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ARTICLE in TROPICAL MEDICINE & INTERNATIONAL HEALTH · SEPTEMBER 2000
Impact Factor: 2.33 · DOI: 10.1046/j.1365-3156.2000.00598.x · Source: PubMed

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Leishmaniasis in the Sudan: a literature review with emphasis on clinical aspects

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Summary

The literature on the leishmaniasis in the Sudan is reviewed with an emphasis on clinical aspects and on literature related to the recent outbreaks in the south and east of the country. The numbers of cases of subclinical infection and post-kala azar dermal leishmaniasis in the recent outbreaks are remarkable. New diagnostic techniques have been introduced and evaluated, notably the direct agglutination test and polymerase chain reaction technology. The latter gives very promising results and further research into application of the technique is warranted. Treatment with pentavalent antimony is still satisfactory. The reservoir host has not been identified definitely.

keywords Sudan, leishmaniasis, kala-azar, PKDL, clinical features, diagnosis, treatment, entomology

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Introduction

The leishmaniasis are a group of diseases with a broad range of clinical manifestations caused by several species of parasites belonging to the genus Leishmania (Family: Trypanosomatidae). The Leishmania parasite, a haemo-flagellate protozoan organism, is exclusively transmitted by the bite of a female sandfly of the genus Phlebotomus or Lutzomyia. There are three clinical forms of leishmaniasis: visceral leishmaniasis (VL) including post-kala azar dermal leishmaniasis (PKDL), cutaneous leishmaniasis (CL) and cutaneous leishmaniasis with involvement of the mucous membranes, also called mucocutaneous leishmaniasis (MCL).

In Sudan, VL and CL are endemic in several areas (Figure 1). PKDL, a complication of VL of unknown cause, now occurs in up to 30% of cases (Zijlstra et al. 1995), much more frequently than in the past (Kirk & Sati 1940b). A particular form of ‘mucosal leishmaniasis’, different from MCL – which is found in Central and Latin America – occurs in Sudan. It is called Sudanese mucosal leishmaniasis (SML).

VL is one of the most important endemic diseases in the country and Sudan is considered to be one of the main foci of VL in the world. Occasionally, severe epidemics have claimed the lives of thousands of people. In recent years the disease has spread outside established endemic areas, and a resurgence of cases has become apparent in regions with a previously low incidence (Siddig et al. 1990). VL spreads over a wide belt from the Atbara river in the north-east along the Sudanese–Ethiopian border to south of the Sobat river and Nassir and Malakal and extending west across the White Nile. Other foci are the Kaoeta area, the Nuba Mountains and scattered areas in the Darfur region.

Epidemiology in historical perspective

Neave was the first to describe VL in Sudan in 1904 (El-Hassan et al. 1995a), although the disease was already known there in the 19th century (Henderson 1937). At the turn of the 20th century, VL was recognized as a serious health problem in the Sudan. This realization led to the establishment of the Sudan Kala Azar Commission, which operated from 1909 to 1913 (Zeese & Frank 1987). In the 3rd and 4th Wellcome Research Laboratory Reports published in 1908 and 1911, respectively, chapters are devoted to kala azar with notes on epidemiology, clinical and diagnostic aspects, trials at treatment, case descriptions and post mortem reports (Balfour 1908, 1911). Archibald and Mansour (1937) identified the main endemic area as the Kassala and Fung districts bordering the Abyssinian frontier and the Kaoeta district in the south. Sporadic cases were found in the Nuba Mountains and in the western district of Darfur. At that time no epidemics had been described.

The first epidemic was reported in the Upper Nile Province
in 1936–38; at least 300 cases occurred with a recorded death rate of 80% (Stephenson 1940). The second epidemic in the southern Fung area of Blue Nile Province in 1956–60 killed thousands of people (Sati 1958) and led to the establishment of a research team that between 1960 and 1964 provided clear data on medical and zoological aspects of the vector and reservoir hosts (Hoogstraal & Heyneman 1969). In 1979–81 there was an increased number of cases in Melut (Zeese & Frank 1987), an area described as a new focus in 1962 by Van Peenen & Reid. Around 1985 the average number of patients requiring treatment was 1300 per year, 75% of whom were treated in Gedaref and Hawata (Zeese & Frank 1987).

In the last decade, several new outbreaks of VL occurred: a major epidemic in the south of the country (Perea et al. 1991; Ashford et al. 1992; El-Hassan et al. 1993b; Seaman et al. 1993) came to light only after VL had been found in the Khartoum area in 1988 among displaced people from Western Upper Nile Province who had fled the civil war in the south (De Beer et al. 1991). Subsequent studies confirmed this (Zijlstra et al. 1999b; El-Hassan et al. 1993b), and it became clear that a devastating outbreak had been going on in southern Sudan since 1984 (Perea et al. 1991), which affected all age groups and by the end of 1988 had already killed 20–30 000 people (Seaman et al. 1992). During the period 1986–95 an estimated 100 000 from a population of about 280 000 people died of the disease in Western Upper Nile Province. Population movement, civil war and poor nutritional status may have contributed to this high death rate (Seaman et al. 1996).

The Masariya, a nomadic tribe from southern Kordofan in western Sudan, traditionally move their cattle to the northern
part of the epidemic area in Western Upper Nile Province in search of pasture. During this trek they became infected and thus brought VL to their home area (Hashim et al. 1994). In 1994 another outbreak was reported in Nasir District of Eastern Upper Nile Province which was probably related to people travelling to a food distribution centre located in the southern part of the VL-endemic zone in eastern Sudan (Mercer et al. 1995). Until recently, at least 1000 cases of VL occurred each year in Gedaref State, eastern Sudan (Zeece & Frank 1987; El-Hassan et al. 1995b; Osman et al. 1998b); the incidence of the disease was estimated to be stable at 4% (Zijlstra et al. 1994). However, by the end of 1997, a sharp increase in the number of VL cases was reported from this area and also from Eritrea and the north-west Ethiopian focus (McGregor 1998). This has continued through 1998 and 1999 (unpublished data).

The first case of possible PKDL was described by Christopherson (1921). The first definite cases were reported by Kirk and Drew (1938). The number of cases might have been much greater than supposed until recently, or may have increased over time (Zijlstra et al. 1995). PKDL patients may serve as a reservoir for transmission of the parasite (El-Hassan et al. 1992).

The first cases of CL in Sudan described at the beginning of the 20th century had contracted the disease in Egypt (Kirk and Drew 1938). The first reported autochthonous CL case was from the Nuba mountains (Archipald 1911). CL patients mainly come from Darfur and the central belt of Sudan (Abdalla et al. 1973; Abdalla & Sherif 1978). So far, three outbreaks of CL have been reported: the first started in 1976–77 in the region of Shendi-Atbara north of Khartoum, the second in 1983 in and around El-Gerrsa in the White Nile area, and the last major epidemic took place in Khartoum Province with about 10 000 recorded cases in 1985–87. Heavy rainfall after several years of drought, the discontinuation of insecticide spraying for malaria control and rodent outbreaks have all been implicated as factors in the outbreaks (El-Safi & Peters 1991).

SML is uncommon: only 78 cases have been reported since the disease was first described by Christopherson in 1914 (El-Hassan et al. 1995a). SML is seen in adult males in VL-endemic areas: eastern Sudan, Darfur and Kordofan. Cases are sporadic and isolated: SML has never occurred in epidemic form.

**Clinical features of VL**

**Skin manifestations**

After the infectious bite of the sandfly a ‘leishmaniama’ may appear. We do not know how often this happens as it is infrequently reported and generally seems to go unnoticed. A leishmaniama is a nonitching papule that may ulcerate and then resemble CL (Kirk 1938), but in general it evolves gradually into a tuberculoid lesion (Manson-Bahr 1959). Histologically it consists of lymphocytes, macrophages and plasma cells (El-Hassan & Modabber 1999). The leishmaniamya may precede VL or be present when VL becomes manifest. Two of four leishmaniamya patients studied in Upper Nile Province developed VL (Adler et al. 1966). In another study, one of five leishmaniamya cases not treated and followed up 6 months later developed VL, another developed PKDL without apparent VL and the remaining three were without symptoms (Zijlstra et al. 1994). Skin pigmentation did not change (Siddig et al. 1990), in contrast to the situation in India, where the dark skin associated with VL gave the disease its Hindi name kala azar (‘black sickness’).

**Other clinical manifestations**

The clinical features of Sudanese VL have been described by a number of authors (Henderson 1937; Van Peenen & Reid 1962; Ahmed et al. 1988; El-Hassan et al. 1990a; Siddig et al. 1990; El-Safi et al. 1991b; Zijlstra et al. 1991a, b; Hashim & El-Hassan 1994; Hashim et al. 1994, 1995). The disease is characterized by the development of fever, splenomegaly, varying degrees of hepatomegaly, weight loss in combination with a healthy appetite, and pancytopenia. Splenomegaly may be absent: in 4% of cases Zijlstra et al. (1991b) did not observe an enlarged spleen. The number of patients with lymphadenopathy ranges from 36% (Hashim et al. 1994) to more than 80% (Zijlstra et al. 1991a).

**Complications**

Complications such as epistaxis (El-Hassan et al. 1990a; Siddig et al. 1990), severe tinea versicolor due to depressed cell-mediated immunity (Hashim & El-Hassan 1994) and neurological changes such as deafness, foot drop and a sensation of burning feet (Hashim et al. 1995) have been reported.

**Congenital and placental leishmaniasis**

A case of congenital leishmaniasis was reported, together with a patient who a few days after the start of treatment of VL aborted a 5-month-old foetus. The placenta contained many parasites, the foetus did not (Eloum et al. 1992).

**Subclinical infection**

In Sudan subclinical infection was defined as serological conversion and/or conversion in the leishmanin skin test (LST) in the absence of clinical symptoms. Using this definition, the ratio of clinical to subclinical cases was 1.6:1 and 2.4:1 in two successive years in a longitudinal study in eastern Sudan (Zijlstra et al. 1994). This ratio is higher than those in Italy (1:4), Kenya (1:5) (Hoo et al. 1982) and Brazil (1:18.5 for ‘a study area at large’ and 1:6.5 for the ‘area with the highest prevalence of dis-
Clinical symptoms of PKDL

PKDL is a recognized complication of VL of unknown cause. A rash with tiny papules on the face resembling measles and papular lesions on a background of depigmented macules are the most common clinical presentations in eastern Sudan (Zijlstra et al. 1995). Rarely, eye lesions associated with past or concomitant PKDL occur (El-Hassan et al. 1998). In a population-based study 56% of VL patients developed PKDL after treatment (Zijlstra et al. 1995). This figure is higher than the other reported frequencies of 20% (Kirk & Sati 1940b; Zijlstra et al. 1993) and 29% (Osman et al. 1998b). PKDL occasionally occurs in the absence of a history of clinically manifest VL (El-Hassan et al. 1990b) or during treatment of VL, but it generally appears directly or up to 6 months post-treatment (Zijlstra et al. 1995). This is faster than Indian PKDL which typically shows up 1–5 years after cure. The nodular and hypopigmented macular form of PKDL, especially in the absence of a history of VL, may be confused with lepromatous leprosy, as may the pathology (El-Hassan et al. 1993a). Unlike leprosy patients, PKDL patients have no sensory loss or motor power deficit. Finding the parasites in smears by microscopy or polymerase chain reaction (PCR) and a positive DAT may also assist in distinguishing PKDL from leprosy (El-Hassan et al. 1992; Harith et al. 1996; Osman et al. 1998a).

Clinical presentation of CL

CL in Sudan is similar to the disease in other endemic areas. There are 3 types: nodular or nodular-ulcerative, ulcerative and diffuse infiltrative (Abdalla et al. 1973). Most patients have multiple lesions of the nodular or ulcerative type (El-Safi et al. 1991a). Typically, lesions start to heal spontaneously after approximately three months (Abdalla & Sherif 1978).

Clinical symptoms of SML

Unlike American mucocutaneous leishmaniasis, Sudanese mucosal leishmaniasis is not preceded or accompanied by cutaneous lesions. Three clinical presentations of SML have been reported: nasal, which is characterized by nasal obstruction, mucoid discharge and slight bleeding; oral, where the patient complains of a sensation of fullness of the mouth, spontaneous loss of teeth and bleeding from the gum; and oro-nasal, where the hard palate may perforate (El-Hassan et al. 1995a). The disease is almost exclusively found in adult males (20–70 years) (Abdalla et al. 1975; El-Hassan et al. 1995a) and characterized by long duration if not treated (Abdalla et al. 1975).

Diagnosis

Parasitological diagnosis

In the first described VL case in Sudan, the parasite was detected in the spleen, and by the early years of the 20th century, VL was frequently diagnosed by demonstrating parasites in splenic aspirates, a technique described by Bousfield (1911–12) and used by many workers both in the field and in the clinic. Three studies showed sensitivities of at least 92% (Van Peenen & Reid 1962; Siddig et al. 1988; Zijlstra et al. 1992).

Lymph node aspiration was introduced by Kirk & Sati (1940a). At present, microscopy on lymph node aspirates is the most commonly used procedure to confirm a diagnosis of VL. The method is safe (Siddig et al. 1988) but varies in sensitivity from 38.3% (Zijlstra et al. 1992), 78% (Siddig et al. 1988) and 81.6% (Osman et al. 1997b) to 100% (Kirk & Sati 1940a). Microscopy of bone marrow aspirates (70.2%) was less sensitive than microscopy of splenic aspirates (96.4%), but more sensitive than microscopic examination of lymph node aspirates (58%) (Zijlstra et al. 1992).

Many authors mention that it is extremely difficult to find parasites in peripheral blood (Archibald & Mansour 1937; Henderson 1937; Kirk & Sati 1940a; Stephenson 1940; Van Peenen & Reid 1962). In contrast to some contemporaries (Balfour 1908), Marshall (1911) found parasites in 13 of 15 (86%) blood samples. Rohrs (1964) detected parasites in the venous blood of 4 of 20 confirmed VL patients. Archibald & Mansour (1937) claimed that even though no parasites could be found in blood films from the Fung district, all blood films of VL patients from the Kaopea district were positive. Using peripheral blood spots on filter paper from confirmed VL patients, Osman detected Leishmania DNA in 70% of the samples by PCR (Osman et al. 1997b).

Parasites have been found in skin biopsies (Kirk & Sati 1940a; Gumaa et al. 1988) and nasal smears of VL patients (Archibald & Mansour 1937; Henderson 1937; Rohrs 1964). The parasite load in skin samples from PKDL patients is lower.
than from CL patients (El-Hassan et al. 1992). Examination of paraffin-embedded skin biopsies from PKDL patients revealed *Leishmania* parasites in all 14 samples tested (El-Hassan et al. 1992). In contrast, a sensitivity of only 20% was reported by Ismail et al. (1997). Using an immunoperoxidase technique and anti-*L. donovani* monoclonal antibody, they achieved high sensitivity with microscopy. Using slit skin smears of PKDL patients, *Leishmania* DNA was detected in 19 of 23 samples by PCR, whereas with microscopy parasites were only found in seven (Osman et al. 1998a). In CL patients, microscopy on slit skin smears is often positive with sensitivity ranging from 54.5% to 100% (Abdalla & Sherif 1978; El-Safi & Evans 1989; Andersen et al. 1996). In SML patients the sensitivity of microscopy on smear samples was 85.7% (Abdalla et al. 1975) and 100% (El-Hassan et al. 1995a).

**Serological diagnosis**

Serological diagnosis, mainly the direct agglutination test (DAT), has been compared with parasitological methods. In several studies the DAT was highly sensitive (94–100%) and specific (74–100%) (Abdel-Hameed et al. 1989; El-Safi & Evans 1989; Zijlstra et al. 1991b). 333 of 654 displaced persons from southern Sudan who were clinically suspect of VL but without parasites in the bone marrow tested positive with the DAT (De Beer et al. 1991) and responded to specific therapy. In war-torn southern Sudan, struck by an extensive outbreak, high titres in the DAT together with suggestive clinical symptoms were considered sufficient evidence of VL to start treatment (Seaman et al. 1993). The performance of the DAT using both aqueous and freeze-dried antigen under field conditions has been evaluated in separate studies in southern and eastern Sudan. Both antigens performed equally well (Meredith et al. 1993; Zijlstra et al. 1997), giving identical titres or a difference of only ±1 dilution in 92–98% of the samples tested in two successive surveys (Zijlstra et al. 1997). Boelaert (1999) reports a series of evaluations of the utility of DAT in Sudan and elsewhere.

The immunofluorescent antibody test (IFAT) and ELISA have also been used in Sudan, but only in a few research studies. Abdalla (1980) found all 50 sera from confirmed VL patients positive in the IFAT at a dilution of 1:200; 33 sera (66%) were positive at a dilution of 1:400, but 16% of 150 controls from the endemic area tested positive at the same dilution and 3.3% of nonendemic controls were positive at a dilution of 1:100. El Amin et al. (1985) found all 25 VL patients’ sera positive in an ELISA. Using another ELISA, El-Safi & Evans (1989) found all 25 confirmed VL patients and 10 of 14 VL suspects positive.

El Amin et al. (1986) compared ELISA, IFAT and indirect haemagglutination (IHA) in 24 sera from confirmed VL patients: all sera tested positive in the three tests, with the ELISA giving higher titres. All three tests gave cross-reactions with sera from patients with African trypanosomiasis which disappeared at higher dilutions in ELISA. In another comparative study, all 25 sera from confirmed VL cases were positive in both ELISA and DAT. The two tests did not differ significantly in VL suspects: 9 of 14 were positive in DAT and 10 were positive in ELISA (El-Safi & Evans 1989).

**Leishmanin skin test**

There are only few reports on the use of the leishmanin skin test (LST) in Sudan. The LST is characteristically negative during active VL and became positive in 81% of cured cases within 6 months (Zijlstra & El-Hassan 1993). Only 59% of PKDL patients tested positive (Zijlstra & El-Hassan 1993). The LST is a useful tool for epidemiological investigations and surveys and can be used to quantify transmission of leishmaniasis. A team working on the epidemiology of VL in southern Sudan found 59% of the individuals tested were LST-positive, compared to 10% in an area where the disease was unknown (Hooistra & Heyneman 1969). During the VL epidemic in southern Sudan, 43% of survivors in two villages were LST-positive (Seaman et al. 1992). In a longitudinal study in eastern Sudan, most people had a positive LST, possibly due to previous exposure to *L. major* in their homeland in western Sudan from where they had migrated in the 1980s. *L. major* causes CL and a positive LST. As VL was observed to occur only in previously LST-negative individuals, previous CL might protect against subsequent VL, a possibility that warrants further research (Zijlstra et al. 1994). As in CL, the LST is almost always positive in SML (Abdalla et al. 1975; El-Safi et al. 1991b; El-Hassan et al. 1995a).

**Molecular diagnosis**

Recently, the value of PCR for the diagnosis of leishmaniasis has been examined. The technique was tested with VL samples of different clinical materials (peripheral blood, aspirates from lymph nodes and bone marrow); with samples taken at different stages of the disease from the endemic area in eastern Sudan (Osman et al. 1997a, b, 1998b) and in a hospital-based study (Andersen et al. 1997). In parasitologically confirmed patients PCR was as sensitive as microscopy. In clinically suspect individuals (clinical features of VL, positive serological test and response to treatment but with negative microscopy), PCR was positive in about 50% of cases (Osman et al. 1997b). PCR was positive in 70% of confirmed cases on peripheral blood and in 17% of suspected cases (Osman et al. 1997b). Thus PCR is likely to be of value in the diagnosis of VL and further studies are warranted. Where the ‘gold standard’ of the diagnosis of VL, i.e. demonstration of parasites, is difficult or impossible, clinicians have to make decisions based on the best evidence available. PCR can be helpful here with proper inter-
pretation in the full context. PCR was also used to diagnose PKDL (Osman et al. 1998a) and CL (Andersen et al. 1996) and proved more sensitive than routine microscopy in all cases.

**Treatment**

Since its introduction in Sudan, sodium stibogluconate continues to be the drug of choice, although treatment is expensive at USS 60–200 per course (Desjeux 1992; Veeken et al. 2000). Pentamidine has been used in the past (Kirk 1947) and more recently 49 patients were treated with different schedules of liposomal amphotericin B with high cure rates of 88% to 94% in higher-dosed regimens (Seaman et al. 1995). The cost of this treatment precludes use at any scale. Antimony is the drug in general use and is discussed here. In the 1960s, Van Peenen & Reid (1962) used a total dose of 600 mg/kg spread over 14 days or more and achieved an initial cure rate of 65%; 20% died. Fearing toxicity of sodium stibogluconate, many physicians used 10 mg/kg/day for 15 days (Zijlstra et al. 1993) instead of the WHO-recommended dose of 20 mg/kg/day for 30 days (World Health Organization 1990).

In a comparative trial in southern Sudan, 134 patients were randomized to treatment with sodium stibogluconate at 20 mg/kg/day for 30 days or the same drug at a dose of 20 mg/kg/day plus amotosalen at 15 mg/kg/day for 17 days. Five patients (7%) in group I and three patients (4%) in group II died. All patients who completed treatment were clinically cured. At days 15–17, the parasite clearance rate was 95% in group II and 81% in group I. At the end of treatment, 93.4% of splenic aspirates in group I were negative, comparable to group II (Seaman et al. 1993). Follow-up was not possible in this trial.

In another comparative randomized trial in Khartoum, Zijlstra et al. (1993) compared a regimen of stibogluconate at 10 mg/kg/day for 30 days with 20 mg/kg/day for 15 and for 30 days. They found no significant difference between the three regimens, but the groups were small (29, 37 and 38 patients). Khalil et al. (1998) reported that in the period 1989–95, 98% of 1593 VL patients responded well to treatment with Pentostam using the three treatment regimens described above. However, this was a retrospective, descriptive study, not comparative, not randomized. It included patients from different endemic areas, treated at different hospitals in Khartoum and follow-up data were often not available.

In contrast, 23 of 49 (47%) patients in eastern Sudan were not cured after well-supervised treatment with daily stibogluconate at a dose of 20 mg/kg/day for 4 weeks: 14 (28.5%) developed PKDL and nine (18%) had recurrent VL with reappearance of parasites in aspirates. Four of these patients died (Osman et al. 1998b).

PKDL often clears by itself (Zijlstra et al. 1995), but once systemic antimony treatment is deemed necessary, a dose of stibogluconate 20 mg/kg/day for at least 30 days seems advisable (El-Hassan et al. 1992). Indications for treatment, the optimum dose and duration have yet to be determined. Ketoconazole at 10 mg/kg/day for 4 weeks was ineffective (El-Hassan et al. 1992), as was a combination of two antifungal drugs, terbinafine and itraconazole (Khalil et al. 1996).

If it is not extensive, CL may clear by itself and does not necessarily require treatment. In extensive and disfiguring disease or when multiple lesions are present, treatment with antimony 600 mg/day for 3–4 weeks was successful (El-Safi et al. 1991a). The response of SML patients to pentavalent antimony (ten patients, one death, seven cures, one lost and one relapse/cure after ketoconazole) or ketoconazole (four patients, three cured) was good (El-Hassan et al. 1995a).

Treatment of VL with pentavalent antimony resulted in death rates of 4.8% to 20% (Van Peenen & Reid 1962; El-Hassan et al. 1990a; De Beer et al. 1991; Zijlstra et al. 1991a; Seaman et al. 1993, 1997). Relapse rates of VL after sodium stibogluconate therapy varied between 1 and 2% (Sati 1958), 6% (Siddig et al. 1989), 3% (Zijlstra et al. 1993) and 18% (Osman et al. 1998b). In lymph node aspirates obtained from Sudanese VL patients immediately after treatment, Leishmania DNA was detected by PCR in 82% of the samples (Osman et al. 1998b). Incomplete treatment and suboptimal dosing have both been implicated in the occurrence of complications after treatment (Zijlstra et al. 1995; Khalil et al. 1998), although in the small study of Osman et al. (1998b) treatment was well supervised.

**Strain identification**

Most epidemiological evidence suggests that VL in Sudan is a zoonosis caused by *L. donovani* sensu lato (Kirk 1956; Hoogstraal & Heyneman 1969; Elnaiem et al. 1997; Oskam et al. 1998). Isoenzyme analysis showed that isolates from Sudanese VL patients were all *L. donovani s.l.* with zymodemes belonging to an ancient ancestral cluster (Ashford et al. 1992; Oskam et al. 1998). Restriction fragment length polymorphism (RFLP) analysis showed that in eastern Sudan the causative agent of VL and PKDL was *L. donovani s.l.* (El-Hassan et al. 1993c; Meredith et al. 1993). Using different molecular biological techniques, isolates from this area were identified as *L. donovani s.s.* (Oskam et al. 1998).

CL is caused by *L. major* (Abdalla et al. 1973; El-Safi et al. 1991a; Ibrahim et al. 1995; Andersen et al. 1996) and *L. tropica* (Abdalla & Sherif 1978). *L. donovani* and *L. major* seem to be the causative agents for SML (Ghalib et al. 1992; El-Hassan et al. 1995a).

**Entomology**

Nine *Phlebotomus* and 29 *Sergentomyia* species have so far been found in Sudan (Elnaiem et al. 1997). The only proven
vector of VL in Sudan is *P. orientalis*, which abounds in woodlands dominated by *Acacia seyal* and *Balantites aegyptiaca* trees (Quate 1964; Adler et al. 1966; Hoogstraal & Heyneman 1969; Ashford & Thomson 1991; Elnaiem et al. 1997, 1998a; b). *P. orientalis* had an exceptionally high infection rate (10%) in southern Sudan (Schroder & Goris 1992). In the Kapoeta area in south Sudan, where *P. orientalis* is not known to be present, *P. martini* may, as in Kenya, be the main vector of VL (Minter et al. 1962). Elnaiem & Osman (1998) confirmed intravillage transmission by PCR of sandfly material.

*P. papatasi* was incriminated as a vector for CL during the epidemics in central and northern Sudan (where *P. orientalis* is absent) in 1976–78 (Abdalla & Sherif 1978). Earlier studies had indicated that *P. papatasi* is not a suitable vector for *L. donovani* (Hoogstraal & Heyneman 1969).

**Reservoir studies**

Outbreaks of leishmaniasis in troops in uninhabited areas (Kirk 1956) and infected *P. orientalis* (3.5–7.1%) in the uninhabited Dinder National Park (Elnaiem et al. 1998a) strongly suggest a reservoir host other than man in Sudan. Man-to-man transmission via sandflies is also likely, especially during epidemics.

A number of studies have been devoted to the identification of the reservoir host of *Leishmania* in Sudan. Archibald & Mansour (1937) did not find the parasite in dogs, cats, fowl, rats, mice, sheep, goats, squirrels, bats, lizards and geckos. In later reports the parasite was isolated from *Cercopithecus aethiops* and *Vulpus pallida* (Kirk 1956), *Rattus rattus*, *Acomys albigena*, *Arvicanthis niloticus*, *Genetta senegalensis* and *Felis serval* (Adler et al. 1966; Hoogstraal & Heyneman 1969). El-Hassan et al. (1993c) detected *Leishmania* DNA in *Arvicanthis niloticus*, the incriminated reservoir of *L. donovani* in eastern Sudan. Despite repeated investigations and trials of experimental infection, no infected dogs, the main reservoir host in the Mediterranean area, were found (Archibald & Mansour 1937; Hoogstraal & Heyneman 1969). Thus the dog is unlikely to be a vertebrate reservoir host in Sudan. Both Kirk (1956) and El-Hassan et al. (1992) suggest that PKDL patients may serve as a reservoir for the parasite.

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