LEISHMANIASIS CONTROL IN EASTERN AFRICA: PAST AND PRESENT EFFORTS AND FUTURE NEEDS

Situation and Gap Analysis

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AAU	Addis Ababa University
ADRA	Adventist Development and Relief Agency
AECID	Spanish Agency for International Cooperation for Development
AHRI	Armauer Hansen Research Institute
AMREF	African Medical and Research Foundation
CBRD	Centre for Biotechnology Research and Development
CL	Cutaneous Leishmaniasis
CMA	Christian Mission Aid
COSV	Comitato di coordinamento delle organizzazioni per il servizio volontario
CPA	Comprehensive Peace Agreement
DACA	Drug Administration and Control Authority
DAT	Direct Agglutination Test
DCL	Diffuse Cutaneous Leishmaniasis
DNDi	Drugs for Neglected Diseases Initiative
DOT	Diocese of Torit
ECHO	European Commission Humanitarian Aid
EHNRI	Ethiopian Health & Nutrition Research Institute
GHC	Gedo Health Consortium
HAPCO	HIV/AIDS Prevention and Control Office
HMIS	Health Management Information Systems
IDSR	Integrated Disease Surveillance and Response
IEND	Institute for Endemic Diseases
IMRF	International Medical Relief Fund
IRS	Indoor Residual Spraying
ITECH	International Training and Education Centre for Health
ITN	Insecticide Treated Bed Net
KEMRI	Kenya Medical Research Institute
KEMSA	Kenya Medical Supplies Agency
LCL	Localised Cutaneous Leishmaniasis
LCP	Leishmania Control Programme
LRTC	Leishmaniasis Research and Treatment Centre
ML	Mucosal Leishmaniasis
MERLIN	Medical Emergency Relief International
MoH	Ministry of Health
MSF-B	Médecins Sans Frontières Belgium
MSF-G	Médecins Sans Frontières Greece
MSF-H	Médecins Sans Frontières Holland
MSF-S	Médecins Sans Frontières Swiss
NAMRU-3	United States Naval Medical Research Unit no. 3
NDL	National Drug List
NGO	Non Governmental Organisation
NLB	Nairobi Leishmania Bank
NMSLA	National Malaria, Schistosomiasis and Leishmaniasis Administration
NTD	Neglected Tropical Disease

ACRONYMS (continued)

PHC	Primary Health Care
PHCC	Primary Health Care Centre
PKDL	Post Kala-Azar Dermal Leishmaniasis
PSF	Pharmaciens Sans Frontières
PSI	Population Services International
RDT	Rapid Diagnostic Test
SACB	Somalia Aid Coordination Body
SNNPR	Southern Nations and Nationalities People's Region
SSG	Sodium Stibogluconate
TWG	Technical Working Group
UNICEF	United Nations Children's Fund
VL	Visceral Leishmaniasis
WHO	World Health Organization

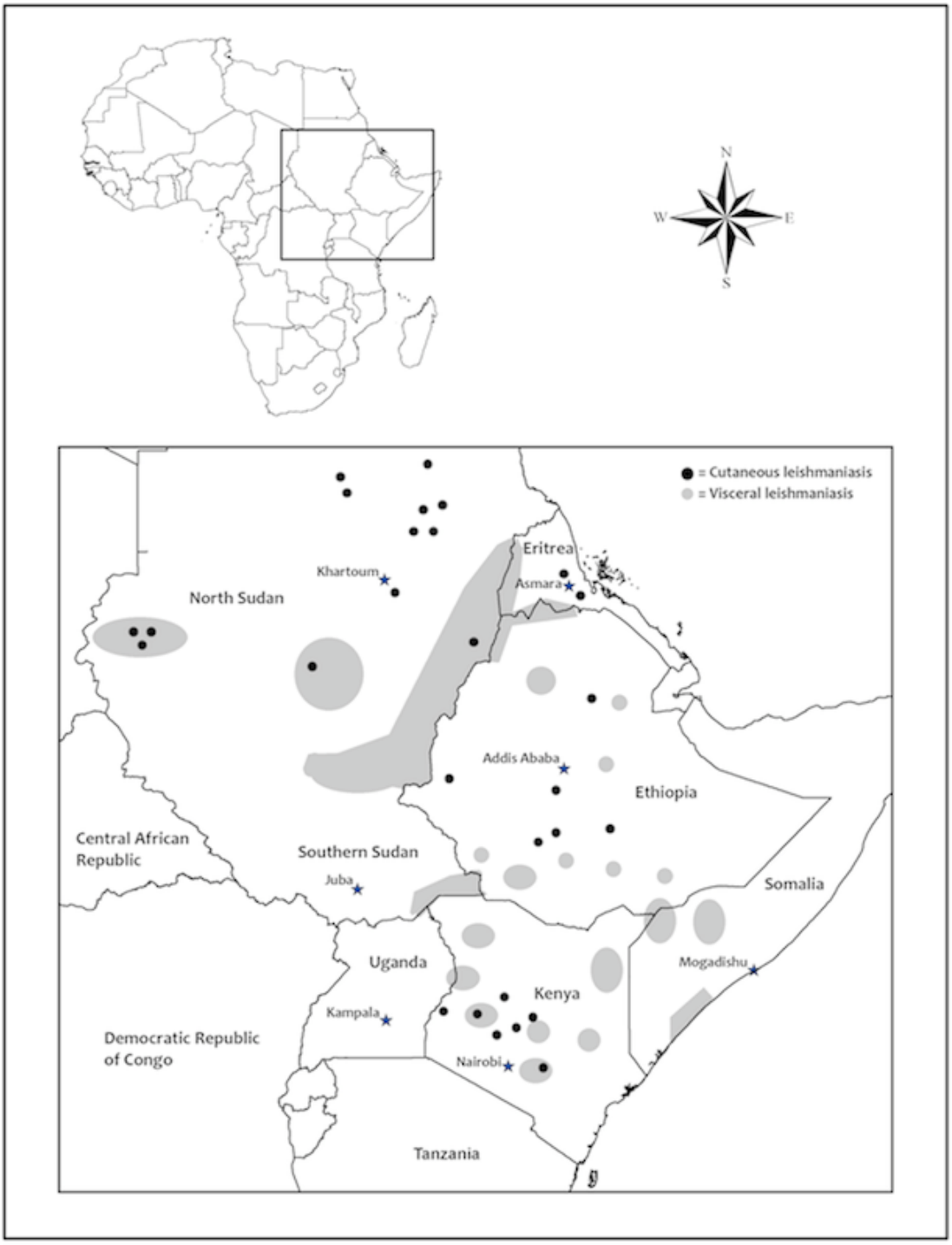
Table 1: Summary of leishmaniasis foci in eastern Africa

Country	Leishmaniasis Type	Endemic Foci		Parasite	Vector
Eritrea	Visceral	Ghash Barka, Anseba and Debub regions	Unknown	Unknown	Unknown
	Cutaneous			*L. tropica*	
Ethiopia	Visceral	SNNPR Region	Omo woreda: Omo plains Konso woreda: Segen Valley (Aba Roba focus), Weyto Valley Sidamo woreda: Lake Abaya, Dawa Valley, Galena Valley	*L. donovani, L. infantum (Libo Kemkem only)*	*P. orientalis (Omo), P. martini (Konso)* Suspected: *P. celiae (Konso)*
		Oromia Region	Moyale, Genale valley		*N/A*
		Somali Region	Afder woreda, Liban woreda		*N/A*
		Tigray Region	Humera plains		*P. orientalis*
		Amhara Region	Metema plains, Libo Kemkem woreda, Fogera woreda		*P. orientalis*
		Afar Region	Awash Valley		*N/A*
	Cutaneous	SNNPR Region	Ochollo village, Sidamo province, Silti woreda	*L. aethiopica* *L. major* *L. tropica*	*P. longipes* *P. pedifer (SNNPR)*
		Oromiya Region	Wollega province – Aleku area, Bale zone	*L. aethiopica*	
		Amhara Region	Kutaber woreda		
Kenya	Visceral	Rift Valley Province	Districts: Turkana, Baringo, West Pokot	*L. donovani*	*P. martini* Suspected: *P. celiae* & *P.vansomeranae (N. E. Province)*
		Eastern Province	Districts: Kitui, Meru, Machakos		
		North Eastern Province	Districts: Mandera, Wajir		
	Cutaneous	Rift Valley Province	Baringo district	*L. major*	*P. duboscqui* *P. guggisbergi*
			Laikipia, Samburu, Nakuru districts	*L. tropica*	
		Eastern Province	Kitui district	*L. major*	
			Isiolo district	*L. tropica*	
		Central Province	Nyandarua district	*L. tropica*	
		Western Province	Bungoma district	*L. aethiopica*	*P. pediffer*

Table 1 (continued): Summary of leishmaniasis foci in eastern Africa

Country	Leishmaniasis Type	Endemic Foci		Parasite	Vector
Somalia	Visceral	Shabelle Region	Giohar – Middle Shabelle river valley	*L. donovani*	Likely: *P. martini*
		Bay Region	Baidoa town		
		Lower Juba Region	Lower Juba river valley		Likely: *P. martini* Possible: *P. vansomerenae*
		Gedo Region			Likely: *P. martini* Possible: *P. vansomerenae* or *P. celiae*
		Bakool Region	Haddur district, Tijeglow district		
North Sudan	Visceral	Gedarif State	Gedarif City, Atbara and Rahad river basins, Dinder National Park	*L. donovani*	*P. orientalis*
		Sennar State	Atbara and Rahad river basin		
		Kassala State	Atbara and Rahad river basin		
		Blue Nile State	Fung province		
		White Nile State	Nile river basin		
		South Kordofan State	Nuba mountains		
		Khartoum State	Nile river basin		
		West Darfur State			
	Cutaneous	Khartoum	Shendi-Atbara region	*L. major* *L. tropica*	Suspected: *P. papatasi*
		White Nile			
Southern Sudan	Visceral	Upper Nile State	Counties: Malakal, Tongo, Ulang, Latjor, Nasir, Kiechkuon, Baliet, Wuror	*L. donovani*	*P. orientalis*
		Unity (Western Upper Nile) State	Counties: Leer, Duar, Guit, Jekany, Niemme		
		Jonglei State	Counties: Lankien, Pieri		
		Eastern Equatoria State	Kapoeta County		Suspected: *P. martini*
Uganda	Visceral	Pokot County	Nakapiripirit district	*L. donovani*	*P. martini*

Figure 1: Map of leishmaniasis foci in eastern Africa



Note: Map adapted from figures in Osman *et al.* (2000), Elnaim *et al.* (2003), Marlet *et al.* (2003), Alvar *et al.* (2007) and Kolaczinski *et al.* (2008), and refined through georeferencing of additional leishmaniasis endemic areas mentioned in the published literature.

1. INTRODUCTION

Available data from eastern Africa show that the leishmaniasis burden, especially that of visceral leishmaniasis (VL), is a major problem to public health in the region. Every year, health facilities report thousands of cases and hundreds of deaths, and in epidemic years the toll can be much higher. VL epidemics during the 1980s and 90s killed 100,000 people in Sudan alone. With routine surveillance in the region mostly limited to passive case detection at a few health facilities equipped to diagnose and treat the disease, the current morbidity and mortality figures likely underestimate the regional leishmaniasis burden. Prevalence surveys in a few sites and epidemiological simulations indicate that there is a large underlying pool of infected and infectious individuals.

It is highly likely that the leishmaniasis burden will increase, as a result of: i) increasing migration, ii) regional climate change, and iii) impaired immunity, resulting from malnutrition and/or HIV. Despite this, efforts to control the disease are either non-existent or remain sub-optimal, and are usually conducted in response to epidemic outbreaks. Measures needed to control leishmaniasis include standardized surveillance and reporting procedures, prompt and effective treatment, community education, and targeted distribution of long-lasting insecticide-treated mosquito nets (LLINs).

In an attempt to reverse the current leishmaniasis trend and strengthen regional control, this report provides an up-to-date picture on the distribution and burden of leishmaniasis in eastern Africa, past and present control efforts, as well as research activities. Based on these findings we identify key gaps in current intervention efforts in the region and put forward some recommendations on how control could be improved.

Objectives of present analysis

1. Present a detailed overview of the distribution and burden of leishmaniasis in eastern Africa.
2. Provide a picture of the national resources and structure available for leishmaniasis control.
3. Provide an overview of the main past and present control activities, and the implementing organisations involved.

The methods used to conduct this analysis included:

- A detailed literature review of published and 'grey' literature;
- Visits to endemic countries and discussions with key representatives of the Ministries of Health, lead implementing partners and key researchers;
- Sharing the draft report with partners to identify updates, gaps, and any additional information that should be included

2. BACKGROUND – LEISHMANIASIS IN EASTERN AFRICA

2.1 Epidemiology

Leishmaniasis is a neglected tropical disease (NTD) caused by protozoan parasites of the *Leishmania* genus, and transmitted by sandfly bites (Figure 2) from about 30 species that are proven vectors. There are three forms of leishmaniasis, visceral (VL), cutaneous (CL), and mucosal (ML). Of the three forms, VL is the most prevalent in eastern Africa, followed by CL and ML.

VL is the most severe form of leishmaniasis, almost always fatal if untreated. Over 90% of the estimated annual incidence of 500,000 VL cases worldwide occur in just six countries: Bangladesh, India, Nepal, Sudan, Ethiopia and Brazil. Eastern Africa has the second highest number of VL cases, after the Indian Subcontinent, and the disease is endemic in parts of Eritrea, Ethiopia, Kenya, Somalia, North Sudan, Southern Sudan and Uganda (Desjeux, 2004, Chappuis et al., 2007).

Figure 2. Phlebotomine sandfly

Source: Natural History Museum, http://www.nhm.ac.uk/about-us/news/2007/june/news_11804.html

VL in eastern Africa is usually caused by *L. donovani* and *L. infantum,* and sometimes *L. major*, and is characterized by a range of symptoms, including fever, weight loss, weakness, hepatomegaly, lymphadenopathy and splenomegaly. VL is also known as "kala-azar", which translates to "black disease", because of the skin pigmentation that can be a symptom. The incubation period ranges from three to eight months. Infected individuals are therefore unlikely to develop symptoms for several months after infection.

Post kala-azar dermal leishmaniasis (PKDL) can occur in patients who have been treated and recovered from VL. PKDL is characterized by a rash, usually starting around the mouth and spreading to other parts of the body. PKDL is primarily associated with *L. donovani* infection and in eastern Africa is most common in North Sudan, where it affects about 50% of treated VL patients (Zijlstra et al., 2003). The presence of PKDL is important, as continuing infection in the patient can provide a reservoir for parasites and facilitate infections of others. The majority of cases spontaneously heal, but severe cases can be treated with anti-leishmanial drugs.

CL is the most common form of leishmaniasis globally, with an annual incidence of 1-1.5 million cases (Desjeux, 2004). 90% of infections are concentrated in Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia, and Syria. The disease is of limited importance in eastern African where it occurs in small foci in North Sudan, Kenya, and Ethiopia. CL is

characterized by sores on the skin that can enlarge over time and ulcerate. Unlike VL, CL is rarely fatal and heals on its own over time, but this may take between three to eighteen months (Piscopo and Mallia Azzopardi, 2007). CL often results in considerable scaring of the affected areas, which may in turn lead to stigmatisation of people affected.

Transmission of *Leishmania* parasites can be zoonotic (i.e. from animals such as dogs and rodents to humans) or anthroponotic (i.e. from infected humans to non-infected humans). Several sandfly species have been incriminated as vectors of leishmaniasis. Feeding and resting patterns may differ between sandfly species, but typically they feed close to their breeding grounds and mostly between dusk and dawn.

2.2 *Risk Factors*

In areas where leishmaniasis has been endemic for a long time, children are at greatest risk. At their young age they have not yet developed immunity to the disease; many adults in endemic communities are reservoirs of infection, facilitating continuing disease transmission to those without immunity. Acacia trees and termite hills (Figure 3), common in many of the endemic countries in eastern Africa, are common breeding and resting sites for certain species of sandflies, and proximity to them is thought to be a risk factor of infection. Nomadic populations, and men who work in agricultural or pastoral settings are also often at increased risk, due to increased time spent outdoors and thus higher exposure to the sandfly vector, especially for those who sleep outside.

Figure 3. Termite hill in a compound, Pokot County, Uganda

Source: J. Kolaczinski

Conditions such as malnutrition and HIV have also been shown to increase the risk of developing VL and exacerbating the severity of the disease. Rainfall and temperature have been cited as associated with transmission, but the nature of the association seems to vary depending on the country. Information on country-specific risk factors will be presented below.

2.3 Diagnosis

Because of the diverse epidemiology of leishmaniasis across countries and regions, the most appropriate diagnostic method to detect infection and disease can vary. Generally, the gold standard VL diagnosis is the microscopic confirmation of parasites in tissue aspirates from the spleen, lymph nodes or bone marrow. Splenic aspirates have the highest sensitivity, but due to the clinical and laboratory expertise and resources needed to perform such a test, and the potential risk of fatal bleeding, it is not used as a routine diagnostic test in developing countries. Serological testing is increasingly used, usually using a rapid dip-stick test (rK39) or a direct agglutination test (DAT). The rK39 rapid diagnostic test (RDT) is easy to use and can usually be performed in the field or at the lowest level health facility; it has become the first line diagnostic in many places. Though DAT samples are easy to collect and can be performed from a few drops of blood, it requires well-trained technicians and good laboratory facilities to assess the samples. Most diagnostic algorithms utilize two or three diagnostic methods for confirmation of negative results.

2.4 Treatment

Current treatment options are very limited; most are expensive and problematic due to issues of resistance, toxicity and side-effects. Country-specific drug information is shown in table 2. Pentavalent antimonials (sodium stibogluconate (SSG) or meglumine antimonate) are traditionally the first line treatment for VL and CL (Davidson, 1998). There are significant disadvantages to using antimonials though, including potentially toxic effects and increasing reports of treatment non-responsiveness (i.e. a sign for possible emergence of drug resistance). Amphotericin B, particularly its lipid formulation AmBisome®, is often used to treat VL and CL, especially in areas where SSG resistance is increasing. However, with Amphotericin B there are also serious issues with toxicity, and its cost is often prohibitively high.

The Institute for OneWorld Health has tested the safety and efficacy of paromomycin, a comparatively inexpensive treatment for VL, and it was approved for use in India in 2006. A topical form of paromomycin can also be used to treat CL. Paromomycin trials are currently underway in eastern Africa. The first oral treatment for leishmaniasis, Miltefosine®, has been developed and is in the process of being registered and studied in some countries of eastern Africa. Despite the advantage of being orally administered and having a shorter duration of treatment (2 weeks), there are some moderate gastro-intestinal side-effects. Due to reported teratogenicity in laboratory animals it also is contra-indicated for used in pregnant women and women of child-bearing age. Several trials are underway in the region to investigate the safety and effectiveness of various combination therapies, which may improve survival and cure rates, and decrease side-effects.

Table 2: Drugs used to treat VL in eastern Africa

Country	First line	Second line	Registered drugs	Drugs in registration process	Drugs supplied by
Eritrea	SSG or meglumine antimonate	None	Antimonial therapy	None	MoH
Ethiopia	SSG	Amphotericin B, AmBisome®	SSG, Amphotericin B, Pentamidine (AmBisome® on National Drug List)	Miltefosine®, Glucantime®	MSF-H, WHO, HAPCO (in HIV co-infected patients)
Kenya	SSG	AmBisome®	SSG	Glucantime®	WHO
Somalia	SSG	AmBisome®			WHO
North Sudan	SSG	AmBisome® (SSG/ paromomycin as alternative)	SSG, antimonials (AmBisome® on essential drugs list)	Miltefosine®	MoH, MSF-CH, WHO
Southern Sudan	MoH: SSG MSF-H: SSG/ paromomycin	MoH: SSG/ paromomycin MSF-H: AmBisome®	SSG (Glucantime® & paromomycin on essential drugs list)		MSF-H, WHO
Uganda	SSG, Glucantime®	Amphotericin B	SSG, Glucantime®		DNDi

3. ERITREA

3.1 Background

Eritrea covers an area of 122,600 km^2 on the Red Sea, between Djibouti and North Sudan, bordering Ethiopia to the south. The country is divided into six administrative regions, called zoba (plural zobatat), namely Anseba, Debub, Southern Red Sea, Gash Barka, Maekel and Northern Red Sea. The population was estimated to be around 3,5 million in 2007 (MoH Eritrea, unpublished), 43% of which were below the age of 15 years (CIA, 2009a). The landscape is dominated by north-south trending highlands, which descend to a coastal desert plain in the east, to hilly terrain in the northwest and to rolling plains in the southwest. The climate varies considerably as a result of altitude. The desert strip on the Red Sea coast is hot and dry, while the central highlands benefit from cooler and wetter climate with up to 61 cm of rainfall annually (heaviest from June to September); the western hills and lowlands are semiarid. In general, rains are scarce and the country is prone to recurrent droughts, interfering with agricultural production. Eritrea's recent harvests have been unable to meet the food needs of the country. As in many other African countries, the economy is largely based on subsistence agriculture, with 80% of the population involved in farming and herding.

In 2006, Eritrea had 26 hospitals, 56 health centres, 182 health stations and 114 clinics. Out of these facilities 63% were operated by the MoH and about 18% by the Catholic Church, the second largest health care provider. Access to basic health services has been estimated to be 70% (MoH Eritrea, unpublished). Despite this relatively good access to health care, about 43 infants die per 1000 live births (CIA, 2009a) and about 58 children die before the age of five; life expectancy at birth is 65 years (WHO, 2010). Malaria continues to be the vector-borne disease of greatest importance to public health (Sintasath et al., 2005), although control has been highly successful (Nyarango et al., 2006, Mufunda et al., 2007). Lymphatic filariasis, dengue and leishmaniasis have also been reported as endemic, but there are limited data on the distribution of these diseases (MoH Eritrea, unpublished).

Control of vector-borne disease is overseen by the Division for Disease Prevention and Control (DPC) in the Health Services Department of the MoH. DPC oversees both communicable and non-communicable diseases. To date, limited NTD control activities have been undertaken in Eritrea, but a strategic plan for integrated control is under development, addressing all endemic NTD including leishmaniasis. The national plan clearly identifies the government's aim to control leishmaniasis to a level where it is no longer a public health problem, and to eventually eliminate it (MoH Eritrea, unpublished). The plan also foresees the formation of a steering committee, to ensure overall facilitation, implementation and monitoring and evaluation of NTD activities. The committee will also support the collaboration between different stakeholders and conduct coordination of activities.

No specific funding to support integrated NTD control has been identified, but Eritrea along with ten other countries in the East and South African region have been included in a proposal for integrated NTD control developed by the World Health Organization's (WHO) regional office for Africa (AFRO) for consideration by the African Development Bank.

3.2 Visceral Leishmaniasis Epidemiology

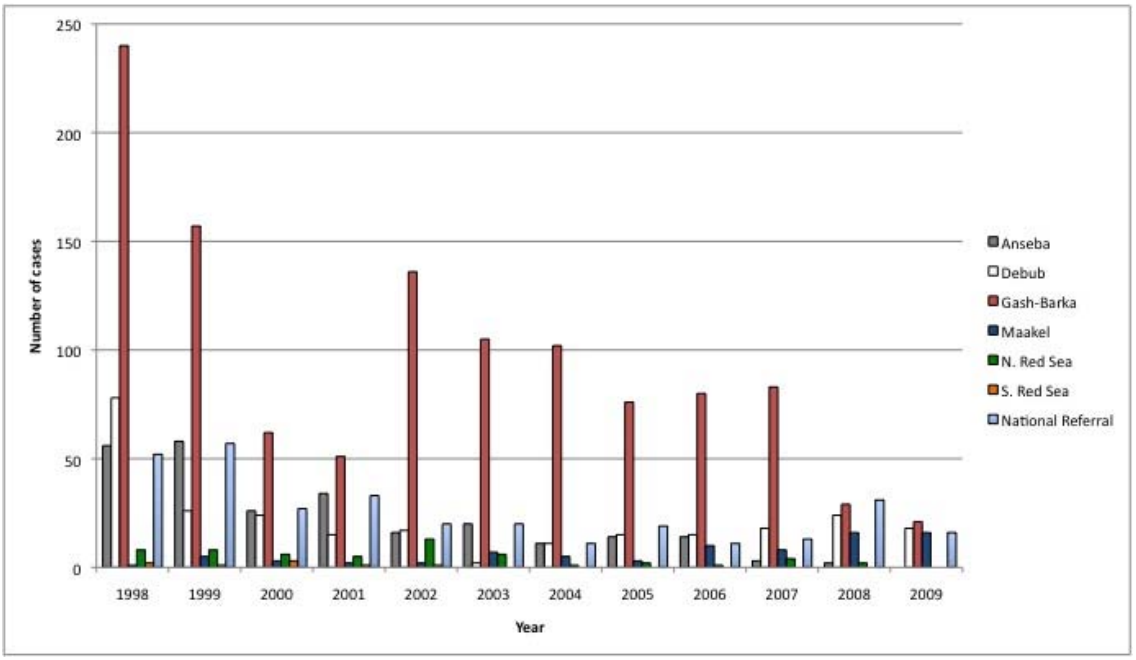
3.2.1 Parasite and vector

Both the parasite causing VL and the vector(s) responsible for transmission have not been identified in Eritrea, nor is it clear whether transmission involves hosts other than humans (i.e. is zoonotic).

3.2.2 Geographical distribution

Passive case-detection data collected through the health information management system (HMIS) indicate that leishmaniasis cases have been reported from all six zobatat (Figure 4). Gash Bharka zoba is worst affected, followed by Debub and Anseba; only a few cases have been reported each year from the other three zobatat, with no cases having been reported from Southern Red Sea since 2002. The three main affected zobatat of Eritrea border North Sudan and/or Ethiopia; the border areas of both of these countries are also leishmaniasis endemic (Ayele & Ali, 1984; Osman et al., 2000; Lyons et al., 2003) and cross-border transmission is likely to occur.

Figure 4: Cases of leishmaniasis recorded by the Eritrean HMIS system, 1998-2009



Note: Visceral and cutaneous manifestations are not being differentiated by the HMIS. Data are shown for the six regions and the national referral facility, Orotta hospital, in the capital Asmara.

Unfortunately, the HMIS system does not separately record data on the visceral and cutaneous manifestations of the disease, and it thus remains unclear whether all of the above regions are affected by both pathological forms, or whether there are specific foci of each form that may not be overlapping. Reports of MoH officials and medical doctors working in Eritrea indicate that VL predominantly occurs in the lower lying border areas with Sudan and Ethiopia, while CL transmission is confined to areas of higher altitude in Anseba and Debub region (Personal communication, Dr Goitom Mebrahtu, MoH, and Dr Margot Anderson, Orotta School of Medicine).

3.2.3 Risk factors

There are no data on leishmaniasis risk factors in Eritrea.

3.3 Cutaneous Leishmaniasis Epidemiology

It is presently unclear where exactly CL is endemic in Eritrea, which vector(s) is/are responsible for transmission and whether transmission is anthroponotic or zoonotic. Parasitological examination of skin samples by dermatologists in Asmara has, however, identified *L. tropica* as the causative agent for CL in Eritrea (MoH Eritrea, unpublished).

3.4 Leishmaniasis Control – Prevention, Diagnosis and Treatment

3.4.1 Surveillance

A national HMIS has been in place since 1998, collecting data on a monthly basis from nearly all governmental and non-governmental health facilities. Data collection forms, unfortunately, do not differentiate between the cutaneous and visceral forms of leishmaniasis, and data are group into two age categories (< 5 years of age and ≥ 5 years of age); disaggregation by sex is presently also not possible. Due to lack of diagnostic facilities at the peripheral level (see below), it is likely that some leishmaniasis infections are misdiagnosed as other diseases, particularly because the leishmaniasis endemic areas are co-endemic for malaria (Sintasath et al., 2005), which has similar symptoms to VL. Since 2002, Eritrea also implements an Integrated Disease Surveillance and Response (IDSR) system, which has been able to substantially increase reporting of data on priority disease from health care centres (Somda et al., 2009). The IDSR system, however, does not include leishmaniasis.

3.4.2 Diagnosis

To date, the Eritrean MoH has not developed diagnostic algorithms for VL or CL, nor any case-definitions. At the periphery, diagnosis is purely based on clinical signs, while parasitological diagnosis of VL is conducted on aspirates from bone marrow or the spleen at some regional hospitals and at the National Referral Centre, Orotta Hospital, in Asmara. At the latter facility skin smears are used to confirm CL infection. RDTs, the DAT or other diagnostic tests are not used for leishmaniasis in Eritrea.

3.4.3 Treatment

Pentavalent antimonial drugs are the sole leishmaniasis treatment used in Eritrea and are only available at the regional hospitals and at Orotta hospital in Asmara. Both SSG and meglumine antimonate have been used for treatment, depending on availability from the manufacturers. Drugs for leishmaniasis treatment are managed by Pharmecor, a company based in Asmara that provides all medical supplies to the public sector and to some private sector facilities. Procurement of antimonial drugs is entirely funded by the MoH. Leishmaniasis treatment is currently in short supply, but an order for 5,000 ampoules of meglumine antimonate has been placed with Sanofi and is expected to arrive shortly. Drug orders are calculated assuming that an average of 100 patients need treatment per annum, as indicated by the available passive case-detection data. Regional hospitals in leishmaniasis endemic areas usually hold a buffer stock of antimonial treatment, and request additional supplies from Pharmecor when the need arises.

3.4.4 Prevention

To date, no prevention activities with the specific aim of controlling leishmaniasis have been conducted; for such activities a better understanding of the vector(s) and their behaviour would be required (Killick-Kendrick, 1999). However, since 2000 Eritrea has massively scaled up vector control activities targeting *Anopheles* mosquitoes as part of implementing the strategic plan for malaria control (Nyarango et al., 2006), which has been financed by the Eritrean Government, the World Bank, WHO, UNICEF, USAID and the Global Funds. By 2004, approximately 81% households owned at least one net, of which 73% were insecticide-treated nets (ITNs), and 59% of children 0–5 years slept under a net. The number of houses sprayed with either DDT or Malathion increased from 39,838 in 2000 to 92,107 in 2004, covering about 13% of the population at risk of malaria. As a result of these and concerted case-management improvements, the malaria control programme exceeded the national targets of 80% reduction in malaria morbidity and mortality after only five years, and surpassed its objective of ensuring that 60% of households owned an ITNs (Nyarango et al., 2006, Mufunda et al., 2007). As it happens, zobatat endemic for malaria are also affected by leishmaniasis, in particular Gash Barka (Sintasath et al., 2005), and it would not be surprising if the concerted malaria control efforts had also led to a reduction in leishmaniasis transmission, if the Eritrean vector(s) is/are peridomestic (Killick-Kendrick, 1999). By 2004, at least 75% of households in Gash Barka were observed to own more than one ITN (Eisele et al., 2006, Nyarango et al., 2006), nets were used by 76% of children under five years and 52% of pregnant women and 42% of the households had been covered by indoor residual spraying (IRS).

3.4.5 Implementing Partners

All VL cases are managed in MoH facilities; the WHO is providing technical support on the development of an integrated NTD control strategy for Eritrea, but no commodity support.

4. ETHIOPIA

4.1 Background

Ethiopia is a landlocked country in the horn of Africa covering an area of 1,104,300 km^2, bordered by Djibouti and Somalia in the east, Sudan in the west, Eritrea in the north, and Kenya in the south. The country is dominated by northern and central plateaus and divided by the Great Rift Valley, surrounded by lowlands areas in the east and west. The climate ranges from cold and wet weather in the highlands, with average annual rainfall above 1,000mm, to hot and dry in the lowlands with unreliable rainfall, usually below 500mm annually. With an estimated population of over 88 million in 2010, Ethiopia is one of the most populous countries in sub-Saharan Africa. The population is young, with 46% aged under 15 years and less than 3% over the age of 60 (CIA, 2009b).

Ethiopia's administrative structure consists of nine regional states, two city administrations, 80 zones, and 551 districts (so-called woredas). Health care in the public sector is delivered through a three-tier health system, comprised of hospitals (specialised referral, regional or district), district-level health centres and community-level health posts. The health centres and satellite health posts also constitute the so-called primary health care unit. Management of the health system is decentralised, with many decisions made at the Regional Health Bureaus, Zonal or District Health Offices. Although only 17% of the population lives in cities, the healthcare infrastructure is disproportionately skewed towards urban areas, and the majority of the rural population has only limited healthcare access (CIA, 2009b).

Limited access to care is reflected in the life expectancy of 57 years, and high infant and under-five mortality rates of 75 and 119 per 1000 live births, respectively. Maternal mortality is also high at 720 per 100,000 live births, with only 6% of births attended by skilled health personnel, which is much lower than the figure of 46% for the WHO African region as a whole (WHO, 2009). The Ethiopian government spends 10% of its budget on health care, which is above average for the WHO African Region (8.7%), but there is less than one physician for every 10,000 people (WHO, 2009). Over 40% of national spending on health comes from private expenditure, 80.6% of which is out of pocket spending (WHO, 2009).

To increase access for rural populations, the government launched the Health Extension Programme (HEP) in 2003 as part of the Accelerated Expansion of Primary Health Care Coverage plan, aiming to provide universal primary health care coverage by 2009. HEP focuses on providing accessible and equitable services, particularly in rural areas, by improving prevention skills and behaviours within the household, and involving fewer facility-based services than traditional primary health care. However, despite increased government efforts, many problems remain and scale up of HEP is far from complete. A high burden of communicable disease continues to result from widespread malnutrition, food insecurity and poor sanitation, while quick diagnosis and appropriate treatment are hampered by a lack of trained health staff and well-equipped health facilities.

Leishmaniasis is an important vector-borne disease in Ethiopia and both VL and CL are endemic (Hailu and Frommel, 1993). The MoH estimates the annual burden of VL to be

between 4,500 and 5,000 cases (FMoH Ethiopia, 2006). While there is currently no reliable estimate of the prevalence of CL, experts estimate that the number of CL cases significantly exceeds that of VL (Personal communication, Dr. Asrat Hailu, AAU & Dr. Abraham Aseffa, AHRI). Known VL endemic foci are in the arid south-west, and the Humera and Metema lowlands in the north-west. The definitive reservoir of VL in Ethiopia remains unknown, although transmission is assumed to be anthroponotic (WHO, 1996). CL is confined mainly to the highlands, although occasional cases have occurred in the Omo Valley, and transmission is currently thought to be zoonotic.

4.2 Visceral Leishmaniasis Epidemiology

4.2.1 Parasite and vector

VL in Ethiopia is caused by infection with *L. donovani,* although *L. infantum* was identified in six splenic aspirate isolates during an outbreak in Libo Kemkem, Amhara Region (Alvar et al., 2007). Both *P. orientalis* and *P. martini* have been confirmed as vectors of VL in Ethiopia, and both species breed and rest in the termite mounds common to the area. *P. celiae* is a possible auxiliary vector in Aba Roba and Weyto valley in the southwest. Detailed information about parasites and vectors found in specific disease foci is shown in table 3. Although some studies propose that there is evidence of zoonotic transmission due to the presence of VL in usually uninhabited areas or the isolation of *L. donovani* in some animal species (e.g. dogs), there is currently no conclusive evidence of zoonotic VL transmission in Ethiopia (Ayele and Ali, 1984, Ali and Ashford, 1994, Bashaye et al., 2009).

4.2.2 Geographical distribution

HIV/AIDS co-infection

The north-western VL focus in Ethiopia has the highest known VL/HIV co-infection rate in the world. Approximately 20-30% of VL patients are estimated to have HIV (Lyons et al., 2003, ter Horst et al., 2008). Co-infection, especially when combined with malnutrition, contributes to an increased fatality rate (Mengesha and Abuhoy, 1978, Haile and Anderson, 2006).

Northwest

The north-western VL focus in Ethiopia covers the semi-arid Metema and Humera plains in Tigray and Amhara regional states bordering Sudan. Historically, this area reported only sporadic cases, but a marked increase occurred during the 1970s when migrants from the non-endemic highlands began to arrive in the area to harvest crops on the large-scale agricultural schemes introduced at the time (Tekle et al., 1970, Ashford et al., 1973, Fuller et al., 1976b, Mengesha and Abuhoy, 1978, Maru, 1979, Hailu and Frommel, 1993). VL in the area predominantly affects young male migrant workers, who tend to sleep outdoors thereby increasing their exposure, and cases peak during the dry season from November to March (Fuller et al., 1976b, Mengesha and Abuhoy, 1978, Ritmeijer et al., 2001). PKDL is also endemic to the Metema-Humera focus, which is an extension of the endemic area in North Sudan (Zijlstra et al., 2003). Since 2003, new settlers who

are being relocated from highland areas to Kafta Humera, Tsegede and Armacho woredas also constitute a new vulnerable population in the area. The relocation corresponds with a dramatic increase in VL cases recorded by Médecins Sans Frontières (MSF) in the area during 2002-2003.

In 2005, an outbreak of VL in Libo Kemkem woreda, a highland area of Amhara regional state, was identified by MSF-Greece. The outbreak began in Bur kebele in 2003, with cases peaking in 2005 and occurring mainly in Libo Kemkem and Fogera woredas, ultimately becoming a low-incidence endemic area by 2007 (Alvar et al., 2007, Herrero et al., 2009). By 2007, around 2,450 primary cases and 120 deaths had been reported since the outbreak began in 2003, with the majority of cases treated at Addis Zemen health centre (Bashaye et al., 2009). Data showed that over 70% of cases occurred in males. It is likely that agricultural workers returning from Humera and Metema introduced the disease to the predominantly agricultural area (Bashaye et al., 2009, Herrero et al., 2009). These cases, and some reported in the 1970s in Belessa, an area in the Gondar region north of Libo Kemkem, are the only recorded VL cases from highland areas in Ethiopia (Ashford et al., 1973). The vector species in this area has yet to be identified. Infected dogs were identified during the survey, and VL infection in humans was strongly associated with dog ownership, suggesting that domestic dogs may play a role in the transmission cycle in this area (Bashaye et al., 2009).

Southwest

The southwest foci include the Omo plains, Aba Roba plains and Weyto River Valley in Southern Nations and Nationalities People's Region (SNNPR) – all areas of lowland savannah with low rainfall. The lower Omo plains are the oldest known VL focus in Ethiopia, first identified in the 1940s (Coles et al., 1942). Most of the population has been exposed to the disease and acquired some immunity, as indicated by a positivity rate of up to 64% using the leishmanin skin test in some tribes (Fuller et al., 1979). The majority of people in these foci are nomadic or semi-nomadic pastoralists.

The other main focus in the southwest occurs in the lower course of the Rift Valley, most notably the Segen (Aba Roba focus) and Weyto valleys in the drainage basin of the Chew Bahir lake, near Konso woreda. The Aba Roba focus has a particularly high VL endemicity and high population immunity, with 36.4% testing positive with the leishmanin skin test (Ali and Ashford, 1993). The majority of cases occur in young males who have yet to develop immunity but experience high exposure to the disease (Ali and Ashford, 1994). The onset of disease in this area tends to be gradual and is characterised by enlarged lymph nodes (Lindtjorn and Olafsson, 1983). Cases in this area peak during the wet seasons, from February to May, and September to October (Gebre-Michael and Lane, 1996).

Sporadic cases have also occurred further north in the middle course of the rift valley in SNNPR, with cases reported from Lake Abaya, and the Dawa and Galena valleys in Sidamo woreda (Lindtjorn, 1980, Lindtjorn, 1987, Ayele and Ali, 1984). Cases here are relatively rare, and the prevalence of skin test positives in the area is low (Berhe et al., 1998). VL has also been reported further east in the Moyale area and Genale river basin near the Kenyan border, Oromia regional state (Ayele and Ali, 1984).

Table 3: VL epidemiology in Ethiopia

Regional State	Disease foci	Parasite	Vector	Main outbreaks (area: year)
SNNPR	• Omo woreda - Omo plains • Lower Rift Valley, Konso Woreda: - Segen Valley (Aba Roba focus) - Weyto Valley • Middle Rift Valley, Sidamo Woreda: - Lake Abaya - Dawa Valley - Galena Valley	*L. donovani*	Omo: *P. orientalis* Konso: *P. martini (confirmed)* *P. celiae (suspected)*	
Oromia	• Moyale • Genale valley	*L. donovani*	-	
Somali	• Afder & Liban Woreda	*L. donovani*	-	border with Kenya and Somalia: 2001
Tigray	• Humera plains	*L. donovani*	*P. orientalis*	Humera: 1970s & 1996, now endemic
Amhara	• Metema plains • Libo Kemkem & Fogera Woredas	*L. donovani* Libo Kemkem: *L. dononvani; L. infantum*	*P. orientalis*	Metema: Outbreak - 1970s & 1996 Libo Kemkem: 2003 - 6, now endemic Belessa highlands, Gondar: 1972
Afar	• Awash Valley			

Southeast

In 2001 an outbreak on the border between Kenya, Somalia and southeast Ethiopia was identified, affecting Afder and Liban zones in Ethiopia's Somali Region (Marlet et al., 2003a). The majority of cases occurred within nomadic tribes who graze their cattle over the borders. Although few previous reports of VL had been made in this area, all the Ethiopian cases occurred in children, which could indicate existing transmission (Marlet et al., 2003a). *L. donovani* was found to be the causative agent.

In March 2010, some DAT samples taken in Afder and Gode zones by MSF-H (Dutch Section) from areas that previously were thought to be VL-free tested positive for VL. There is currently no estimate on the number of cases in this area, as the new cases were identified very recently.

Northeast

Cases of VL have also been recorded in the Awash Valley in Amhara and Afar regional states in the northeast, which also experienced expanding agricultural development and an influx of migrant workers during the 1970s (Fuller et al., 1976a).

4.2.3 Risk factors

Various risk factors have been associated with VL transmission in Ethiopia. The majority of VL cases throughout the country occur in males, a pattern caused by increased exposure to the sandfly vector during agricultural or pastoral work. The age groups affected tend to reflect exposure, and the length of time VL has been present in the area. In areas where the disease has been endemic for many years, more cases occur in younger age groups as they have yet to develop the acquired immunity seen in adults. In outbreaks or areas where the disease has recently been introduced, all ages are susceptible, and most cases occur in groups that have regular contact with sandfly habitats (Ali and Ashford, 1994).

VL transmission also seems to be associated with humidity, as measured by the amount of rainfall, although no universal pattern has been established (Gebre-Michael and Lane, 1996). For example, in the southwest foci, the greatest risk of infection is likely to occur in the rainy season, during which the vector population increases and the human population is more exposed to sandfly biting due to intensified farming and grazing activities (Ayele and Ali, 1984). In the northwest, however, cases peak just after the rainy season when the majority of migrant workers leave the highlands to work on lowland farms during the harvest. These workers also sleep outdoors, thereby increasing their exposure to the vector.

The high rate of HIV infection in this migrant population has an impact on treatment outcomes. The case fatality rate for VL patients in an MSF-supported control programme in Tigray was much higher compared to areas with lower rates of HIV. HIV positive cases were four times more likely to die than those who were not (Lyons et al., 2003).

A recent study investigating risk factors associated with the outbreak in Libo Kemkem identified dog ownership and habitual outdoor-sleeping to be risk factors for infection (Bashaye et al., 2009). The study also found that keeping cattle indoors, lack of mosquito net ownership and un-plastered walls were also associated with increased VL risk. The Armauer Hansen Research Institute (AHRI) is currently in the final year of a three-year risk factor assessment in Libo Kemkem, which focuses on the interaction of malnutrition and immunology (Personal communication, Dr. Abraham Aseffa, AHRI). Other studies in Ethiopia have found additional factors such as proximity to termite hills and poor nutritional status to be associated with increased VL risk (Ali, 1997a, Ali, 1997b).

4.3 Cutaneous Leishmaniasis Epidemiology

CL was first described in Ethiopia in 1913 and is common in highland areas between 1,400 to 2,700 m (Balzer et al., 1960, Ashford et al., 1973, Hailu and Frommel, 1993). The majority of CL in Ethiopia is caused by *L. aethiopica*, (Lemma et al., 1969, Ashford et al., 1973, Lindtjorn, 1981) with rare cases caused by *L. major* and *L. tropica* (Fuller et al., 1979). CL due to *L. aethiopica* manifests itself in three forms, all of which are found in Ethiopia: localised cutaneous (LCL), ML and diffused cutaneous leishmaniasis (DCL) (Ashford et al., 1973, Gebre-Michael et al., 2004). Infection is largely transmitted by *P. longipes*, although *P. pedifer* is also known to transmit the infections (Table 4). CL transmission in Ethiopia is zoonotic, with the rock hyrax acting as the main reservoir (Ashford et al., 1973).

CL has been extensively studied in the western highlands and lake areas of the Rift Valley. The main areas of transmission include the Ochollo focus in the Rift Valley escarpment above Lake Abaya, the Kutaber area in the eastern Ethiopian plateau near Dessie, the Aleku area of Wollega zone, the south-west highlands of Bale and Sidamo, and the Sebeta area near Addis Ababa. The Ochollo focus is highly endemic for the disease, with higher prevalence in younger age groups. An outbreak in Silti woreda, SNNPR, 150km south of Addis Ababa, was reported in 2005. A CL prevalence of 4.8% was recorded, which exceeded prevalence rates previously reported from Ochollo (Ashford et al., 1973, Negera et al., 2008). Unlike endemic areas such as Ochollo, where prevalence is highest in children aged 0-10 years, the majority of cases in the Silti outbreak occurred in those aged 11-20 years. This indicates a difference in immunity in the two areas, with adults in high prevalence areas demonstrating protective immunity, suggesting that the disease has only been recently introduced to Silti woreda.

Table 4: CL epidemiology in Ethiopia

Regional State	Disease foci	Parasite	Vector	Main outbreaks
SNNPR	Ochollo village Sidamo zone Silti woreda	*L. aethiopica* *L. major* *L. tropica*	*P. longipes* *P. pedifer*	Ochollo: highly endemic; most prevalent in those 0-10 years Silti woreda: 2005 outbreak with a prevalence of 4.8% recorded, majority of cases in those 11-20 years
Oromia	Wollega province: - Aleku area Bale	*L. aethiopica*	*P. longipes*	
Amhara	Kutaber woreda	*L. aethiopica*	*P. longipes*	

4.4 Leishmaniasis Control – Prevention, Diagnosis and Treatment

Leishmaniasis in Ethiopia was formerly overseen by the MoH's Communicable Disease Department, but after the MoH underwent a large reorganisation in 2007, responsibility for leishmaniasis has been decentralized. The MoH is now organized into three directorates, including the Directorate for Health Promotion and Disease Prevention, which covers most communicable disease including NTDs. The directorate is organized in urban, agrarian, and pastoralist sub-directorates, each responsible for a set of regional states. Health officers are assigned to the regional state to manage overall health promotion and disease prevention, and thus oversee all diseases, instead of having disease-specific duties. However, there is also a group of MoH staff working specifically on NTDs in collaboration with WHO and other partners to finalize a strategic plan for integrated NTD control. The group is currently chaired by Dr. Tizita Hailu (Personal communication, Hunegnaw Mekonnen, MoH).

A National Leishmaniasis Task Force was established in 2007 with the aim of eliminating VL by 2015. The task force includes members from the Institute of Pathobiology at Addis Ababa University; the Drugs for Neglected Diseases Initiative (DNDi); MSF-H; International Training and Education Centre for Health (ITECH); WHO; MoH HIV/AIDS Prevention and Control Office (HAPCO); AHRI; Ethiopian Health and Nutrition Research Institute (EHNRI); Spanish Agency for International Cooperation for Development (AECID); and affected regional offices. Meetings are held on an ad hoc basis and are chaired by the MoH NTD focal person.

There is no specific governmental budget allocated to leishmaniasis control. The MoH supplies salaries and office space, but does not provide diagnostics or drugs. The first national guidelines for VL case-management were developed in 2006, providing diagnostic and treatment algorithms for each level of the health system. The guidelines are currently being revised by MoH in collaboration with WHO and other partners, and will also include guidelines for care of CL patients.

Hospitals and health centres in endemic regions equipped to treat VL include: Humera Hospital, Axum Hospital and Makelle Hospital in Tigray regional state, Gondar University Hospital, Metema Hospital, Bahir Dar Hospital and Abderafi health centre in Amhara regional state, Arba Minch Hospital in SNNPR, and Tikur Anbessa Hospital in Addis Ababa.

4.4.1 Surveillance

At present there is no standardised national reporting system for leishmaniasis in Ethiopia, but a HMIS for the collection of national health statistics has recently been introduced by the MoH and includes leishmaniasis in its surveillance categories. However, there are still no available data on number of cases nationally or by regional state. WHO, along with the MoH and other partners have developed a standardised reporting format for VL for use between the districts and regional states, which is pending endorsement from the task force. Except for Amhara regional state, leishmaniasis is not included in the IDSR Strategy (Personal communication, Merce Herrero & Abate Mulugeta, WHO).

WHO are collaborating with the MoH to map the geographic distribution of VL nationwide, funded by the Spanish Government. The first phase includes mapping the

disease in Amhara, Tigray, Oromia and Somali regional states, and the second phase will include expansion into SNNPR, Afar, Gambella and Benishangul Gumuz regional states. This mapping exercise will assess VL distribution through leishmanin skin tests, serology, active case finding and community based surveys, investigate the presence of animal reservoirs, and conduct entomological studies.

Much less is known about the distribution and burden of CL in Ethiopia. AHRI began a GPS mapping project in 2009 to identify areas of Ethiopia where CL is currently present. A team of clinicians, laboratory technicians, and geographic information system (GIS) experts are sent to locations where CL had been reported to confirm its presence and to inquire about other endemic areas. This mapping project is ongoing and no results have been released to date (Personal communication, Abraham Aseffa, AHRI).

4.4.2 Diagnosis

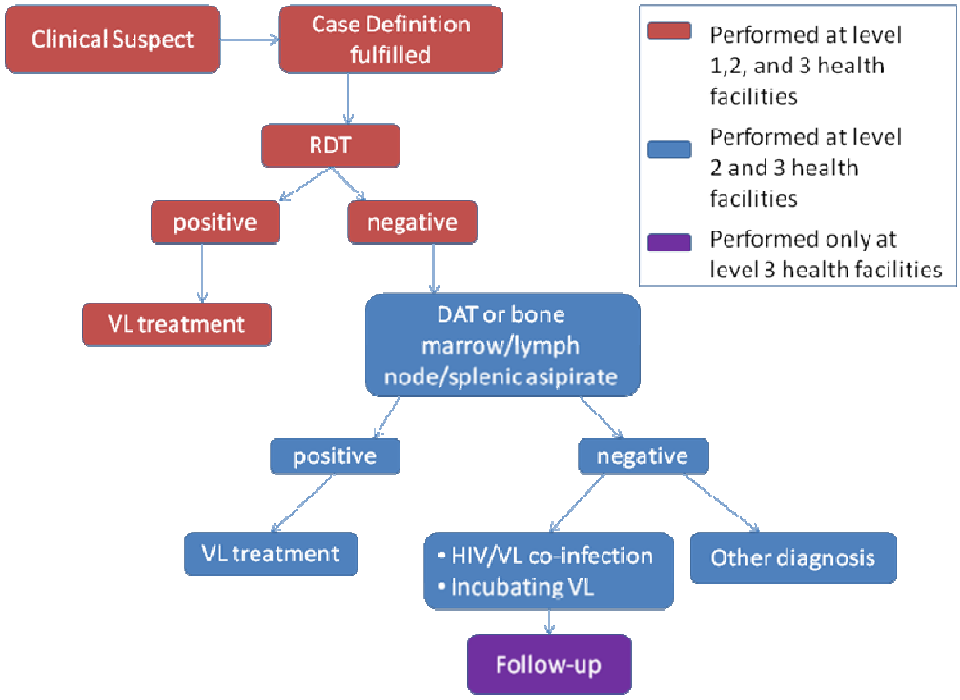
The national guidelines recommend clinical diagnosis and use of rK39 RDTs at health centres, with treatment of positive cases occurring on site (Figure 5). Clinical cases that are negative with the rK39 RDT are referred for further diagnosis using DAT and/or lymph node or bone marrow aspirate at district or zonal hospitals. Diagnosis using splenic aspirate is only recommended at zonal or specialised referral hospitals. Despite these guidelines, there seem to be few staff adequately trained to conduct such procedures in government-run facilities. RDTs used at MoH facilities are provided by WHO or MSF-H.

MSF-H diagnoses clinically suspected cases with rK39 RDT at outreach health centres, and refers cases for confirmation or treatment to its treatment centres. Cases with negative rK39 RDT results are referred to facilities fully supported by MSF-H for further diagnosis by DAT or splenic/lymph node aspirate if DAT is negative. Lymph node aspirates are conducted at the two centres currently supported by MSF-H, but splenic aspirates are only conducted at Kahsay Abera General Hospital in Humera, Tigray Region.

A number of studies have been conducted on the accuracy of diagnostic methods for VL in Ethiopia. The rK39 RDT has been reported to have a sensitivity of 71.7% (Diro et al., 2007), which is lower than DAT with a sensitivity as high as 97.7% (Hailu and Berhe, 2002). This high sensitivity is also retained when DAT is used to diagnose VL in HIV co-infected patients (Hailu and Berhe, 2002). However, the specificity of the rK39 RDT appears to be higher than DAT, at 82.4% compared to 62.7% specificity, respectively (Diro et al., 2007).

In 2009, MSF-H published results from a study conducted in 2006-2007 in Humera investigating the accuracy of the rK39 RDT. Sensitivity of the rK39 RDT was found to be 84%, which was lower than that found for DAT (94%). However, specificity of the rK39 RDT was higher than that of DAT, at 99%, compared to 92%, respectively. Sensitivity was also disaggregated by HIV-positive and HIV-negative patients, as Humera has a high prevalence of HIV. For both the rK39 RDT and DAT, sensitivity in HIV patients was significantly lower than that of the overall study sample, at 77% and 89%, respectively (ter Horst et al., 2009).

Figure 5: Ethiopian National Guidelines - VL Diagnostic Algorithm



AHRI has developed a simplified molecular diagnostic test for CL, in particular for infection with *L. aethiopica*. Past diagnostic methods such as electrophoresis are labour-intensive and slow, and the molecular differentiation between *L. aethiopica* and *L. tropica* has been difficult. The newly developed diagnostic test allows for immediate genotyping of the infection, which is particularly useful for outreach teams. The epidemiology of CL and its response to treatment vary according to infecting parasite species, therefore species-specific treatment is recommended. The results have been submitted for publication, and field tests for the diagnostic test are being planned (Personal communication, Abraham Aseffa, AHRI).

4.4.3 Treatment

Drugs registered for VL by the Drug Administration and Control Authority (DACA) in Ethiopia are pentamidine, SSG and amphotericin B. AmBisome® has been approved by the National Drug Advisory Committee and included on the National Drug List (NDL). Steps are also being taken to register Miltefosine®, and Sanofi Aventis are in the process of submitting Glucantime® for registration in Ethiopia, Kenya and Sudan. DNDi have recommended that all available drugs for leishmaniasis treatment are included in the NDL and in the national guidelines.

The government guidelines recommend SSG as the first line treatment for VL, and amphotericin B as second line treatment to be used in cases of toxicity, relapse and treatment failure. Amphotericin B is also recommended as a first line treatment for pregnant women. However, due to the high toxicity resulting from the use of

amphotericin B, AmBisome® is preferable despite its high cost. The guidelines also include recommendations for treatment of VL co-infection with malaria or HIV, relapses, PKDL, and evaluating cures. WHO provide SSG and AmBisome® to government-run facilities in VL endemic areas. HAPCO, the government office that manages HIV/AIDS in Ethiopia, plans to provide SSG and AmBisome® to HIV/VL co-infected patients.

MSF-H uses SSG as a first line treatment for VL, and use AmBisome® for HIV positive cases, relapse or treatment failures. The organisation provides these drugs to Humera and Axum hospitals in Tigray regional state, and Abderafi health centre in Amhara regional state.

In 2006, DNDi opened the Leishmaniasis Research and Treatment Centre (LRTC) within Arba Hospital, Arba Minch, SNNPR. LRTC is Africa's first research facility focusing on VL and is part of the DNDi supported LEAP, implemented in collaboration with the MoH, Addis Ababa University (AAU) and DACA. A trial testing a 17-day short-course of SSG/paromomycin combination therapy, compared to each drug used alone, finished in January 2010 with results to be reported later in 2010.

A Miltefosine®/AmBisome® combination trial planned for Sudan and Kenya will be expanded to Ethiopia in 2010, and, if successful, provide further support for the registration of Miltefosine®. A trial to determine the lowest, safe, single dose of AmBisome® commenced in Arba Minch and Gondar Hospitals in 2009, scheduled to be completed in June 2011. A study investigating the effectiveness of pentamidine as a secondary prophylaxis in HIV co-infected patients, led by the Institute of Tropical Medicine (ITM) in Belgium in collaboration with AAU, Gondar University, DNDi, and MSF-H, is currently under ethics committee review (Personal communication, Endeshaw Mengistu, MSF-H & Asrat Hailu, AAU).

EHNRI has conducted a pilot study on the efficacy of plants used by traditional healers to treat leishmaniasis, and obtained potentially promising results. The institute is now embarking on a more thorough research project to screen the active ingredients of about five to seven of these plants in the laboratory, to more conclusively determine their benefits. EHNRI estimates that up to 85% of the population in Ethiopia rely on traditional healers in some way, and therefore research into treatments provided through these providers is considered important (Personal communication, Amha Kebede & Geremew Tasew, EHNRI).

Currently there are no standard guidelines for the treatment of CL in Ethiopia. AHRI presently prefers to treat with cryotherapy, a topical treatment consisting of repeated sessions of applying liquid nitrogen to lesions, instead of the available drugs, which are potentially toxic. AHRI has been in discussions with WHO to initiate a clinical trial to test the efficacy of various available treatments for CL, particularly for CL due to *L. aethiopica* (Personal communication, Abraham Aseffa, AHRI).

4.4.4 Prevention

There are limited data on the use and effectiveness of ITNs in the control of VL in Ethiopia, although during the Libo Kemkem outbreak it was noted that ITN possession was associated with a decreased likelihood of becoming infected.

4.4.5 Implementing Partners

Due to the lack of government resources for VL control in Ethiopia, the support of various organisations is required to sustain surveillance, diagnosis, treatment and training, including MSF-H, WHO, DNDi, and AECID (Table 5).

MSF-H has been able to hand over some of its programmes to the MoH in recent years. Until January 2009, MSF-H provided full support for VL control to Humera Hospital (target population: 150,000), including staff, laboratory technicians, diagnosis, treatment and active outreach and case finding. In January, the hospital was handed over to the Tigray Regional Health Bureau although MSF continued to provide some support until June 2009. Axum Hospital, also in Humera, was also formerly supported by MSF-H, but had since been handed over to the government (Personal communication, Julius Olenge, MSF-H).

WHO is involved in procurement of drugs and diagnostics for VL, monitoring and evaluation, disease mapping, training of MoH staff, and capacity building at the federal level. WHO also works with ITECH in a programme funded by the AECID to standardise training materials, and develop a training manual aimed at clinicians, nurses and lab-technicians for VL diagnosis and treatment, and conduct training on the manual in VL endemic areas.

CL is currently mainly being treated at AAU, Gondar Hospital, and ALERT hospital (AHRI). AHRI staff also travel about once a week to Silti woreda to provide care, as they had been conducting research on CL in Silti and the local facilities are not yet equipped to manage CL cases (Personal communication, Asrat Hailu, AAU & Abraham Aseffa, AHRI).

Table 5: Leishmaniasis partners in Ethiopia

Organisation	Leishmaniasis Activities	Regions/Health Facilities
AAU	Diagnostic and treatment, research	Addis Ababa: Tikur Anbessa Hospital
AHRI	Research, diagnosis and treatment of CL	
DNDi	Clinical research, diagnosis, and treatment	SNNPR: Arba Minch Hospital Amhara: Gondar University Hospital
EHNRI	Research	Addis Ababa
MoH	Diagnosis and treatment	Tigray; Humera Hospital, Axum Hospital, Makelle Hospital Amhara; Metema Hospital, Addis Zemen Health Centre Addis Ababa: Tikur Anbessa Hospital
MSF-H	Training, diagnostic, treatment, health education, active case finding & referral	Amhara: Abderafi Health Centre Outreach sites: Tsegede, Metema and Tach Armacho
WHO	Diagnostics and treatment	Tigray: Makelle Hospital Amhara: Gondar University Hospital, Metema Hospital Addis Ababa: Tikur Anbessa Hospital

5. KENYA

5.1 Background

Kenya covers an area of 580,367 km^2, and is bordered by Ethiopia, Somalia, Southern Sudan, Tanzania and Uganda. Its environment is diverse, ranging from a tropical coast to arid interior, low plains rising to central highlands, and highland plateaus in the west. The country is administratively divided into eight provinces. In July 2009 there were 254 reported districts, but in August 2009 the High Court of Kenya ruled that all districts created after 1992 were created illegally, and thus there are only 46 legal districts (Machuka, 2009). The total population in 2009 was estimated to be 39 million, with 43% aged under 15 years and only 4% aged over 60 years (CIA, 2009c, WHO, 2009).

Health indicators in Kenya continue to be poor, with a life expectancy at birth of 54 years, and infant and under-five mortality of 80 and 121 per 1,000 live births, respectively. Maternal mortality is 560 per 100,000 live births and only 42% of births are attended by a skilled health worker. Prevalence of HIV in adults aged 15-49 years is 6.7%, with an estimated 1.2 million people living with HIV/AIDS (WHO, 2009). Government-run dispensaries are the lowest point of contact between the public and the national health system, which include national hospitals, through provincial and district hospitals, to health clinics. The number of physicians for each member of the population is one per 10,000 people, which is relatively high compared to the average of two per 100,000 for the WHO African region. Only 9.7% of the total government budget is spent on health, while private health expenditure constitutes 52.2% of all spending on health, 80.0% of which is out of pocket expenditure (WHO, 2009).

The first VL cases were reported from Wajir and Mandera in North Eastern province as early as 1935 (Ashford and Bettini, 1987). Since then both VL and CL have been identified, although comprehensive epidemiological data on both diseases are still lacking. The estimated average VL caseload per year is about 600, according to the MoH, though in epidemic years caseloads can surpass 1,000 (Njau, 2010). The occurrence of CL is rare compared to VL, and the two diseases do not tend to overlap geographically. VL is found predominantly in the arid, low-lying areas of the Rift Valley, Eastern and North Eastern provinces, whereas CL occurs over a wider range of environmental conditions, from semi-arid lowlands to high plateaus in the Eastern, Rift Valley, Central and Western provinces. VL cases in highland areas have been recorded, probably as a result of spreading epidemics (Southgate and Oriedo, 1962).

5.2 Visceral Leishmaniasis Epidemiology

5.2.1 Parasite and Vector

VL in Kenya is caused by *L. donovani* (Table 6), and previous reports of *L. infantum* are now considered misidentifications (Jamjoom et al., 2004). The main sandfly vector is *P. martini*, which breeds in termite hills, animal burrows, tree holes and house walls (Mutinga et al., 1990). It was first identified as the vector of *L. donovani* during an outbreak in Meru district in 1966, and has since then been incriminated as the VL vector in Rift Valley, Eastern and North Eastern Provinces, but the full extent of its geographical distribution remains unknown (Heisch et al., 1962, Johnson et al., 1993). Other possible vectors have been identified in North Eastern Province, including *P. celiae* and *P.*

vansomeranae, both of which are associated with termite hills (Heisch et al., 1962, Marlet et al., 2003a, Heisch et al., 1956). The only confirmed VL reservoir in Kenya is man, with no animal reservoir yet identified (Mutinga et al., 1989).

Table 6: VL epidemiology in Kenya

Province	Current foci (district)	Parasite	Confirmed vector	Main outbreaks (district: year)
Rift Valley	Turkana Baringo West Pokot	*L. donovani*	*P. martini (confirmed)*	None
Eastern	Kitui Meru Machakos	*L. donovani*	*P. martini (confirmed)*	Kitui : 1953 & 1980s Meru: 1953 & 1966 Machakos: 1970s
North Eastern	Mandera Wajir	*L. donovani*	*P. martini (confirmed),* *P. celiae (suspected),* *P. vansomeranae (suspected)*	Garissa, Wajir and Mandera :2000 to 2001 Wajir: 2008 to present

5.2.2 Geographic Distribution

Rift Valley Province

The first recorded VL outbreak occurred in 1940 at Lake Turkana among the King's African Rifles troops, a military battalion that travelled through southwest Ethiopia, northern Kenya and southeast Sudan (Coles et al., 1942). The Rift Valley focus was first identified in Turkana district in 1955 (Mutinga, 1975), with cases subsequently reported in Baringo and Marakwet districts, followed by West Pokot district, eventually spreading across the border to Uganda (McKinnon, 1962, Schaefer et al., 1995a, Schaefer et al., 1995, McKinnon and Fendall, 1955). Transmission in these areas tends to be more stable than in the eastern foci, but West Pokot, Baringo and Turkana continue to be endemic for the disease (Lawyer et al., 1989). In Baringo district, 66% of reported cases are male, and 50% are between 5-14 years of age (Tonui, 2006). In 1991, three cases of VL were reported from Kajiado district in Rift Valley Province (Johnson et al., 1993).

MSF-CH (Swiss Section) has been collecting data from Kacheliba Health Centre in West Pokot since November 2006 (Table 7). Cases increased considerably from 2006 to 2007, which MSF-CH attributed to a backlog of cases presenting to the Kacheliba facility, rather than to an outbreak (Personal communication, John Kitui, MSF-CH). A similar observation was made a few years earlier in Uganda, when MSF-CH started to support Amudat Health Centre (Kolaczinski *et al.* 2007).

Table 7: Case data from Kacheliba Health Centre, Kenya

Year	Primary VL cases	PKDL cases	Relapses
2006	112	0	2
2007	706	5	27
2008	524	10	18
2009	434	28	22

Source: Personal communication, John Kitui, MSF-CH

Eastern Province

Historically, the main outbreaks have occurred in Eastern Province where VL has presumably been endemic the longest. The first outbreak occurred in Kitui district, beginning in October 1952 and peaking in June 1953. By May 1954 a total of 2,725 cases had been recorded which, at the time, was the largest ever-reported VL outbreak in Africa. 70% of cases were male, and over 60% were under 18 years of age (Heisch, 1954). The next outbreak occurred in Tharaka district in 1961 resulting in at least 500 cases, followed by another outbreak in Meru district in 1966 with 1,500 reported cases (Wijers and Mwangi, 1966). In the late 1970s, an outbreak in Machakos affecting over 2,000 people (Njau, 2010). Another outbreak was reported from Kitui in the 1980s, but no estimates of the caseload are available (Ngoka and Mutinga, 1978, Ho et al., 1982, Wijers and Kiilu, 1984). All of these districts are still considered VL endemic.

North Eastern Province

Although the first VL cases were reported in this province as early as 1935, the first outbreak was only reported in 2000/01 across the borders of eastern Kenya, southern Somalia and southeast Ethiopia (Ashford and Bettini, 1987, Boussery et al., 2001). The outbreak affected Wajir, Garissa and Mandera districts in Kenya. The majority of patients were nomadic tribesmen who grazed their cattle over the border area, although Somali refugees in Kenyan refugee camps were also affected (Boussery et al., 2001, Marlet et al., 2003a). Various causes of the outbreak have been proposed. Unusual increases in rainfall patterns may have affected the sandfly population and caused drought, food shortages and increased malnutrition, and the subsequent migration of infected populations from endemic areas to seek food and security may all have contributed (Marlet et al., 2003a, Tonui, 2006).

There have been several other outbreaks in this province since 2001. The first from September 2006 – April 2007 in Wajir and Isiolo districts, with 40-60 cases occurring mostly in children. Between April – July 2008, a further 92 cases and seven deaths were reported, suspected to have spread from Isiolo in Eastern Province through Wajir to Mandera district. Again, most cases in this outbreak were children (Njau, 2010). Most recently, in 2010, an outbreak was reported in Isiolo district, but no information on the caseload is presently available (Njau, 2010).

Other areas

Sporadic VL cases have also been reported in Tana River district, Coastal Province, although no data on the overall caseload are available (Southgate and Oriedo, 1962).

5.2.3 Risk factors

Few studies have investigated VL risk factors in Kenya, and many reports are restricted to an examination of distribution by age, sex and occupation, or evaluations of immunity based on the leishmanin skin test (Manson-Bahr, 1961, Southgate, 1964, Southgate and Oriedo, 1967). Several risk factors, including socio-economic status, proximity of compounds to termite hills, indoor transmission, cattle ownership, low use of mosquito nets and malnutrition, have been proposed, although a clear and consistent relationship between these factors and VL risk has been difficult to demonstrate (Schaefer et al., 1995a). For example, various studies have investigated the association between VL and

living close to termite hills, which are thought to be the resting and breeding place of *P. martini* (Wijers and Mwangi, 1966, Johnson et al., 1993). Results are inconsistent and varied, with some studies in Kitui finding a positive association (Heisch, 1954, Southgate, 1964, Southgate and Oriedo, 1962), while no relationship was found in other areas such as Baringo and Machakos (Schaefer et al., 1995a, Ho et al., 1982).

VL tends to be restricted to dry, hot lowland areas, while CL is found over a wide range of climatic conditions, including high altitudes areas with low temperature and high rainfall (Kungu et al., 1972). Increases in VL incidence have been associated with the rainy season. Sandfly density is greatest during and shortly after the rainy season, and thus it is likely that transmission during this period is greatest. Evidence from Kitui district supports this hypothesis, as peak VL incidence lagged six months behind the rainy season and peak sandfly density, correlating with the approximate six-month incubation period of the disease (Southgate, 1977).

During VL outbreaks more men than women tend to be affected. For example, 70% of cases occurred in males during the Kitui outbreak of 1953, and 66% of cases reported in Baringo were males (Southgate and Oriedo, 1962, Tonui, 2006). It is likely that this is due to an increased exposure of men to sandfly bites due to their role in farming and cattle herding. Men herding livestock often tend to sit on termite mounds as these provide a vantage point to guard the herd. The age distribution of VL cases is also affected by the exposure and immunity of those bitten. VL is more likely to affect immunologically naive hosts, and the length of time VL has occurred in a particular area or population is reflected in the age distribution of those infected. For example, in established foci such as Kitui, a higher proportion of children became affected, as more adults had acquired immunity, whereas in areas more recently affected by VL the percentage of infection in adults was higher (Southgate, 1964, Southgate and Oriedo, 1962).

Infection with HIV is also a known VL risk factor, as it lowers the immune system's ability to respond to infection. HIV and VL co-infection has been reported in fifteen cases in Kenya and there are likely to be many more unreported cases (WHO, 2007c).

5.3 Cutaneous Leishmaniasis Epidemiology

CL was first described in Kenya in 1969, and is caused by three parasites – *L. major*, *L. tropica* and *L. aethiopica*. The disease occurs in a broad range of settings, ranging from river valleys and semi-arid lowlands to the hills and cliffs of highland plateaus. The specific parasites and vectors are presented in table 8 for each CL focus. CL is most endemic in the central part of Rift Valley Province, in the districts of Naivasha and Laikipia. In April 2009, an outbreak with at least fifty CL cases was reported from Gilgil district in Rift Valley Province (Njau, 2010).

Transmission of both *L. major* and *L. aethiopica* is thought to be zoonotic. Isolates of both species have been found in rodents and *L. major* has also been identified in non-human primates (Mutinga, 1975, Githure et al., 1984, Gicheru et al., 2009). Baringo and Kitui are the only districts from where both CL and VL have been reported (Tonui, 2006). Although zoonotic transmission of *L. tropica* has not been confirmed in Kenya, it has been

identified in the rock hyrax in Rift Valley Province (Sang et al., 1994, Sang et al., 1992). This and the occurrence of the disease in the human population of a previously uninhabited area support the hypothesis of zoonotic transmission (Sang et al., 1994).

Table 8: CL epidemiology in Kenya

Province	Current foci (district)	Parasite	Confirmed vector	References
Rift Valley	Baringo	*L. major*	*P. duboscqui* *P. guggisbergi*	• Beach et al., 1984 • Mebrahtu et al., 1987 • Mebrahtu et al., 1992 • Sang et al., 1993 a&b • Mutinga et al., 1994 • Tonui, 2006
	Laikipia Samburu Nakuru	*L. tropica*		
Eastern	Kitui	*L. major*	*P. duboscqui* *P. guggisbergi*	
	Isiolo	*L. tropica*		
Central	Nyandarua	*L. tropica*	*P. duboscqui* *P. guggisbergi*	
Western	Bungoma	*L. aethiopica*	*P. pediffer*	

5.4 Leishmaniasis Control - Prevention, Diagnosis and Treatment

Leishmaniasis control is the responsibility of the Division of Vector-Borne and Neglected Tropical Diseases (DVBNTD), formerly the Division of Vector-Borne Diseases, within the Department of Disease Control of the Ministry of Public Health and Sanitation (MoPHS). The department was formed in 2008 and a leishmaniasis focal person within the DVBNTD has been appointed. A national plan of action for NTD control for 2010-2015 is being developed and is anticipated to be finalized in late 2010 (Personal communication, Eric Muchiri, DVBNTD). However, there is no specific budget to support day-to-day leishmaniasis prevention and control activities in the MoPHS (Njau, 2010). Outbreaks, including those of VL, are managed by the Disease Outbreak Management Unit, which operates at national rather than district level.

Currently there are no national statistics on VL or CL and no consistent centralised case reporting. This is due to weak reporting systems between district hospitals and government, and in part also due to lack of coordination between the various non-governmental organizations (NGOs) involved in leishmaniasis control. Only service providers in districts with currently confirmed outbreaks report regularly. These reports are provided to the Disease Outbreak Management Unit instead of DVBNTD. Due to poor reporting and data collection, the caseload in each endemic focus is unknown (Njau, 2010).

Leishmaniasis is not a notifiable disease in Kenya, although the country has implemented an IDSR strategy, and is receiving weekly reports on priority diseases from 85% of districts. If the leishmaniases could be added to the list, this would create an opportunity for regular reporting and surveillance (Njau, 2010). The existing diagnosis and treatment

guidelines were developed in 2001, but are being updated with the input of WHO, the Kenya Medical Research Institute (KEMRI) and MSF-CH.

5.4.1 Diagnosis

Diagnosis at public hospitals is conducted using splenic aspirate, and slides are read on site. Both MSF-CH and Medical Emergency Relief International (MERLIN) use clinical diagnosis confirmed by rK39 RDT or splenic aspirate. The rK39 RDT has not been validated in most VL endemic areas of Kenya and is therefore neither included in the current diagnosis guidelines nor is it technically approved for use in Kenya. To facilitate registration in Kenya, MSF-CH, in collaboration with KEMRI, is currently conducting an evaluation of the rK39 RDT, comparing it to splenic aspirates at Kacheliba health centre in West Pokot district. The study began in March 2010 and is aiming to finish around the end of 2010.

5.4.2 Treatment

An SSG dosage of 20mg/kg for 30 days is used in Kenya, as a high relapse rate occurs at lower dosages (Mebrahtu et al., 1989, Wijers, 1971). However, relapses have still been reported at this high dose, as well as major side effects (Nyakundi et al., 1995). Pentostam® and SSG are both registered in Kenya. WHO supplies SSG for use in public health facilities and provides diagnosis and treatment support. SSG remaining from the 2008 outbreak is used for first line treatment. Ordinarily drugs would be distributed by the Kenya Medical Supplies Agency (KEMSA), but it is currently undergoing organisational restructuring and is non-functional.

MSF use SSG as first line treatment and AmBisome® as second line treatment for elderly, pregnant or relapsed patients, although the latter drug is not yet registered. MSF patients treated with AmBisome® are followed up for longer, to ensure no relapse has occurred, as the most affective dosage has yet to be finalised. Sanofi Aventis has begun the process of registering Glucantime® in Kenya. A validation study to finalise a recommended dosage is being conducted, as required for registration.

In Baringo and Kimalel health centres, KEMRI, with the support of DNDi, conducted a trial to evaluate the impact of SSG/paromomycin combination therapy compared to each treatment alone, as part of a regional multi-centre trial. The trial was completed in January 2010, and results will be published and disseminated shortly. KEMRI and DNDi also initiated a study in March 2010 to evaluate the efficacy of shorter combinations of SSG plus single dose AmBisome®, Miltefosine® plus single dose AmBisome® and Miltefosine® alone. Participants are currently being recruited, and the study is scheduled to finish in June 2011. Sitamaquine is another orally administered treatment for leishmaniasis, and although it is not approved for use in Kenya, studies have demonstrated efficacy and tolerability of the drug in Kenyan patients (Wasunna et al., 2006).

There is little to no support for CL control in Kenya, and no information CL treatment was available from partners consulted for this analysis.

5.4.3 Prevention

The MoH does not provide ITNs for VL prevention in Kenya, and only MSF give out nets to cases at treatment centres. Some have reported that use of ITNs, treated wall cloths, repellents and other personal protective measures are not effective in preventing VL transmission in Kenya (Tonui, 2006, Mutinga et al., 1993). Others have found more favourable results for ITN use. One field study that installed ITNs in homes and re-treated them every six months for over four years found that the percentage of sandfly reduction inside the houses increased with each re-treatment. After a maximum of eight re-treatments, an 81% reduction in *P. martini* indoors was found (Basimike and Mutinga, 1995). Research testing the efficacy of Olyset®, PermaNet® and a local ITN brand against *P. duboscqi*, the vector for CL, found that Olyset® seemed more effective in preventing sandfly biting than the other products. The authors recommended that the mesh sizes of ITNs deployed for leishmaniasis prevention should be smaller than of nets used for malaria prevention, to ensure more effective control of sandflies (Kasili et al., 2010).

MSF-CH conducts community education in its project areas, often during public gatherings such as market days or public meetings. It provides basic information such as how to identify symptoms of VL, teaching people that it is a treatable disease, and where to seek diagnostic and treatment services (Personal communication, John Kitui, MSF-CH).

5.4.4 Implementing Partners

The MoH aims to make VL diagnosis and treatment available at all district hospitals in endemic areas, although in practice there is a lack of the drugs required and of staff adequately trained to conduct splenic aspirates or monitor treatment outcomes. This can be particularly problematic in HIV infected or severely malnourished patients, and the outcomes of relapsed or PKDL patients are rarely followed up. In Wajir district, North Eastern Province, MERLIN used to support five diagnosis and treatment centres with inpatient facilities, but this programme terminated in 2009.

In West Pokot, Rift Valley Province, MSF-CH has supported the MoPHS-run Kacheliba Health Centre through provision of staff, diagnostics, training and drugs since 2006 (Table 9). MSF-CH originally supported VL case-management at Amudat Health Centre, Uganda, but because most of the patients reporting to Amudat originated from the West Pokot area of Kenya, the organisation moved its support to Kacheliba in late 2006. MSF also supply rK39 RDTs and diagnostics training to five health facilities in West Pokot district, with positive cases referred to Kacheliba Health Centre for treatment. Two family-size LLINs are given to each VL patient when discharged.

Patients used to travel from Turkana to West Pokot to seek treatment, but the long distance and animosity between the populations in the two regions made travel difficult. To ease the hardship, MSF-CH has recently begun to provide training and expertise to health centres in the Turkana region, to build case-management capacity for VL. In this region, however, the organization does not provide diagnostic and treatment supplies or case-management (Personal communication, John Kitui, MSF-CH).

MSF also supported Baringo and Kimalel Health Centres in Rift Valley Province between 2008 and 2009, before KEMRI took over support to these facilities. These sites are now included in the multi-country DNDi trial, run by the Centre for Clinical Research at KEMRI, investigating the efficacy of SSG/paromomycin combination therapy, as well as AmBisome® and Miltefosine®. World Vision supports health centres in Turkana district and has been involved in provision of VL diagnosis and treatment. KEMRI also run the Nairobi Leishmania Bank (NLB), part of the Centre for Biotechnology, Research and Development (CBRD), which preserves *Leishmania* isolates from Kenya and other African countries, to allow work on (molecular) characterisation of Leishmania species. KEMRI has also established laboratory-reared sandfly colonies for research on sandfly biology and control, and on parasite-vector interactions (Tonui, 2006).

Table 9: Leishmaniasis partners in Kenya

Organisation	Activities	District	Treatment centres
MoH	Diagnostics and inpatient treatment	Wajir	Wajir District Hospital
MSF-CH	Staff, training, diagnostics, inpatient treatment, community education. Two family nets to positive patients. Diagnostics, but no treatment Training and capacity-building	West Pokot Turkana	Kacheliba health centre Five health centres
KEMRI	Diagnosis, transport and referral to treatment centre Diagnosis, transport and referral to treatment centre	Baringo	Baringo health centre Kimalel health centre
World Vision	VL diagnosis and treatment	Turkana	
WHO	Supply of SSG Support with diagnosis and treatment		MoH-run treatment facilities

6. SOMALIA

6.1 Background

Somalia covers an area of 637,700 km^2 that largely consists of desert. It is located on the east coast of the horn of Africa, bordering Kenya, Ethiopia and Djibouti. From December to February the country experiences a north-eastern monsoon, and from May to October a south-western monsoon. The terrain is mostly flat undulating plateau rising to hills in the north (CIA, 2009d). In 2007, the total population was estimated to be around eight million, with 44% below 15 years of age, while only 3% were 65 years old and above (WHO, 2009). Although Somalia is technically divided into 18 administrative regions, it effectively consists of two independent states (Somaliland and Puntland) and small government controlled areas, with the remainder under the control of Islamist groups.

Since the collapse of the government in 2001, factional fighting has left large parts of the country without any form of health care. Large numbers of people have been displaced and food aid is often diverted (Guha-Sapir and Ratnayake, 2009). In 2006, fighting began between the transitional government and insurgents, resulting in an upsurge in violence and the displacement of over a million people. Currently, the government only retains control over small areas in Baidoa and Mogadishu. The majority of health care is provided by NGOs operating remotely from Nairobi, with very limited population coverage. Other than physical violence, the main causes of death are malnutrition, preventable disease and birth complications, all symptoms of the poorly functioning health, water and sanitation systems, mass displacement and poor food supply (Guha-Sapir and Ratnayake, 2009).

The available health indicators show that the health status of Somalis is poor in almost every aspect. Only 28% of the population have access to local health services. Vaccine preventable diseases continue to be a leading cause of death and morbidity among children (International Crisis Group, 2010), and an estimated 72% of all deaths are caused by communicable diseases. Life expectancy at birth is 52 years, while under-five mortality is 142 per 1,000 live births (WHO, 2009). Maternal mortality is high, at 1,044 per 100,000 live births, only 33% of births are attended by skilled health personnel, and antenatal care coverage is 26%. There are few qualified health care workers, only 0.4 per 10,000 population or a total of 310 in the whole country. HIV prevalence is estimated to be 0.5%, with approximately 24,000 people living with HIV/AIDS, of which only 413 people are reported to be receiving ART (WHO, 2009).

Cases of VL have been described in all parts of Somalia, but current foci are concentrated in Bay and Bakool regions near the border of Ethiopia, and Gedo and Lower Juba regions along the Kenya border. There have been no reports of CL (Ruiz Postigo, 2010) and few reports of PKDL in Somalia (Personal communication, Mohammed Fuje, WHO).

6.2 Visceral Leishmaniasis Epidemiology

6.2.1 Parasite and Vector

VL in Somalia is caused by *L. donovani* (Table 10). There has been little research on VL vectors, but it is highly likely that the disease is largely transmitted by *P. martini,* the major vector throughout Kenya and southwest Ethiopia (Marlet et al., 2003b). Both *P.*

martini and *P. vansomerenae* were found to be present during the 2001 outbreak on the borders of Somalia, Ethiopia and Kenya. *P. celiae* is also a potential vector, present in Konso woreda in southwest Ethiopia and Wajir in northeast Kenya. Transmission in Somalia is thought to be anthroponotic (Raguenaud et al., 2007).

6.2.2 Geographic Distribution

Anecdotal cases were described as early as 1935, but VL was first officially reported in 1943 (Penso, 1934), with the first outbreak reported in 1952 from Daarbuluk, Hargeisa (Personal communication, Mohammed Fuje, WHO). The first VL endemic focus was described in 1965, with 12 cases diagnosed in Middle Shabele region, the majority of which occurred in young age groups and originated from the province capital Giohar (Baruffa, 1965, Cahill et al., 1967, Shiddo et al., 1995). Further VL cases were reported in 1995-6 from the Lower Juba region by MSF-B (Belgian Section) and a case was identified in 1995 in Baidoa, Bay region (Woolhead, 1995).

In 2001, an outbreak on the borders of Kenya, Ethiopia and Somalia began, with the majority of cases occurring in ethnic Somalis from nomadic tribes grazing cattle in the border area. Cases first occurred in Lower Juba, Bakool and Gedo regions, although VL in Gedo may have been introduced by the arrival of people displaced from Bakool in 1998. Cases continued to occur in Bakool, with approximately 140 cases reported annually from 2002 to 2004. A marked increase to 1,002 patients was observed in 2006, 80% of which came from two districts, Haddur and Tijeglow, in Bakool (Raguenaud et al., 2007).

The outbreak continued into 2008, with the number of patients treated by MSF-B in Somalia rising from approximately 700 in 2006 to 911 in 2008 (Personal communication, MSF-B). World Vision also collected data towards the end of the outbreak, and had 153 cases admitted for treatment between July 2008 and February 2009. Among these cases there were 20 deaths; 42 confirmed cases defaulted before being admitted to treatment (Personal communication, Sharif Mohamed, World Vision). The low case fatality rate and paediatric profile of this outbreak differ from the general East African profile of high mortality and a high infection rate in adults (Marlet et al., 2003b). Although no previous cases had been reported from Bakool, its paediatric profile suggests that the region was long endemic for VL (Marlet et al., 2003a, Raguenaud et al., 2007). This idea is supported by the fact that the population has a local word for VL, 'dedabse' (Marlet et al., 2003b).

In 2009, MERLIN reported that the total number of VL cases country-wide was about 500. However, due to interruptions and suspension of activities among many NGOs around 2008-2009, this number is likely to be an under-estimate (Personal communication, Mohammed Fuje, WHO). SOS Children's Villages International (SOS) has collected data from its facility in Baidoa, Bay region, since late 2008. Thirty-one VL cases were treated from September to December 2008, and 115 VL cases were treated during the entire year of 2009. In 2010, no activities were conducted in January, but from February through April 45 cases were treated. About 60% of cases seen by SOS are male, 43% are age five or below, 53% are aged between five and 14 years, and only 3% are over 15 years old (Personal communication, Ahmed Ebrahim, SOS).

Table 10: VL epidemiology in Somalia

Region	Disease foci	Parasite	Vector	Main outbreaks (area: year)
Shabele	Giohar – Middle Shebelle River Valley	*L. donovani*	*P. martini (suspected)*	
Lower Juba	Lower Juba river valley	*L. donovani*	*P. martini (suspected)* *P. vansomerenae (suspected)*	Outbreak 2001
Bay	Baidoa	*L. donovani*	*P. martini (suspected)*	
Gedo		*L. donovani*	*P. martini (suspected)* *P. vansomerenae (suspected)* *P. celiae (suspected)*	Outbreak 2001
Bakool	Haddur & Tijeglow district	*L. donovani*	*P. martini (suspected)* *P. vansomerenae (suspected)* *P. celiae (suspected)*	Focus of outbreak 2001 – 2008

6.2.3 Risk Factors

There are no data on leishmaniasis risk factors in Somalia, but the presence of termite hills and acacia trees, common in Bakool, may be associated with transmission as these are the favoured breeding and resting sites of *P. martini* (Robert et al., 1994, Ngumbi et al., 1998). Children aged five years and below are the main age group affected, and malnutrition has been observed to be associated with symptoms of VL (Personal communication, Mohammed Fuje, WHO). There are currently no data on HIV/VL co-infection in Somalia (WHO, 2007b).

6.3 Leishmaniasis Control - Prevention, Diagnosis and Treatment

Due to the lack of government control over the majority of Somalia, almost all health care is provided by NGOs. The government provides no resources for VL control and collects no data. MERLIN attempted to collect data from partners working on VL until activities were suspended in September 2009. MSF-B had been collecting information regarding death rate, age, sex and origin of each patient from 2002 until it stopped operating in Somalia in 2009 (Personal communication, Mohammed Fuje, WHO & Ahmed Ebrahim, SOS). In 2010, VL was added to the IDSR as a reportable disease and standardized reporting systems have been implemented since, but no data are available yet and reporting continues to be irregular (Personal communication, Mohammed Fuje, WHO).

Even with VL having been added to the list of reportable diseases, its true magnitude in Somalia is likely to remain unknown and implementation of effective control interventions will remain inadequate while there is no safe access to the population (Raguenaud et al., 2007). Additionally, the fact that people are regularly forced to move between geographic areas means that it is often unclear where cases originate or where exactly transmission occurs (Ruiz Postigo, 2010).

6.3.1 Diagnosis

WHO and MERLIN developed diagnosis and treatment protocols in collaboration with MSF-B in 2006, based on MSF's existing protocols, and are currently being updated by WHO. The protocols state that if the clinical diagnosis indicates VL, an rK39 RDT should be conducted and treatment be initiated if the test is positive. Negative rK39 RDTs should be confirmed with DAT and individuals with a positive DAT be put on treatment (Personal communication, Mohammed Fuje, WHO). However, DAT samples must be flown to Nairobi, and insecurity or a lack of flights often result in delays of up to three weeks until results are sent back to the facility. Because the target time for receiving the results is eight to ten days after taking the sample, use of DAT has largely been discontinued and treatment is usually initiated based on clinical diagnosis and rK39 RDT results (Personal communication, Sharif Mohamed).

6.3.2 Treatment

MERLIN used to provide anti-leishmanial drugs to World Vision, but because operations were discontinued in 2009 World Vision had no supplies from July 2009 until June 2010, when WHO began to provide diagnostic and treatment supplies to NGOs. Introduction of SSG/paromomycin combination treatment had been planned by MSF-B in 2009, but was delayed due to security issues causing programme interruption. MSF-B has stopped operations since.

Treatment Protocol

First line: SSG (20 mg for 30 days)
Second line: AmBisome

6.3.3 Prevention

When MSF-B was operational, VL cases and their families were provided with health education sessions to increase awareness on VL symptoms, on preventive activities such as staying away from acacia trees and termite hills, and on the importance of sleeping under ITNs. World Vision continues to conduct awareness-raising on VL in Tijeglow district, Bakool region, among village health committee leaders, women's groups, and community elders. The organisation also distributes ITNs to all families of confirmed VL cases and is planning an evaluation of the utilization of these nets (Personal communication, Sharif Mohamed, World Vision).

6.3.4 Implementing Partners

In the past, organisations involved in VL control included WHO, Somalia Aid Coordination Body (SACB), HNI, MSF-B, Gedo Health Consortium (GHC), COSV, Inter SOS, World Vision, Caritas, UNICEF and the African Medical and Research Foundation (AMREF). MERLIN used to coordinate partners working on VL and data collection since 2004. Most of these organisations have since discontinued work in Somalia, with only SOS and World Vision continuing to manage VL cases and support being provided by WHO (Table 11). No organisation has stepped into the coordinating role left vacant by MERLIN (Personal communication, Mohammed Fuje, WHO, Ahmed Ebrahim, SOS & Sharif Mohamed, World Vision).

SOS operates a VL programme in Baidoa in Bay region, which was handed over by Caritas in August 2008. Due to the few VL services available in Somalia, especially after the

departure of MSF and MERLIN, the Baidoa facility now receives patients from across Bay, Bakool, and Gedo regions. Dry food rations are provided to patients that are not from Baidoa twice a month during treatment. Because treatments take 30 days, and many patients travel from far away, food rations prevent patients from defaulting on treatment, which used to occur frequently. The rations allow patients to contribute food to the families they stay with in the town and provide an incentive to stay for the full length of treatment. Baidoa is not an inpatient facility, so patients with complications or that otherwise need to be hospitalised must be referred to the hospital in Mogadishu (Personal communication, Ahmed Ebrahim, SOS).

World Vision has been working on VL control in Somalia for about three years. Due to lack of resources and funding, activities are presently only implemented in Tijeglow district; past activities also included Bay region. World Vision manages VL cases, and is involved with community education and capacity building of medical staff. In addition to providing anti-leishmanial treatment, the organisation also provides micronutrient supplementation, de-worming, and measles vaccinations to all VL cases (Personal communication, Sharif Mohamed, World Vision).

Table 11: Leishmaniasis partners in Somalia

Organisation	Leishmaniasis Activities	Ongoing Health Facilities
SOS	Diagnosis & Treatment	Bay Region: Baidoa
WHO	Technical and financial to NGOs	
World Vision	Diagnosis & Treatment, Education, Nutritional support	Bakool Region: Tijeglow

7. NORTH SUDAN

7.1 Background

North Sudan, officially the Republic of the Sudan, is situated in northern Africa, bordering Egypt, Eritrea, Ethiopia, the Central African Republic, Chad, Libya and Southern Sudan. North Sudan is one of the largest countries in Africa, covering an area of over 1,865,800 km^2 and with a population of approximately 33.7 million people. A large portion of the country is dominated by desert while the rest consists mostly of Savannah grassland. The rainy season is from July to September in the north, but starts a little later in the southern areas.

Management of the public health system is three-tiered, with a Federal Ministry of Health (FMOH), State Ministries of Health (SMOH), and a local health system. Health delivery is also divided into three tiers, with primary health care units (PHCUs) as the lowest level facility, followed by health centres and rural/community hospitals (WHO, 2007a). The most recent figures for North Sudan (as opposed to all of Sudan) date from 2004 and estimated that 51% of the population was under 18 and 3% over 65 years of age, and life expectancy at birth was estimated at 56 years (WHO, 2007a, NSCSE, 2004).

VL is one of the most important infectious diseases in North Sudan with an estimated 20,000 cases occurring annually (Burki, 2009). The main endemic area is in the east between the White Nile and the Ethiopian border, including White Nile state, the Blue Nile river basin and Atbara and Rahad tributaries in Kassala, Gedarif and Sennar states, and reaches across the border of Southern Sudan into Upper Nile state (Siddig et al., 1988, Kirk, 1939, Perea et al., 1991, el-Hassan et al., 1993, de Beer et al., 1991). Scattered cases have also been reported from the Nuba mountains in South Kordofan state, from areas along the Nile north of Khartoum, and from western Darfur (Osman et al., 2000).

CL is also present, mainly being reported from Darfur and the central belt of North Sudan (Abdalla et al., 1973). Mucosal leishmaniasis (ML) can occur as part of VL or as a primary type, which is not preceded or accompanied by cutaneous lesions, known as Sudanese Mucosal Leishmaniasis (SML) (el-Hassan et al., 1995). SML is not common, however, and cases are sporadic and isolated.

7.2 Visceral Leishmaniasis Epidemiology

7.2.1 Parasite and vector

VL in North Sudan is caused by *L. donovani* (Table 10), and the only confirmed vector is *P. orientalis* (Hoogstral and Heyneman, 1969, Schorscher and Goris, 1992, Elnaiem et al., 1998a), which is abundant in the acacia/balanite forests common throughout the country (Quate, 1964, Elnaiem et al., 1997). It should also be noted that there are a high number of VL cases in the east of the country despite a scarcity of *P. orientalis.* Nevertheless, it is thought that *P. orientalis* is the main VL vector in the area, as the infection rate of sandflies is high and post kala-azar dermal leishmaniasis (PKDL) is common. Skin lesions of PKDL may act as reservoirs of infection, allowing a small number of sandflies to play a major role in disease transmission during inter-epidemic periods (Zijlstra et al., 1994, Elnaiem and Osman, 1998).

Both anthroponotic and zoonotic VL transmission are thought to occur. Outbreaks of VL in troops moving through otherwise uninhabited areas, and the existence of infected *P. orientalis* in the uninhabited Dinder National Park, strongly suggest that zoonotic transmission takes place (Kirk, 1956, Elnaiem et al., 1998a). The parasite has also been isolated from various mammals. Anthroponotic transmission via sandflies is also likely, especially during epidemics. In villages near Dinder National Park in Gedarif and Sennar states, both near the Ethiopian border, there is intense transmission with a significant number of individuals being asymptomatic carriers, indicating that humans are a reservoir for the disease in this area (Ibrahim et al., 1999).

7.2.2 Geographic distribution

East

VL was first reported in the eastern part of North Sudan in 1908, followed by increasing disease incidence in the area (Cummins, 1908). The area has a savannah climate with acacia/balanite forests and cracked alluvial 'black cotton' soil, a short rainy season (July to October) and dry hot season (November to June). In response to these cases and reports of VL from further south, VL was soon recognised as a major public health problem. In response, the Sudan Kala-Azar Commissions was established, operating from 1909 to 1913 (Zeese and Frank, 1987). Over the following years, Kassala and Fung in Blue Nile state were identified as endemic areas (Kirk, 1939, El-Safi et al., 2002, Osman et al., 2000, Archibald and Mansour, 1937).

Cases continued to be recorded along the Atbara river in the east. In Wad Arud, Blue Nile state, a small outbreak in a military patrol was recorded in 1928 (Kirk, 1939). Further cases then occurred during the resettlement of people from Wadi Halfa, Northern State, during an agricultural programme in 1930, resulting in the death of over one sixth of the population (Hoogstral and Heyneman, 1969). A high incidence of VL was also recorded among soldiers stationed in Gallabat town, Gedarif state, in 1942 (Bayoumi, 1979). More cases were recorded in Wadega-Kurmuk in Blue Nile state and neighbouring Upper Nile state during the 1950s (Hoogstral and Heyneman, 1969). A major epidemic then occurred in Fung, Blue Nile state, from 1956-60 in which thousands of people died and the tribe most affected, the Jum Jum, experienced a mortality rate of over 50% (Sati, 1958, de Beer et al., 1991).

By 1985, approximately 1,300 patients were being reported in Sudan each year, 75% of which from Gedarif and Hawata (Zeese and Frank, 1987). The numbers of cases in the east began to decline from 1985, but rose again from 1991 onward particularly around the Rahad and Dinder rivers (Zijlstra et al., 1994, el-Hassan et al., 1995). Further outbreaks were recorded in Dinder National Park, Gedarif state, from 1988 to 1989 and from 1994 to 1995 following the transfer of game wardens from the southern region to the park. In 1996, another larger outbreak occurred in Gedarif state spreading to Eritrea and northwest Ethiopia, continuing through 1998-9 (Osman et al., 2000).

During the 1996 outbreak, MSF treated 1,233 cases in 1996, rising to 4,618 in 1997, and 4,432 in 1998. Half of the cases originated from a single village, Barbar El Fugara (El-Safi

et al., 2002). The majority of cases were children, suggesting a high level of immunity among adults, indicating a long-term presence of the disease in the area. High-incidence villages were clustered around the Atbara and Rahad rivers and in areas of low altitude and high rainfall (Elnaiem et al., 2003).

The east continues to be the main VL focus in North Sudan. Gedarif currently has two main endemic zones: a low endemicity zone in the central region around Gedarif city and a high endemicity zone around the Rahad and Atbara rivers, both tributaries of the Blue Nile (Elnaiem et al., 2003, El-Safi et al., 2002). In January 2010, MSF-CH started a VL programme at Tabarak Allah hospital in the Atbara area, and from January to August treated 574 primary VL cases, 56 relapses and 69 PKDL patients (Personal communication, Khalid Ahmed, MSF-CH). The second focus includes villages near Dinder National Park on the Ethiopian border, where the high degree of transmission and significant number of asymptomatic human carriers suggest anthroponotic transmission (Ibrahim et al., 1999).

Central

An outbreak occurred on the western bank of the White Nile in 1983, 100 km south of Khartoum (Khalil et al., 2008). Over 100 individuals, both adults and children, died (Ahmed et al., 1988). No further cases were reported in the area until 2006, when there was another outbreak, possibly caused by resurgence of the sandfly population due to re-growth of the acacia/balanite trees after a period of drought, intense grazing and tree felling (Khalil et al., 2008).

Table 12: VL epidemiology in North Sudan

State	Current foci	Parasite	Vector	Main outbreaks (district: year)
Gedarif	Gedarif City Atbara and Rahad river basins Dinder National Park	*L. donovani*	*P. orientalis*	Wad Arud: 1928 Gallabat town: 1942 Dinder National Park: 1988-9 & 1994-5 Atbara & Rahad river basins; Barbar El Fugara: 1996-9
Sennar	Dinder National Park Azaza Damous area	*L. donovani*	*P. orientalis*	Dinder National Park: 1988-89 & 1994-95
Kassala	Kassala city suburbs	*L. donovani*	*P. orientalis*	Kassala: 1910-11
Blue Nile	Fung area, Damazin, Roseires	*L. donovani*	*P. orientalis*	Fung: 1956 – 60
White Nile	White Nile river basin	*L. donovani*	*P. orientalis*	White Nile river basin (100 kilometres south of Khartoum): 1983 & 2006
Kordofan	Nuba mountains, Melut, Abu-Gubeiha and Um-Ruaba	*L. donovani*	*P. orientalis*	1923, 1939, 1969 & 1982
Western Darfur	Geneina town area	*L. donovani*	*P. orientalis*	2004

Migration between North Sudan and Southern Sudan

Besides the various established endemic areas in Sudan, there are also examples of the disease being transferred between North and Southern Sudan by migrating nomadic tribes. A major outbreak occurred in Unity State, Southern Sudan between 1984 and 1994, which may have been triggered by nomadic pastoralists from Blue Nile importing the disease from the north (see section on Southern Sudan). In 1990 and 1991, 200 patients from the Masairiya tribe from southern Kordofan state were diagnosed with VL in Khartoum, having been infected in the Bentiu area of Unity state before importing the disease into Kordofan (el-Hassan et al., 1993). In 1994, another outbreak was reported in Nasir district, which may have been related to people returning from a food distribution centre in the VL endemic zone of eastern Sudan (Mercer et al., 1995).

7.2.3 Clinical features and risk factors

The most notable feature of VL in North Sudan is the high rate of PKDL that occurs during or shortly after treatment. PKDL was first described in Sudan in 1921, with the first definite case identified in 1938 (Christopherson, 1921, Kirk and Drew, 1938). It is now reported with increasing frequency, occurring in at least 50% of cases, which is higher than in any other VL endemic area (Kirk and Sati, 1940, Zijlstra et al., 1995). The frequent occurrence of PKDL may also play a role in VL transmission, as PKDL patients can serve as a human reservoir for the parasite (el-Hassan et al., 1992). HIV/VL co-infection is also a growing concern in North Sudan, particularly in the east, with the percentage of cases co-infected in hospitals in Khartoum increasing from 5% in 1998 to 8% in 2002. Co-infections in Gedarif state accounted for 8% and 3.6% in 2002 and 2003, respectively (Alvar et al., 2008).

PKDL in Sudan

Dermatological lesions have been traditionally described as one of the main characteristics of Sudanese VL, and rates of PKDL here are higher than in other eastern African countries (Kirk, 1944, Sati, 1963). Rates of PKDL as high as 9% have been recorded in VL patients, with rates in children under five twice that of children aged five to nine years, and 20 times that of adults aged 45 years and over (Collin et al., 2004).

Various risk factors for infection with VL have been identified. In the eastern focus, rainfall and altitude are the best predictors of VL incidence (Elnaiem et al., 2003). As the humidity rises and temperature falls due to the rains, numbers of *P. orientalis* increase, in turn increasing transmission (Elnaiem et al., 1998b). There are also significant differences in VL incidence and ratios of clinical to subclinical infection in the different tribes and ethnic groups of Gedarif state, with marked vulnerability in the Nilotic Baria and Nuba tribes, suggesting a genetic predisposition to VL infection (Ibrahim et al., 1999, Bucheton et al., 2002, Elnaiem et al., 2003).

Other factors that have been found to reduce risk of infection include the lack of cattle ownership and presence of the *Azadirachta* (neem) tree (Bucheton et al., 2002). A negative association between those with a positive Leishmanin (Montenegro) skin test

and the likelihood of infection with VL has also been reported, suggesting that previous exposure to leishmaniasis (both visceral and cutaneous, or subclinical infection) may result in protection from later VL infection (Zijlstra et al., 1994). The endemic nature of VL in North Sudan means that those affected are often children who have not yet acquired immunity to the disease.

7.3 Cutaneous Leishmaniasis

CL in North Sudan is caused by *L. major* and *L. tropica* (Abdalla et al., 1973, el Safi et al., 1991, Ibrahim et al., 1995, Andresen et al., 1996). *P. papatasi* has been considered a possible vector of CL during the epidemics in central Sudan, where *P. orientalis* is absent (Abdalla and Sherif, 1978). The first case of CL in North Sudan was described at the beginning of the 20th century (Kirk and Drew, 1938). The majority of CL patients now come from Darfur and the central belt, and three outbreaks of CL have been reported in the past (Abdalla et al., 1973). The first outbreak occurred from 1976-77 in the Shendi-Atbara region north of Khartoum province (Abdalla and Sherif, 1978). The second outbreak started in Khartoum in 1985 on Tuti, an island of about 20,000 inhabitants at the junction of the White and Blue Nile rivers; approximately 10,000 cases were recorded between 1985 and 1987. Heavy rainfall after several years of drought, the discontinuation of IRS for malaria control and an increase in rodent numbers have all been implicated as triggers of the outbreaks (el Safi and Peters, 1991). The third epidemic occurred along the main Nile, north of Khartoum up, to the border with Egypt; all age groups were affected (el Safi and Peters, 1991).

As mentioned above, a particular form of ML, SML, also occurs in North Sudan. Only 78 sporadic and isolated cases have been reported since the disease was first described by Christopherson in 1914 (el-Hassan et al., 1995). SML occurs almost exclusively in adult males in VL-endemic areas in the east, Darfur and Kordofan, and is characterised by a long disease duration if it is not treated (Abdalla et al., 1975, el-Hassan et al., 1995). The great majority of SML cases reported to date are caused by *L. donovani* (el-Hassan, personnal communication).

7.4 Leishmaniasis Control - Prevention, Diagnosis and Treatment

In 1996, the Federal Ministry of Health (FMoH) created the Leishmania Control Programme (LCP), within the Division of Endemic Disease Control (DEDC). In 1998 the programme separated from the DEDC and a national coordinator was nominated. In 2001, the LCP was merged with the Malaria and Schistosomiasis Control Programme, under the National Malaria, Schistosomiasis and Leishmaniasis Administration (NMSLA). Leishmaniasis focal persons have also been appointed in some of the endemic states.

A workshop on 'Developing a National Policy on Leishmaniasis control in Sudan' was held in 2003 with the support of WHO and MSF-H. The workshop led to formulation of a draft strategic plan for VL control (2003-2007) and to efforts to develop a national VL protocol and policy at federal level. There now is some level of financial support for VL control from the MoH.

Currently, no laboratory quality control system exists for VL diagnosis at state or federal

level, with the exception of the Institute of Endemic Diseases, University of Khartoum laboratories and its facilities in eastern Sudan, namely Kassab rural hospital and the recently opened Centre for Tropical Medicine run by Professor EL-Hassan. VL is a notifiable disease in the two endemic states of Gedarif and Sennar. National guidelines for the diagnosis and treatment of VL have been published and are currently being updated by the Institute for Endemic Diseases (IEND).

7.4.1 Diagnosis

The national guidelines recommend the use of rK39 RDT and DAT for VL diagnosis in the field, although it is suggested that these tests are not used as stand-alone diagnostic tools. Parasitological confirmation via a lymph-node or bone marrow aspirate is recommended. MSF-CH uses the rK39 RDT and DAT for diagnosis of primary VL, and lymph node aspirates in cases of relapse and for test of cure (Personal communication, Khalid Ahmed, MSF-CH).

DAT was the main method of diagnosis used during the 1984 to 1994 outbreak (Seaman et al., 1996), with studies demonstrating a high sensitivity and specificity (Abdel-Hameed et al., 1989, el Safi and Evans, 1989, Zijlstra et al., 1991). Splenic aspirate has been shown to have a sensitivity of at least 92% in Sudan (Van Peenen and Reid, 1962, Siddig et al., 1988), but is not regularly used (Personal communication, Ahmed Musa). Lymph node aspirate is a safer method, but reports of sensitivity have varied from 58.3% to 100% (Kirk and Sati, 1940, Siddig et al., 1988). Bone marrow aspirate has had a reported sensitivity of 70.2% (Zijlstra et al., 1992). In 2006, a study conducted in both North and Southern Sudan found the rK39 RDT to have a sensitivity of 81% and specificity of 97% in clinically suspected cases (Ritmeijer et al., 2006).

7.4.2 Treatment

SSG has been registered in North Sudan, while Glucantime® was never specifically registered because its use is covered by the general registration of antimonials provided for SSG. While not registered, AmBisome® is on the essential drugs list. The MoH and WHO supply SSG and Glucantime® free of charge for treatment of leishmaniasis, while patients are required to pay for their food and accommodation during treatment at MoH run facilities.

The national guidelines currently recommend SSG for 30 days as first line treatment or, if unavailable, Glucantime® for 21 days. AmBisome® is the recommended second line treatment. Combination therapy of SSG/paromomycin has also been suggested as an alternative second line treatment. MSF-CH uses 20 mg/kg/day SSG for 30 days as its first line treatment for confirmed primary VL and AmBisome® for second line in cases of SSG failure or when SSG is relatively or absolutely contra-indicated (Personal communication, Khalid Ahmed, MSF-CH).

The use of amphotericin B is not recommended due to possible side effects, although permitted in unavoidable circumstances. It is planned to include Miltefosine® in the revised treatment guidelines. Treatment for PKDL is only recommended if it is severe or if it persists for over six months, and it is treated with SSG for at least two months. However, this treatment is expensive and can be toxic for this length of time.

AmBisome® is effective in the majority of PKDL cases, but it is required at double the dose used to treat VL.

There has been some indication of poor cure rates with SSG in the eastern part of the country. One study reported that 47% of patients were not cured after well-supervised treatment (Osman et al., 1998). Case-fatality rates after treatment with SSG have ranged from 4.8% to 20% (Van Peenen and Reid, 1962, el-Hassan et al., 1990, de Beer et al., 1991), with the current rate being around 2% following close patients management (Ahmed Musa unpublished data). Relapse rates after treatment have varied from 1% to 18% (Sati, 1958, Osman et al., 1998). However, incomplete treatment and suboptimal dosing have both been implicated in the occurrence of complications after treatment. This suggests that treatment outcomes could be improved through better training and implementation of correct treatment (Zijlstra et al., 1995, Khalil et al., 1998).

DNDi completed a four-country trial in January 2010, in North Sudan, Ethiopia, Kenya, and Uganda, to assess the efficacy and safety of SSG monotherapy versus paromomycin monotherapy versus an SSG/paromomycin combination therapy for VL. The study in North Sudan took place at Kassab Hospital in Gedarif State, which treats approximately 1,000 VL patients a year (Personal communication, Manica Balasegaram, DNDi). In April 2009, DNDi started another trial at Kassab Hospital to determine the lowest and safest single dose of AmBisome® for treatment of VL in non-HIV positive patients. This trial is scheduled to finish in June 2011. In March 2010, DNDi also initiated a trial to evaluate the effectiveness of shorter combinations of SSG plus single dose AmBisome®, Miltefosine® plus single dose AmBisome® and Miltefosine® alone. The trial is taking place in Kenya and in North Sudan at the Doka health centre in Gedarif, and is scheduled to finish in June 2011.

The guidelines for diagnosis and treatment of VL are under review. Following the multi-centre clinical trial of SSG/ paromomycin, this combination therapy will become the first line treatment, while SSG or AmBisome monotherapy will become the second and third line treatment, respectively.

7.4.3 Prevention

Vaccines studies were conducted using killed *L. major* + BCG vaccine without adjuvant and with adjuvant (ALUM) in Sudan. There was no difference between the group who received the vaccine (without adjuvant) and the group who received the placebo (Khalil et al., 2000). Version of the vaccine that contained adjuvant gave promising results in Phase I and II trials, but no funds were available to initiate phase III trials (Kamil et al 2003, Khalil et al 2005, Khalil et al 2006).

MSF has been involved in ITN distribution in the eastern region since the epidemic of 1995. It was considered that ITNs were a better option than IRS, as the extent to which *P. orientalis* rests indoors is unclear. Additionally, people often sleep outdoors during the dry season when sandfly infection rates are highest, and ITNs would also have the benefit of protecting against malaria (Elnaiem et al., 1998b). ITNs have been shown to be protective against the bite of *P. orientalis*; an intervention trial conducted during the

1990s showed a reduction of cases in villages where ITNs were distributed compared to control villages (Elnaiem et al., 1999a).

Between 1999 and 2001, MSF distributed over 350,000 ITNs in Gedarif state. VL incidence subsequently declined, with the largest decrease of 59% occurring 17-20 months after distribution. A two-year follow up study showed that 44% of nets were still reasonably intact, and data from 114 villages indicated a statistically significant reduction in VL after ITN provision. Based on these data, it was estimated that 1,060 VL cases were prevented and that ITNs have a protective effect of 27% (Ritmeijer et al., 2007).

7.4.4 Implementing partners

MSF-H used to be the main organisation currently involved in VL control in North Sudan. It became involved in 1996, when the Institute of Endemic Diseases at the University of Khartoum invited MSF-H to intervene in response to an outbreak in Um el Kher, Gedarif state. From 2001, MSF-H supported five hospitals (Dooka, Hawata, Sifawa, Kassab and Gedarif teaching hospital) in Gedarif and two hospitals (Azaza Damous and Dinder Rural hospital) in Sennar state, to improve diagnosis and treatment standards and introduce a surveillance system for HIV/VL co-infection. MSF-H phased out support to these sites in 2004. In January 2010, MSF-CH started to support diagnosis, treatment and medical follow-up for VL at Tabarak Allah hospital in Gedarif State.

8. SOUTHERN SUDAN

8.1 Background

Southern Sudan, officially known as the Autonomous Government of Southern Sudan, lies within the Nile basin and shares borders with five countries: North Sudan, Ethiopia, Kenya, Uganda and the Democratic Republic of Congo. The region's autonomous status was brought about in 2005 by a comprehensive peace agreement (CPA) between the North and the South after decades of conflict. A referendum to decide whether Southern Sudan will remain part of the Republic of the Sudan is scheduled for January 2011.

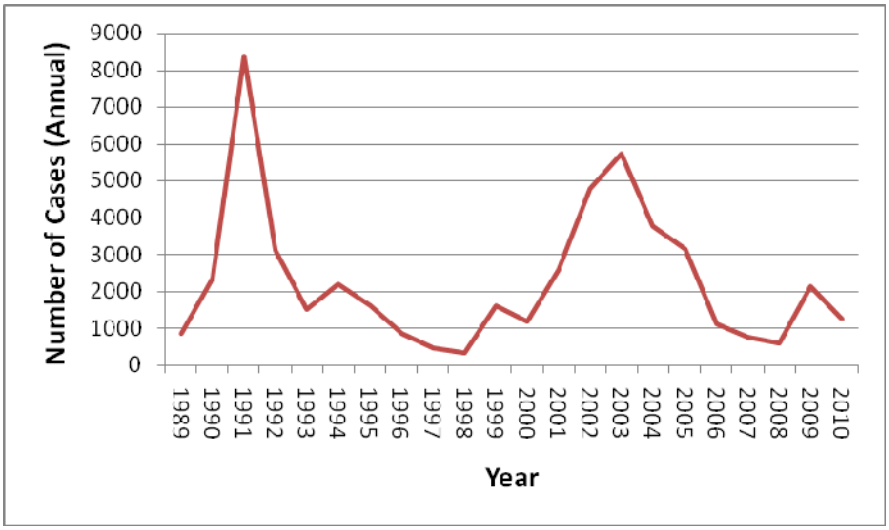
Southern Sudan covers an area of 640,000 km^2 and is divided into a three-tiered administrative system; at the 2008 census there were 10 states, 79 counties and 517 payams. The terrain consists of flat savannah grasslands with scattered acacia/balanite forests. The rainy season lasts from April to November and causes large parts of the country to become flooded and inaccessible.

The 2008 census estimated the population to be around 8.26 million people and showed it to be the youngest in the world; 49% were under 17 years of age and only 2% above age 65. Life expectancy at birth is 42 years, one of the lowest in the world. Infant and under-five mortality is high at 150 and 205 deaths per 1000 live births, respectively. Under-five mortality accounts for 57% of total deaths. Extreme lack of health services is evidenced by the fact that only 5% of births are attended by skilled health personnel (NSCSE, 2004).

Infrastructure, including health services, is being reconstructed. Currently, severe financial and human resource constraints result in limited healthcare access. A Health Sector Recovery Strategy was introduced after the CPA, with the ultimate goal of providing one hospital per 300,000 people, one Primary Health Care (PHC) Centre for 50,000 people, and one PHC unit for 15,000 people. These targets represent a substantial expansion of the present health care infrastructure (MoH-GOSS, 2008). The MoH of the Government of Southern Sudan (MoH-GoSS) at central, state and county level is in great need for management and human resource capacity strengthening and commodity support, and NGOs continue to provide a key role in healthcare delivery.

VL was first reported in Southern Sudan in 1904 (Zijlstra and el-Hassan, 2001) and is characterised by periodic outbreaks and high mortality rates. Passive case-detection data from NGOs providing VL diagnosis and treatment services between 1989 and 2006 indicate that VL occurs in a cyclical pattern, with caseloads fluctuating year to year, from under 500 to over 8,000 cases, with peaks in 1991 and 2003 (Kolaczinski et al., 2008a). Figure 6 displays the changes in annual incidence from 1989 through 2010, as reported to WHO. It has been suggested that in certain areas as many as 45% of cases and 91% of deaths caused by VL may go undetected, and current passive case-detection data may provide a significant under-estimate of the actual caseload, as many cases never seek care from health facilities (Collin et al., 2006).

Figure 6: Total annual VL cases reported to WHO in Southern Sudan, 1989-2010



Source: Personal communication, Justin Rubena, WHO

There are two VL foci (Figure 7), a large endemic area covering parts of Upper Nile, Unity and Jonglei states in the north (Zeese and Frank, 1987,), while a much smaller endemic focus is located in the east of Eastern Equatoria state in the south of the country (Hamza et al., 1976, Kolaczinski et al., 2008a, Ruiz Postigo, 2010). Transmission of VL is highest during or shortly after the rains (from April to November), leading to a peak in clinical cases during the dry season, which usually lasts from November to January. CL is very rare in Southern Sudan and there are no detailed data on number or origin of cases.

8.2 Visceral Leishmaniasis Epidemiology

8.2.1 Parasite and vector

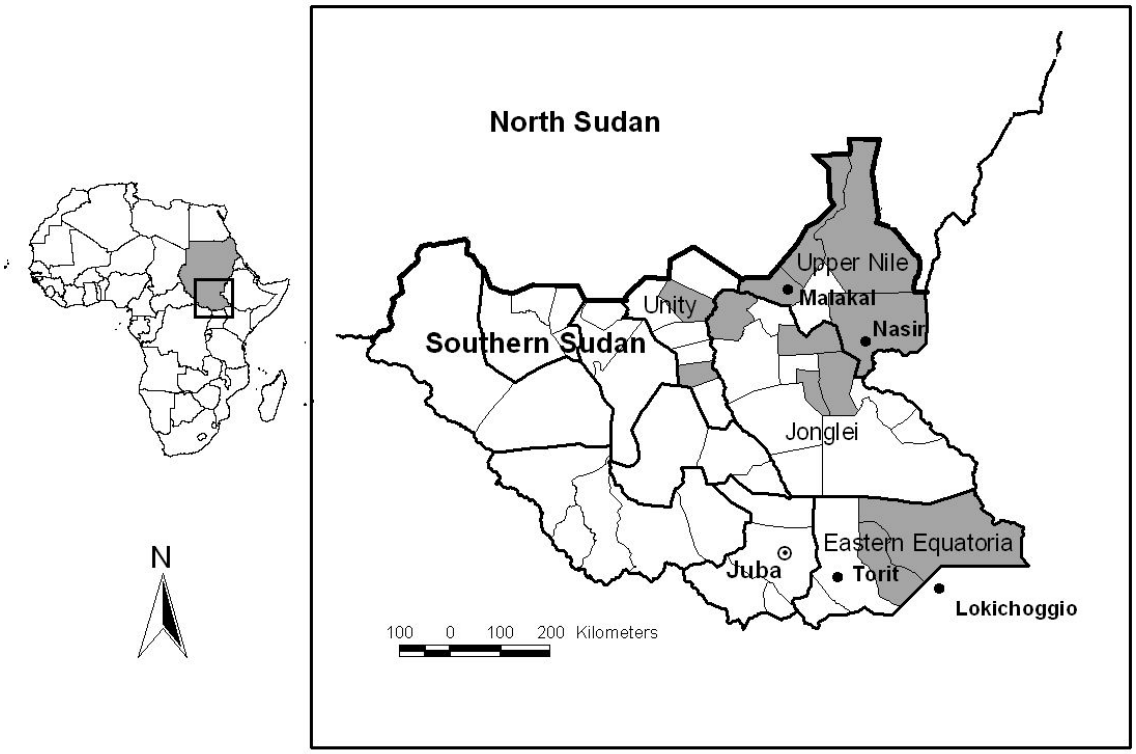
Between 1960 and 1964 a leishmaniasis research laboratory was established in the northern focus, at Malakal, by the United States Naval Medical Research Unit No. 3 (NAMRU-3) to investigate leishmaniasis outbreaks in the area. Staff at the laboratory identified the causative agent to be *L. donovani,* and confirmed the local sandfly vector to be *P. orientalis* (Table 13). This vector was subsequently shown to have exceptionally high infection rates in Southern Sudan (Schorscher and Goris, 1992). *P. orientalis* is associated with the acacia-balanite forests and cracked black cotton soil, both of which provide ideal breeding and resting sites for the vector (Hoogstral and Heyneman, 1969). *L. donovani* has been identified as the causative agent and its transmission is thought to be anthroponotic. Infected domestic animals have been found in the area, but none of these have been confirmed as a reservoir host (Dereure et al., 2000). The main tribes in this leishmaniasis endemic area are semi-nomadic pastoralists of the Dinka, Nuer and Shilluk tribes.

8.2.2 Geographical distribution

Northern Focus

The first recorded VL epidemic in Southern Sudan occurred in Melut, Upper Nile state in the 1940s, with at least 300 cases and 80% mortality (Table 13). It affected the Dinka and Shilluk tribes living in the area (Stephenson, 1940), and may have been imported by nomadic herdsmen from Fung district in Blue Nile state. Outbreaks in the area increased in frequency and intensity throughout the 1950s, with a particularly severe outbreak affecting Melut and Paloich in Upper Nile in 1952 (Hoogstral and Heyneman, 1969). Although the characteristics of these outbreaks were not well-documented, heavy casualties were again reported among the Dinka, which is the dominant tribe in the area (Perea et al., 1991). The case-load in the Melut-Paloich area decreased during the 1970s, before peaking again in Melut between 1979 and 1981 (Zeese and Frank, 1987).

Figure 7: Map of Southern Sudan showing the northern and southern VL focus



Note: Shaded areas represent those counties where primary cases were reported from January through June 2007. Source: Kolaczinski et al. 2008

Another large outbreak was recorded in 1994 in Nasir, Upper Nile state, probably as a result of by non-immune villagers returning from a feeding centre in the west of the province where VL is endemic (Mercer et al., 1995). Again, the high infection rate reflects the lack of natural immunity to VL and high malnutrition rates in the population. MSF established an emergency treatment centre in 1994, which had to be shut down in 1995 due to deteriorating security conditions (Mercer et al., 1995). Upper Nile is now considered endemic for VL, with most transmission taking place from March to May.

The most serious epidemic to date in Sudan occurred in Unity state (formerly Western Upper Nile) between 1984 and 1994, affecting the Dinka and Nuer tribes (Table 13). This was the first large outbreak reported in Sudan since 1964, and was only discovered when cases among displaced people fleeing the civil war were diagnosed in Khartoum, as war made the detection and reporting of outbreaks in remote areas difficult (Perea et al., 1991). As the disease had not previously been present in this state, the entire population of 300,000 was considered at-risk.

Table 13: VL epidemiology in Southern Sudan

State	Current foci (county)	Parasite	Vector	Main outbreaks (district: year)
Upper Nile	Malakal, Tongo, Ulang, Latjor, Nasir, Kiechkuon, Baliet, Pieri, Wuror	*L. donovani*	*P. orientalis*	Melut: 1940, 1952, 1979-81 Paloich: 1952 Nasir/Malakal: 1994-6 Baliet: 2009
Unity (Western Upper Nile)	Leer, Duar, Guit, Jekany, Niemme	*L. donovani*	*P. orientalis*	Unity state: 1984–1994 Peaking in Jekany: 1988–1989
Jonglei	Lankien, Pieri	*L. donovani*	*P. orientalis*	
Eastern Equatoria	Kapoeta	*L. donovani*	*P. martini (suspected)*	

The epidemic caused an estimated 100,000 deaths in both North and Southern Sudan over a ten-year period and affected all age groups, with a mortality rate of over 90% (Seaman et al., 1992, Seaman et al., 1996). It is likely that nomadic tribes who had travelled through a VL endemic area (Zijlstra et al., 1991a) and/or troops who had trained on the Ethiopian border introduced the disease to the non-immune population of Unity state (Perea et al., 1991). It is thought that the epidemic peaked in 1988-1989 in Jekany, coinciding with widespread famine in Sudan (Seaman et al., 1992, Seaman et al., 1996), and was probably exacerbated by both increased transmission due to migration and persistent malnutrition (Cerf et al., 1987, el-Hassan et al., 1993). The first treatment centre in Unity state was set up in 1988 by MSF, which went on to treat a total of 18,948 patients between 1989 and 1995 at centres in Leer, Duar, Niemme and Jekany (Seaman et al., 1996).

The most recent outbreak in Southern Sudan began in September 2009, particularly affecting Upper Nile and Jonglei states. Cases peaked around October and November, and dropped significantly by January 2010. In the last quarter of 2009, there were over 1,200 cases of VL nation-wide, with over 70% of admissions in Jonglei state, especially at Old Fangak health centre. Overall, around 120 deaths and an average case fatality rate of 5.4% were reported during the outbreak (Orkeh and Rubena, 2010). From the beginning of June to early August 2010, Ayod county in Jonglei state reported 149 VL cases, 31 of which resulted in death, compared to eight deaths in the previous six months (Martell, 2010). The caseload stabilized in early 2010, but another dramatic increase started to occur in the third quarter of 2010, prompting a request for further funding and support for outbreak response activities by the MoH-GoSS (BBC, 2010). Health officials attribute the initial outbreak to the onset of the rainy season and to impeded health care access, due to tribal conflict (Martell, 2010).

Southern Focus

Kapoeta in Eastern Equatoria state was the first area identified as VL endemic (Archibald and Mansour, 1937). The leishmaniasis endemic part of Eastern Equatoria is very dry, with desert-like sandy soils, and inhabited by the nomadic Toposa and Nyangatom tribes. In late 2008, around nine DAT samples sent from Narus, Kapoeta county, to MSF's Lokichoggio laboratory were found to be VL positive. MoH-GoSS and WHO staff travelled to the region in December 2008 to deliver supplies and treatment, and to train staff on VL case management. Until recently only a few cases were reported each year, and the situation is considered stable (Personal communication, Justin Rubena, WHO & Mounir Lado, MoH).

8.2.3 Clinical features and risk factors

The clinical disease associated with VL in the northern focus is sudden and severe, usually leading to rapid death in the absence of treatment, while the disease in Eastern Equatoria appears to progress more slowly (Ruiz Postigo, 2010). Reported deaths rates and ratios of clinical to subclinical infection vary widely and case-fatality rates reported by MSF between 2003-2008 vary from 4% to 6% (Collin et al., 2006).

Major outbreaks have tended to follow population movement, flooding, food shortages and conflict (Zijlstra and el-Hassan, 2001). Risk factors associated with death in VL patients include malnutrition, anaemia, splenomegaly, increased age and long duration of illness (Seaman et al., 1996, Collin et al., 2004). Seasonal peaks usually occur in the dry season between November and January, their timing determined by the VL incubation period and the peak sandfly biting period during or shortly after the rains.

MSF conducted research on risk factors for relapse among VL patients treated at MSF clinics between 1999 and 2007. The results showed that splenomegaly upon admission and treatment with 17-day SSG/paromomycin combination therapy (as opposed to 30-day SSG monotherapy) significantly increased the risk of relapse. However, those who were treated with the combination therapy had a smaller risk of death. In addition, the higher relapse rates could be due to improved access to treatment, which occurred at the time of the study. Factors that were not found to be associated with risk of relapse included age, sex, malnutrition, mobility, and complications with treatment (Gorski et al., 2010).

8.3 Leishmaniasis Control – Prevention, Diagnosis and Treatment

MoH-GoSS has identified NTD control as a priority (Rumunu *et al.* 2009). An NTD Department has been established under the Directorate of Preventive Health Services, to oversee the control of leishmaniasis and all other endemic NTDs. Implementation of an IDSR strategy was initiated last year and VL was added to the list of reportable diseases. In theory this requires both weekly and monthly reports from all health centres in the country, but current reporting from some centres has not reached this level (Personal communication, Justin Rubena, WHO & Mounir Lado, MoH).

Until 2004, HealthNet International (HNI), funded by the European Commission Humanitarian Aid Office (ECHO), was the lead organisation coordinating the VL response.

When funding came to an end in 2004, this role was transferred to the WHO-Southern Sudan Office, which receives financial support from the Spanish Government. WHO will continue this role until the MoH-GoSS has developed sufficient capacity to take it over.

Draft diagnostic and treatment guidelines drawn up by the WHO-Southern Sudan office in cooperation with the MoH and MSF-H have been utilised since 2005, with training on these guidelines provided by WHO. A meeting in 2007, held to standardize diagnostic and treatment protocols, recommended the establishment of a Kala-Azar Task Force within the MoH and standardised VL surveillance. The finalisation of these guidelines is planned for late 2010 (Personal communication, Justin Rubena, WHO).

8.3.1 Diagnosis

Although national guidelines for VL diagnosis and treatment have not been finalized, the following diagnostic algorithm has been agreed upon:

- The main diagnostic tool recommended for suspected cases is the rK39 RDT;
- Patients with a positive RDT result are given anti-leishmanial treatment;
- If the rK39 RDT test is negative, a DAT is conducted and, if positive, treatment is initiated;
- If the DAT is borderline or negative, then lymph node aspiration is recommended.

While these are the recommended guidelines, the ability to implement and adhere to this algorithm on the ground is difficult. There are only a few facilities that can conduct DAT. Non-MSF run facilities used to send DAT samples to MSF's Lokichoggio laboratory (by plane), but because of long delays this practice is generally no longer adhered to. Only Old Fangak health centre and the MSF-run facilities have the resources and expertise to conduct lymph node aspirates, and MSF is the only organization performing splenic aspirates (Personal communication, Justin Rubena, WHO & Elin Jones, MSF-H).

In 2006, a study conducted in both North and Southern Sudan found the rK39 RDT to have a sensitivity of 81% and a specificity of 97% in clinically suspected cases (Ritmeijer et al., 2006). The RDT is supplied to the MoH-GoSS and NGOs by WHO, while MSF-H imports it through their headquarters in Amsterdam.

8.3.2 Treatment

All anti-leishmanial treatment in Southern Sudan is procured by MSF-H or WHO. SSG is the only registered drug, although SSG, Glucantime® and paromomycin are all on the essential drugs list. The first line treatment recommended by the draft MoH guidelines is 20mg/kg/day SSG for 30 days, with paromomycin/SSG combination therapy used as second line treatment. WHO provides SSG to NGOs or MoH-run facilities with confirmed positive cases on a case-by-case basis. Drugs procured by WHO are stored at the MoH facility in Juba, not at individual health facilities. This drug procurement and distribution role used to be carried out by Pharmaciens Sans Frontières (PSF), with drugs stored in Lokichoggio, Kenya.

MSF treat positive cases using SSG/paromomycin combination therapy, and use AmBisome as a second line treatment in relapsed and HIV positive cases. MSF started using this combination therapy in response to an increasing number of VL cases in Upper

Nile not responding to SSG monotherapy. The change to combination therapy reduced treatment duration from 30 to 17 days, and increased initial cure rates from 92.4% with SSG monotherapy to 97% (Melaku et al., 2007). Overall, however, SSG seems to retain good efficacy in Southern Sudan (Collin et al., 2004). AmBisome is only available in MSF-run facilities and is shipped from the central MSF supply in Amsterdam.

8.3.3 Prevention

Although ITNs are not routinely given to VL patients, large-scale ITN distribution for malaria prevention is ongoing throughout Southern Sudan. In Jonglei state, Malaria Consortium has distributed 45,000 nets to individuals living around Old Fangak, and Population Services International (PSI) have conducted distribution campaigns in other parts of Jonglei state during 2009. PSI have also conducted a distribution campaign in Tonj, Warrap state. In Eastern Equatoria, Malaria Consortium distributed 14,000 nets in Kanto, Kapoeta. Malaria Consortium and Medair also provide education and awareness activities on VL, aiming to improve treatment-seeking behaviour.

8.3.4 Implementing partners

The main NGO providing VL diagnosis and treatment in the country is MSF-H, although other organisations have became involved since 1999, including Medair, Comitato di Coordinamento delle Organizzazioni per il Servizio Volontario (COSV), Adventist Development and Relief Agency (ADRA), Tearfund, International Medical Relief Fund (IMRF), Diocese of Torit (DOT), United Nations Children's Fund (UNICEF) and Sudan Medical Fund and Christian Mission Aid (CMA). The current organizations involved in VL control and the locations of their projects and facilities are presented in table 12. WHO provides diagnostics and drugs to the MoH-GoSS facilities at Bentiu Hospital in Unity, Malakal Hospital in Upper Nile, and to all NGO-run facilities other than MSF.

MSF-H have operated in Southern Sudan since 1989 and were the first agency to provide VL control in response to the 1984 outbreak in Upper Nile, during which over 20,000 patients were treated. MSF-H also set up temporary centres in Pagil and Rom in Jonglei state during the 2009-2010 outbreak when caseloads in these areas were high, but these were closed when the number of cases had declined (Personal communication, Elin Jones, MSF-H).

Malaria Consortium implemented a project from 2007-2008 to build the capacity of Malakal Teaching Hospital, Upper Nile state, to manage VL cases, as it is the only government VL referral hospital serving northern Jonglei. A total of 93 staff at the Hospital, laboratory staff, and community health workers were trained on VL diagnosis, treatment, and health education. Since December 2009, Malaria Consortium also implements an education and awareness programme in response to the outbreak in Jonglei and Upper Nile states. The project focuses on training community health workers to be able to educate the local community about recognizing VL symptoms and when and where to seek treatment. The project also trains community health workers on testing, treatment, and nutritional supplementation. So far, the project has been implemented in Melut, Longechuk, and Baliet counties, Upper Nile state, and Atar county, Jonglei state (Personal communication, Cathy O'Connor, Malaria Consortium).

Table 14. Leishmaniasis partners in Southern Sudan

Organisation	Leishmaniasis Activities	Ongoing Health Facilities*	Outbreak Health Facilities*
CMA	Diagnosis & Treatment	Jonglei State: Padak County	Jonglei State: Keew PHCC**
COSV	Diagnosis & Treatment	Jonglei State: Ayod PHCC	
DOT	Diagnosis & Treatment	Eastern Equatoria State: Kapoeta County, Narus	
Malaria Consortium	Education & Training		Jonglei and Upper Nile states
Medair	Diagnosis & Treatment, Education & Awareness	Upper Nile State: Melut PHCC	
MoH/WHO	Diagnosis & Treatment	Upper Nile State: Malakal Teaching Hospital	
MSF-H	Diagnosis & Treatment, nutritional support	Upper Nile State: Lankien PHCC, Nasir PHCC	Jonglei State: Boma PHCC, Atar PHCU, Pagil PHCU, Pieri PHCC, Rom PHCC, Baliet PHCC
MSF-B	Diagnosis & Treatment	none	Jonglei State: Pibor PHCC

*Ongoing health facility refers to facilities with continuous VL programmes, whereas outbreak health facilities only addressed VL during an outbreak
**Primary health care centre (PHCC)

9. UGANDA

9.1 Background

The Republic of Uganda is a landlocked country bordering Kenya, Tanzania, Rwanda, the Democratic Republic of Congo, and Southern Sudan. It covers 240,000 km^2 and is currently divided into 80 districts (CIA, 2009e). Uganda's population is about 33.4 million and growing, with a total fertility rate of 6.7 births per woman, which is one of the highest birth rates in sub-Saharan Africa and the world. The country's population is ethnically diverse, with Baganda being the largest ethnic group, comprising about 18% of the population. More than 85% of the population lives in rural areas, and the country's economy is mainly agricultural, with most people depending on subsistence farming and an agriculture-based industry.

In 2009, life expectancy at birth was estimated to be 48 years, and infant and under-five mortality in 2007 were estimated at 82 and 131 per 1,000 live births, respectively. About 42% of births are attended by skilled health personnel, and there is approximately one physician for every 10,000 people. HIV prevalence was estimated to be about 4.1%, constituting the leading cause of death in the country (WHO, 2006).

VL is the only form of leishmaniasis that has been reported in Uganda, and was initially described in the 1950s (Wykoff et al., 1969). However, the disease remained largely unnoticed until 1997, when MSF-CH started to provide support to Amudat Health Centre in Pokot County (Kolaczinski et al., 2007).

9.2 Visceral Leishmaniasis Epidemiology

9.2.1. Parasite and Vector

The only known parasite to cause VL in Uganda is *L. donovani*, which is transmitted by *P. martini.* Termite hills are common in Pokot County, and are thought to be a favourite breeding and resting site for sandflies, as are animal burrows, tree holes and house walls (Sondorp, 1999b). Currently there is no known animal reservoir of *L. donovani* in Uganda, and transmission is therefore thought to be anthroponotic (Wykoff et al., 1969, Stevenson, 2004).

9.2.2 Geographic Distribution

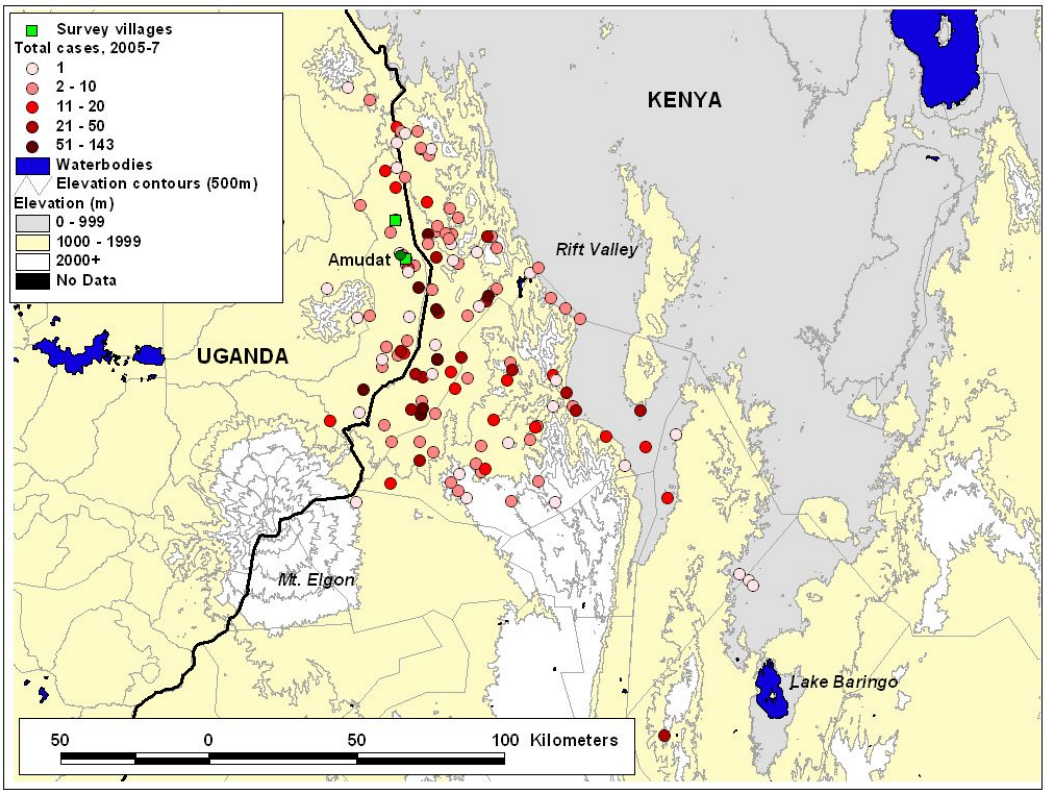
The only VL endemic area in Uganda is in Pokot County, Nakapiripirit district, forming part of the endemic focus in West Pokot district, Kenya (Figure 8). The area is home to the Pokot tribe, estimated to be about 180,000 people, the majority of which live in Kenya. The Pokot in Uganda occupy an area of about 100 km by 30 km, which is now the administrative unit of Pokot County. The Pokot lead a nomadic lifestyle and move freely across the Kenya-Uganda border with their cattle in search of grazing land (Sondorp, 1999a).

When MSF-CH started to provide VL diagnosis and treatment at Amudat Health Centre, Nakapiripirit district, in 1998 it was the first organisation to address the serious need for VL interventions in the Pokot focus. During the first 12 months (April 1998 to May 1999),

204 cases were discharged, accounting for 17% of all patients reporting to the facility. During the same period 10 VL deaths occurred (Sondorp, 1999a).

From 2000 to 2005, VL cases treated more than tripled to about 690 per year. This increase was likely, at least in part, to be the result of a higher case-detection rate once treatment became available (Kolaczinski et al., 2007). Occasionally VL cases are reported from areas of Uganda other than Pokot county, namely the neighbouring districts of Moroto and Kotido, but as yet there has been no confirmation of transmission in these areas (Personal communication, Joseph Olobo, Makerere University; Ngatya and Ariong, 2009).

Figure 8. Villages of origin of VL cases presenting at Amudat hospital, Uganda, 2005-2007



Source: Simon Brooker & Jan Kolaczinski, Malaria Consortium, unpublished

9.2.3 Risk Factors

A case-control study was conducted at Amudat Health Centre in 2006 to investigate risk factors for VL. Some factors found to be significantly associated with increased risk of VL included low socio-economic status, households that only occupied one room, sleeping outdoors some or all of the time, stunting, and infection with malaria (Kolaczinski et al., 2008b). It was also found that sleeping in areas where animals were kept was protective, suggesting that *P. martini* may prefer to feed on animals rather than humans (Kolaczinski et al., 2008b).

Personal beliefs, behaviours, and choices are also possible factors determining VL risk. The above study found that knowledge of VL transmission and symptoms was poor, but

that risk was lower among those who were aware of the symptoms and the same group was more likely to own a mosquito net (Kolaczinski et al., 2008b). MSF-CH in 2002 conducted a survey to assess knowledge, attitudes, and behaviours regarding VL among 292 randomly selected participants from both Pokot county, Uganda, and West Pokot district, Kenya. Though 95% of respondents had heard of VL, locally referred to as "termes", only 64% knew that it is transmitted by sandflies. Most were able to accurately identify symptoms, but many other misperceptions were identified. Thus, 86% of respondents believed VL could be transmitted through consuming un-boiled milk, and eating "fatty food" and animal organs were also cited as possible causes of VL by 66% and 30% of respondents, respectively (Cavailler et al., 2002). While the majority (59%) of respondents preferred to seek VL treatment at a hospital or health post, about 38% expressed a preference for consulting traditional healers or seeking other traditional methods. Only 22% believed sleeping under a mosquito net could protect against VL (Cavailler et al., 2002).

9.3 Leismaniasis Control – Prevention, Diagnosis and Treatment

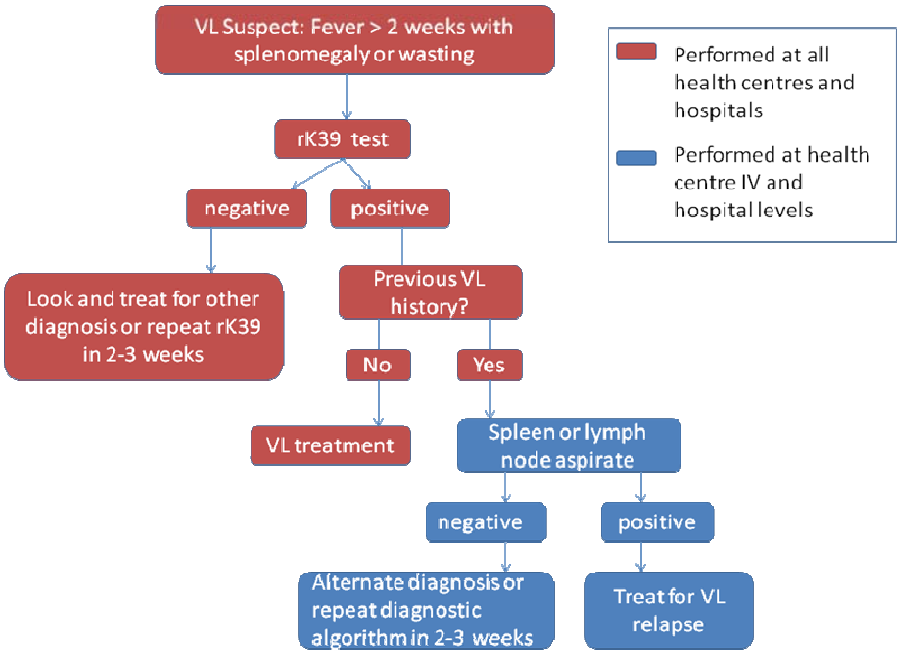
Coordination of VL interventions is the responsibility of the Vector Control Division in the MoH's Department of Community Health. There is no focal person assigned specifically to VL and previously there was no budget allocated. However, VL is included in the new National Health Sector Strategic Plan for the current fiscal year, meaning that the government has the responsibility to provide resources for VL control, although this is not expected to be a large amount initially. VL is not a reportable disease in Uganda, and though there is a system for collecting monthly reports on case information, these have not been submitted regularly. Currently there are plans to develop a Task Force to strengthen VL control, with a meeting being scheduled for November 2010 (Personal communication, Dawson Mbulamberi, MoH).

9.3.1 Diagnosis

In 2005, MSF-CH conducted a study to evaluate the efficacy of the rK39 RDT at Amudat Health Centre. Two VL diagnostics, the DUAL-IT L/M® and the Kalazar Detect® were evaluated against the Formol Gel Test (FGT), a cheap and simple, but poorly sensitive test. The DUAL/IT L/M® had a higher sensitivity (97%) than the Kalazar Detect® (83%) and the FGT (66%). Specificity for Kalazar Detect®, DUAL/IT L/M® and FGT were 99%, 97% and 90%, respectively (Chappuis et al., 2005). The authors concluded that the DiaMed-IT LEISH® should be adopted by MSF-CH as the first line test for VL (Chappuis et al., 2005).

Uganda's national guidelines now provide a diagnostic algorithm that recommends testing patients reporting with a two-week history of fever plus splenomegaly or wasting with the rK39 RDT (Figure 9). Treatment should be initiated for RDT-positive individuals and RDT-negatives should be confirmed with an alternative diagnostic test or be re-tested with the rK39 RDT after 2-3 weeks.

Figure 9. Uganda National Guidelines - VL Diagnostic Algorithm



9.3.2 Treatment

Pentavalent antimonials are the recommended first line treatment. Pentostam®, Glucantime® and generic SSG are all registered. Amphotericin B is the recommended second line treatment (MoH Uganda, 2007). Between September 2003 and April 2004, there was an interruption in MSF-CH's supply of antimonials to Amudat, and all VL cases had to be treated with amphotericin B. This situation allowed MSF to evaluate the safety and efficacy of amphotericin B compared to a historical cohort treated with Glucantime®. Results showed no statistically significant difference in case fatalities or treatment failures between the two, indicating that amphotericin B is similar to Glucantime® with regards to safety and effectiveness in treating VL in Uganda (Mueller et al., 2008).

DNDi conducted a trial on SSG/paromomycin combination therapy at Amudat Health Centre. The trial was completed in 2010 and is being written up for publication. DNDi is also planning to start a trial on Ambisome monotherapy at Amudat as part of a multi-country study including Ethiopia and North Sudan (Personal communication, Joseph Olobo, Makerere University). The MoH currently has no resources to procure anti-leishmanial drugs and all treatment is therefore being provided by DNDi (Personal communication, Dawson Mbulamberi, MoH).

9.3.3 Prevention

Currently there are no VL prevention activities being conducted in Uganda.

9.3.4 Implementing Partners

MSF-CH provided VL case-management at Amudat Health Centre until 2006, when activities were moved to Kacheliba, Kenya. DNDi/LEAP took over provision of VL diagnosis and treatment at Amudat, as a component of its research on the efficacy of VL treatment regiments.

10. KNOWLEDGE AND INTERVENTION GAPS

Present situation analysis highlights several gaps that should be addressed, to improve leishmaniasis prevention and control in eastern Africa:

A) Country-specific information

In most of the region's countries the MoHs do not have complete (or any) records of (passive surveillance) data on leishmaniasis. Reasons for this include leishmaniasis not being a reportable disease in some countries and the incomplete, weak or no reporting systems used by the (mostly public sector) service providers. For example, whilst data may be at facility level, it may not reach a higher-level administrative level, and thus is not reported nationally. Lack of consistent, accurate and complete reporting makes it difficult to monitor disease trends, identify areas of need (and epidemics), and deliver interventions accordingly. In countries where more than one form of leishmaniasis is prevalent, these are often not being differentiated, making it impossible to attribute the respective burden of each form.

Disease burden data in most East African countries is almost exclusively facility-based, i.e. through passive data collection, with only few countries having up-to-date active case detection data collected through specialized surveys or studies. As a result, it can be said that the burden of leishmaniasis in all countries of eastern Africa is certainly an under-estimate, which again makes it difficult to assess programmatic gaps and plan possible interventions.

B) Knowledge and activities on prevention

Prevention is arguably the most neglected aspect of leishmaniasis control in the region. Current prevention activities are limited to small-scale LLIN distribution and health education in select areas, mostly targeting individuals already infected with leishmaniasis. Evidence on the effectiveness of ITNs/LLINs is mixed, but there are data to suggest that regular use of a net is likely to reduce leishmaniasis transmission. No trial to evaluate the effectiveness of LLINs and/or other prevention efforts for leishmaniasis has been conducted in eastern Africa; even the impact of health education efforts has not been assessed.

C) Consistent funding to procure supplies and deliver interventions

Limited and sporadic funding for leishmaniasis prevention and control leads to inconsistent intervention efforts across most of the region. Interventions are primarily initiated in response to outbreaks, rather than to prevent them (i.e. little funding is provided between epidemics). Continuous implementation of activities, particularly longer-term support to strengthen systems, is rare. Most of the limited donor support that is available for leishmaniasis is allocated to research on diagnostics and drugs, rather than to the delivery of existing interventions or to operational research that could improve delivery of existing tools for leishmaniasis prevention and control. As a result, countries often experience stock-outs of diagnostics and drugs, and many health workers in endemic foci are not adequately trained in up-to-date case-management or prevention and control guidelines.

In many of the endemic countries the MoH has not established a budget line for leishmaniasis or, in fact, NTD prevention and control. Diagnostic and treatment supplies are almost exclusively provided by WHO or NGOs.

11. RECOMMENDATIONS

Based on the identified gaps, the following recommendations are put forward:

A) Country-specific Information

Many of the current gaps in leishmaniasis control result from a general lack of resources and capacity for health care delivery. Increased efforts (and funds) are required to strengthen overall health systems, aiming to improve health workers' capacity to diagnose and treat a broad range of diseases including leishmaniasis, and to improve reporting at facility level and generally within the MoHs' administration. Where feasible, activities specific to leishmaniasis prevention and control, such as case-management training, should be addressed as a component of health systems strengthening efforts conducted under the auspices of larger, better-funded programmes (e.g. for HIV/AIDS, tuberculosis or malaria).

Adding leishmaniasis to the list of reportable diseases or IDSR, if in existence, could provide an opportunity to strengthen leishmaniasis reporting. It will be important, however, that details on the various pathological forms of leishmaniasis, and the age, sex and geographic origin of the patient are maintained when data are collected and collated through the prevailing in-country reporting system(s). If collation of surveillance data at national level is currently not possible, efforts should be made to –at least– improve reporting and data analysis in the known highly endemic areas. Maintaining awareness of the situation in these locations will allow a faster response when needed. As part of the process, epidemic thresholds will need to be agreed upon to differentiate seasonal increases in case-loads from actual outbreaks.

B) Knowledge and activities on prevention

Evidence on the effectiveness of different leishmaniasis prevention and control methods is limited for eastern Africa. Prevention efforts do, however, form a key component of malaria prevention and control strategies in the region, and indeed these two diseases are often co-endemic. Depending on the resting and biting habits of the different leishmaniasis vectors in eastern Africa, it could be envisaged that prevention tools used for malaria prevention and control, such as LLINs or IRS, are also effective in reducing leishmaniasis transmission. This assumption is supported by results from studies in Sudan, which have shown that ITNs protected against biting by *P. orientalis* (Elnaiem et al., 1999b), and that ITN users had significantly lower VL incidence compared to non-users (Ritmeijer et al., 2007). It is therefore recommended that, initially, more resources be devoted for operational research to study the behaviour of the main sandfly vectors in eastern Africa. Depending on the results, operational research studies should be conducted to determine the effectiveness of potential prevention and control methods, particularly LLINs. If nets were shown to be effective in preventing leishmaniasis in the

region, this message could be used to advocate for priority targeting of malaria/leishmaniasis co-endemic areas based on cost-effectiveness grounds.

C) Leishmaniasis funding support and commitment

Establishment of a designated MoH budget line provides an important indication to health sector donors that host governments are committed to the prevention and control of NTDs and is –in itself– an important part of leveraging additional funding from outside resources. National advocacy should therefore focus on increasing host government commitment in the form of: i) an NTD line in the national (health sector) budget; and ii) provision of some of the necessary funds to procure supplies and provide adequate case management.

D) Communication and Coordination

Implementing partners in some of the leishmaniasis-endemic countries have established mechanisms to share information and coordinate their activities. It was observed that countries with such coordination mechanisms (e.g. Southern Sudan) tended to have better data and an overall more coordinated approach. Other leishmaniasis-endemic countries may want to follow suit, aiming to better use existing in-country resources and use their combined strengths (and data) to advocate for additional funding support and commitment for interventions.

Increased cross-border communication was also identified as a priority, given that cross-border transmission is common. Furthermore, such communication could be of benefit to some countries as their neighbours may have had more experience with implementation of leishmaniasis prevention and control activities. Sharing such experience could save time and money when case-management guidelines or strategies are being developed or modified.

12. GLOSSARY

AmBisome®, Amphocil®, Abelcet®	Lipid formulations of Amphotericin B
Amphotericin B	Amphoterecin B deoyxcholate (Fungizone®); first-line treatment regimen for treating VL in sub-Indian continent. Second-line treatment option for CL and ML. Fifteen injections are required over 30 days. Disadvantages are cost, toxicity, and side effects.
Anthroponotic transmission	Transmission between humans
Aspirate (splenic/lymph node/bone marrow)	Removal of fluid with a fine needle for diagnostic testing
Cryotherapy	A topical treatment for CL consisting of repeated applications of liquid nitrogen to lesions
Direct agglutination test (DAT)	Serological diagnostic test for VL
Glucantime	Meglumine antimonate, a pentavalent antimony used to treat both VL and CL
Hepatomegaly	Enlargement of liver
Integrated Disease Surveillance and Response (IDSR)	Strategy recommended by the World Health Organization to improve the availability and use of surveillance and laboratory data for control of priority infectious diseases
Lymphadenopathy	Enlargement of lymph nodes
Miltefosine®	Hexadecylphosphocholine; the first oral chemotherapy treatment for VL and CL. Disadvantages are possible teratogenicity, moderate side-effects, and cost.
Paromomycin	Aminoglycoside drug currently being tested for VL treatment. Limited side-effects and toxicity.
Pentavalent antimony	First-line drug regimen to treat the leishmaniases, except in Indian sub-continent. Disadvantages include toxicity and side-effects.
Pentostam®	Sodium stibogluconate, a pentavalent antimony used to treat both VL and CL.

GLOSSARY (continued)

Post kala-azar dermal leishmaniasis (PKDL)	A complication of VL characterized by a rash, usually starting around the mouth and spreading to other parts of the body.
rK39 RDT	A rapid diagnostic test for VL
Sensitivity	The probability that a person having a disease will be correctly diagnosed as positive
Specificity	The probability that a person who does not have a disease will be correctly diagnosed as negative
Splenomegaly	Enlargement of spleen
Zoonotic transmission	Transmission from animals to humans

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