se. africana* and *Se. logonensis*), Logone Birni (*Ph. duboscqi*, *Se. africana* and *Se. antennata*), Garoua, North Region (*Se. africana* and *Se. clydei*), and Douala, Littoral Region (*Se. africana*) (Dondji, 2001).

Depending on the type of animal reservoir host, leishmaniases are classified into two groups: zoonotic and anthroponotic leishmaniases. For the zoonotic type, wild, peridomestic and domestic animals are reservoirs. Some animals incriminated are foxes, jackals, wolves, rats, sloths, marsupials, dogs. For the anthroponotic type of leishmaniases, man is the only reservoir (Dondji, 1999). Unsuccessful attempts have been made to identify animal reservoir hosts of CL in northern Cameroon (Dondji, 1999). Although still debated, there are reports that gorillas may act as reservoir host of *L. major* in the forested southern regions of the country (Bastien et al., 2015; Hamad et al., 2015).

5. History of leishmaniasis in Cameroon neighboring countries

Figure 3 shows Cameroon and different neighboring countries with the leishmaniasis situation indicated in terms of the presence of leishmaniasis cases. Four countries, namely Cameroon, Nigeria, Chad and Central African Republic, are currently known to be endemic. Equatorial Guinea is the only country with neither previous leishmaniasis cases nor vector reports.

5.1. Nigeria

In Nigeria, leishmaniasis is an important tropical disease that is gradually gaining attention (Adediran et al., 2016). As reported by Igbe et al. (2008), northern Nigeria is one of the African endemic cutaneous leishmaniasis foci, especially in Sokoto, Gusau, Katsina, Maiduguri and Azare. Suspicious cases of VL were signaled in the country between 1936 and 1947 (Desjeux, 1991). The first cases of CL in Nigeria were reported since the 1920's. The Annual Reports of the Medical and Health Services of Nigeria recorded 131 cases of CL and 5 cases of VL for the years 1924–1941 (Elmes & Hall, 1944), but there is no indication of

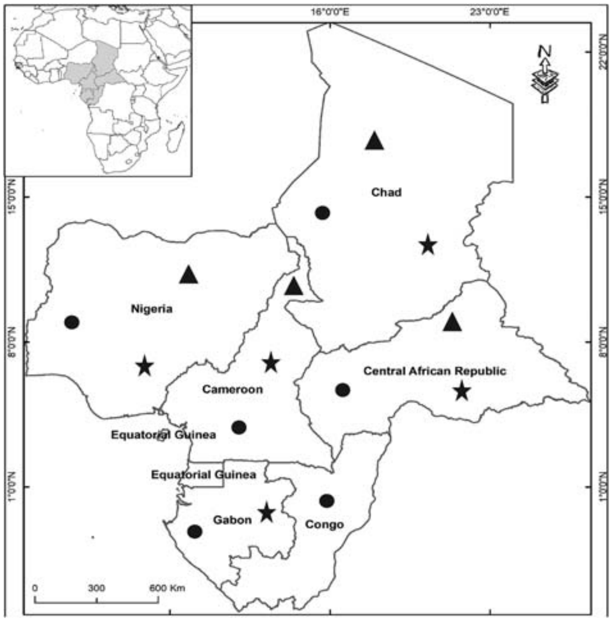

Fig. 3. Cameroon and neighboring countries with reported leishmaniasis cases and sand fly records. Reports available on: sand flies (circles); cutaneous leishmaniasis (triangles); and visceral leishmaniasis (stars).

parasitological confirmation of these cases. Igbe et al. (2008) explained that after reported attempts to confirm clinical suspected cases of cutaneous leishmaniasis, success was achieved in 1942 when *Leishmania* was observed in smears from cutaneous sores of leishmaniasis in Nigeria. Agwale et al. (1993) reported that 63 (5.63%) out of 1120 school children (6–22 years) screened in Keana, northern Nigeria, were positive for cutaneous leishmaniasis.

In a survey performed in 1988, Asimeng (1988) collected two sand fly species of the genus *Phlebotomus* (*Ph. duboscqi* and *Ph. rodhaini*), and eight species of the genus *Sergentomyia* (*Se. affinis*, *Se. africana*, *Se. antennata*, *Se. bedfordi*, *Se. christophersi*, *Se. clycdei*, *Se. ingrami* and *Se. schwetzi*). Later, Asimeng (1990) carried out a survey in northern Nigeria to determine the distribution of the species of phlebotomine sand flies in the major vegetation zones: Sahel, Sudan, Northern Guinea Savanna, and Southern Guinea Savanna. A similar study on the species composition of sand flies was performed by Agwale et al. (1995). A recent study carried out on the occurrence and monthly dynamics of phlebotomine sand flies in Sokoto State, North-West Nigeria, confirmed the occurrence of phlebotomine sand flies and the potential of *Leishmania* transmission in the study area (Usman et al., 2020).

Domestic dogs have been incriminated as reservoir of leishmaniasis in the States of Kwara, Oyo and Ogun; in these three states, the prevalence of canine leishmaniasis was 14.63%, 3.33% and 1.32%, respectively (Adediran et al., 2016).

A recent study carried out to investigate the prevalence of visceral leishmaniasis infection in Gboko Health Division, Benue State showed a VL rate of 13% with a prevalence of 13.5% and 12.5% for female and male patients, respectively (Orpin et al., 2019). In 2019 and 2020, 410 cases and 516 new cases of cutaneous leishmaniasis were reported in Borno State. As of January 2021, a total of 220 affected persons, including Bako and Alhaji Yero's children, have been identified in 26 communities (WHO, 2021).

5.2. Chad

Chad has been identified as a leishmaniasis-endemic country. However, Demba et al. (2015) mentioned that the disease is not included in the Statistical Yearbook of Health of the Ministry of Public Health.

Between 1966 and 1973, 64 cases of visceral leishmaniasis were reported in N'djamena (Demba et al., 2021). In the early 2000s, VL was diagnosed in a French soldier returning from Chad after a two-month mission (Demba et al., 2021). A recent retrospective study in the Léré Health District in southwestern Chad reported 345 cases of VL out of 1141 tested (prevalence of 30%) (Demba et al., 2021). Six cases of mucocutaneous leishmaniasis were recorded between 1969 and 1971 (Sirol et al., 1971). Desjeux (1991) stated that cases of cutaneous leishmaniasis were sporadically reported in Chad in 1968, 1976 and the first semester of 1976 with 121, 836 and 164 cases, respectively. *Phlebotomus duboscqi*, a potential vector, was recorded in the Abéché focus (Desjeux, 1991). A retrospective study using the records of the Laboratory of the District Hospital of Am Timan between January 2008 and December 2012 reported 680 clinical CL cases (Demba et al., 2015). The months with high incidence of cases were June, July, August and September with a male to female sex-ratio of 1:7 (Demba et al., 2015). Recently, a study on the distribution and diversity of sand flies in two geoclimatic zones of the country has been performed. For a total of 2015 specimens collected, 13 species were recorded: one species of *Phlebotomus* and 12 species of *Sergentomyia*. *Phlebotomus duboscqi*, an anthropophilic species, was collected predominantly inside human dwellings and was present at four of the five explored sites. *Sergentomyia schwetzi* and *Se. dubia*, the two species involved in the transmission of canine leishmaniasis, were also found at four study sites (Demba et al., 2022).

5.3. Central African Republic

Cutaneous leishmaniasis is not well known by the health personnel in the Central African Republic. According to Kassa-Kelembho et al. (2003), some sporadic cases have been previously reported in the north-west and south-west parts of the country before 1991. In Bangui, first imported cases of CL were mentioned in 2003 (Kassa-Kelembho et al., 2003). According to the WHO, one suspect case of CL was reported in Birao in 2009 and the first VL case was reported in 1949 (Boua, 2010). Cagnard & Lindrec (1969) reported three other cases of VL in Bangui (Desjeux, 1991).

As far as the vector is concerned, Grépin (1983) reported in the country 33 species and subspecies of sand flies belonging to two genera namely, *Phlebotomus* with two species (*Phlebotomus gigas* and *Ph. rodhaini*) and *Sergentomyia* with 31 species/subspecies (*Sergentomyia adami*, *Se. adleri*, *Se. affinis*, *Se. affinis vorax*, *Se. africana africana*, *Se. antennata*, *Se. bedfordi*, *Se. buxtoni*, *Se. christophersi*, *Se. cincta*, *Se. clydei*, *Se. collarti*, *Se. darlingi*, *Se. decipiens*, *Se. dissimillina*, *Se. dubia*, *Se. dureni*, *Se. emilli*, *Se. hamoni*, *Se. hunti*, *Se. inermis*, *Se. ingrami*, *Se. logonensis*, *Se. magna*, *Se. mirabilis*, *Se. moucheti*, *Se. schwetzi*, *Se. simillima*, *Se. squamipleuris*, *Se. wansoni* and *Se. yusafi*). In 2009, WHO mentioned *Ph. duboscqi* as one of the main vectors of diseases in the country (WHO, 2009).

5.4. Congo

Congo has not been reported as a leishmaniasis-endemic country. Data on the disease cases are scanty. Few studies have described the presence of the vectors in the country. The first mention was in Brazzaville in 1968 by Vattier-Bernard (1968). In 1971, this author noticed the presence of three species of sand flies in the country, namely *Ph. schwetzi*, *Ph. mirabilis* and *Spelaeophlebotomus gigas* (Vattier-Bernard, 1971). Later, in the northern part of the country 2266 phlebotomine sand flies belonging to two genera (*Phlebotomus* and *Sergentomyia*) and 19 species have been gathered at 22 sites classified as forests, villages and habitations (Trouillet et al., 1988). These species are *Ph. rodhaini*, *Se. africana africana*, *Se. decipiens*, *Se. dureni*, *Se. dyemkoumai*, *Se. emilli*, *Se. firmata*, *Se. grjebinei*, *Se. hamoni*, *Se. impudica*, *Se. ingrami*, *Se. magna*, *Se. moreli*, *Se. moucheti*, *Se. richardi*, *Se. schwetzi*, *Se. silva*, and *Sergentomyia* sp. (Trouillet et al., 1988).

5.5. Gabon

A native case of VL was reported by Tournier in Gabon in 1920 (Rahola et al., 2013). Galliard & Nitzulescu (1931) described two new species of sand fly, *P. africanus* and *P. sanneri*, collected from four distant localities of the country. Rahola et al. (2013) captured an unknown sand fly male specimen of the genus *Phlebotomus* by CDC miniature light trap. These authors therefore proposed the erection of a new subgenus, *Legeromyia*, for *Phlebotomus* (*Legeromyia*) *multihamatus* described from the National Park of La Lopé.

5.6. Equatorial Guinea

No data on leishmaniasis and insect vectors were found in our literature search for Equatorial Guinea (Table 2). No report has identified this country as an endemic focus of leishmaniasis.

6. Leishmaniasis challenges in Cameroon and neighboring countries

6.1. Challenges in Cameroon

A study conducted by Kamga et al. (2012) from June 2010 to December 2011 revealed that in Cameroon, amongst neglected tropical diseases, leishmaniasis was the condition for which the population has the least knowledge. In fact, out of 2566 individuals surveyed, only 466 (18.0%) declared to know about the disease. This lack of information can be attributable to the fact that in the list of tropical diseases taught from the primary to the secondary school, leishmaniasis is not mentioned. The awareness needs to be intensified everywhere since the northern part and the southern part of the country are both foci of leishmaniasis. Today, many reported cases in Cameroon are in regions affected by conflicts namely the Far North Region and the North-West Region. Conflicts and other causes of migration have been reported to influence the spread of diseases including leishmaniasis (Berry & Berang-Ford, 2016). Outbreaks and epidemics of leishmaniasis are reported due to movement of populations bringing infected individuals to susceptible vectors or exposing naïve individuals to infected vectors (Kamhawi, 2017). Recently, Tateng et al. (2018) detected *Leishmania donovani*, a known VL-causing species in sand flies collected from the CL-endemic focus of Mokolo. The detection of *L. donovani* in sand flies from Mokolo was likely due to the movement of populations from Kousseri and neighboring Nigeria and Central African Republic due to political unrest in the Sahel region. Consequently, epidemiological and entomological surveys should be conducted in these conflict localities but might be very challenging. Investigators need military protection to investigate in these localities. Due to lack of financial support, investigations in Cameroon have been scarce and only in few parts of the country.

Cases of leishmaniasis associated with HIV have been reported in Cameroon (Ngouateu et al., 2012; Tangie et al., 2017). In the Mokolo leishmaniasis focus, out of 20 patients with cutaneous leishmaniasis (CL) one was reported to be co-infected with HIV. Symptoms in this group of patients are more severe (Ngouateu et al., 2012, 2015). Co-infection with other pathogens such as *Plasmodium*, *Schistosoma* etc. has not yet been investigated in the country and needs to be performed.

Despite the presence of VL causative agent in sand flies collected at Mokolo and cases of VL previously described in the country, information on this clinical form of the disease is very scarce. More in-depth studies on VL in Cameroon are strongly recommended.

In June 2009, from the reports of our studies, the Minister of Public Health reorganized the National Committee for Leprosy and Buruli ulcer Control (CNLP2LUB) and included to this committee yaws and leishmaniasis. Until then, the disease remained relatively ignored and consequently there are no control strategies developed and no effective national policy. There was no mention of the disease in the WHO (2016) annual report for Cameroon. The annual report of WHO (2017) for Cameroon opened a paragraph on leishmaniasis, but in this paragraph suspected cases of another pathology (an eruptive fever) were mentioned.

Overall, we strongly encourage the development of a Cameroon leishmaniasis risk map. Such map should include localities where cases of the disease and sand fly vectors have been recorded. A complete map requires additional information to the current body of knowledge. Consequently, a multidisciplinary team involving physiologists, immunologists, parasitologists (to investigate on the physiopathology and immunology), botanists (to identify plant food sources of sand flies), entomologists and other biologists (for the study of vector and reservoir hosts), geographical information system experts (collect geographical coordinates of sites), and pedologists (analyze the soil, the breeding site of sand flies) should be funded to conduct studies that will identify potential transmission sites of the infection. Data obtained from this team would help develop a risk map of the disease that predicts potential epidemics and is required for the development of a potentially successful control programme of leishmaniasis in Cameroon. In addition to the risk map, we recommend the implementation of a leishmaniasis programme that includes diagnosis and typing of *Leishmania* parasites in order to investigate the parasite diversity in the country.

From this review, it can be observed that the lack of interest in leishmaniasis in Cameroon is obvious. In addition, the lack of financial support for investigations and consequently the gap in data is obvious. Consequently, a national control programme is not yet in place despite the morbidity of the disease and its socioeconomic impact in the affected population. Consequently, more efforts should be directed towards the study and control of leishmaniasis in Cameroon.

Cases of animal (e.g. canine) leishmaniasis are scanty in the country.

6.2. Challenges in the neighboring countries

The Central African Republic is almost totally surrounded by endemic countries namely Sudan (North Sudan: Sulaiman et al., 2019; South Sudan: Abubakar et al., 2014; Al-Salem et al., 2016), Chad (Demba et al., 2015), Democratic Republic of the Congo (Ruiz-Postigo et al., 2020) and Cameroon (Ngouateu et al., 2012). Moreover, the country is in civil war which is a factor for people migration. Forced migration as consequence of war is known to highly correlate with leishmaniasis infection in the migrating population (Al-Salem et al., 2016; Rehman et al., 2018). Despite the above, investigation on leishmaniasis remains extremely poor in the Central African Republic and reports on the vectors are very scanty.

Chad and Nigeria are neighboring countries and are both leishmaniasis-endemic countries. Both countries are surrounded by other endemic countries, namely Benin, Cameroon, Niger, Sudan, South Sudan, Lybia (Ayman et al., 2017) and Central African Republic for Chad, and Cameroon, Niger and Benin for Nigeria. Leishmaniasis is especially found in the North-West and North-East Nigeria, which form the belt of the disease in the country. But recently, an uncommon case of CL has been reported in the South-South Nigeria (Uchechukwu & Ejovwoke, 2020). More surveys should be performed in this part of the country to find more possible cases of leishmaniasis.

The Democratic Republic of the Congo, the Central African Republic as well as Cameroon are leishmaniasis-endemic countries neighboring Congo. Despite the fact that the vector has been reported in Congo, the country is still without endogenous leishmaniasis cases reported. Further investigation is required to provide the real picture of the disease in the country.

With few studies showing the presence of *Phlebotomus* species in Gabon, the country remains potentially a place where leishmaniasis transmission can occur. Both Gabon and Equatorial Guinea share a border with Cameroon which is a leishmaniasis-endemic country. These two countries (Gabon and Equatorial Guinea) are consequently at risk for the disease transmission. Consequently, and like other countries in the region, epidemiological and entomological studies should be conducted to provide a true picture of the disease. Such in-depth studies are necessary for the development of a potentially successful programme that will limit the impact of potential outbreaks.

7. Conclusions

Leishmaniasis is known in Cameroon and almost all the surrounding countries long time ago. The disease is also reported in Chad and Nigeria and Central African Republic. Countries situated southern to Cameroon, namely Gabon, Congo and Equatorial Guinea, have not yet reported endogenous cases of leishmaniasis but remain potential transmission sites of the disease. Leishmaniasis remains a very neglected tropical disease in all the countries covered in the present review. In order to address the shortcomings identified here, the authors recommend training of more scientists in leishmaniasis epidemiology in the region that should be accompanied by necessary funding. This training must be multidisciplinary and includes development of laboratory and field skills for studies of the parasite, the vector, the reservoir, the vegetation, and the soil in potential endemic foci. In addition, prospective studies involving geographers and other experts should develop a disease risk map of the Central Africa region.

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Declaration of competing interests

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