Situational Analysis of Leishmaniases Research in Kenya

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SUMMARY

_Leishmania spp_ are protozoan parasites of the Trypanosomatidae family that cause disease in humans and animals. In general, infections with these parasites can be divided into three main forms namely, cutaneous, mucocutaneous, and visceral leishmaniases. The disease is prevalent in many tropical and subtropical regions of the world, where it is transmitted via the bite of an infected sand fly. Leishmaniasis has been known to be endemic in parts of Kenya from as far back as early in the 20th century. These endemic areas include Turkana, Baringo, Kitui, Machakos, Meru, West Pokot and Elgeyo Marakwet districts which have been reported to be endemic for kala-azar. Recent outbreaks of VL have been reported in the previously non-endemic districts of Wajir and Mandera in North Eastern Kenya between May 2000 and August 2001. The vector for VL in Kenya is _Phlebotomus martini_ though other vectors including _P. orientalis_ have been reported. Baringo district is the only foci reported where both VL and CL are known to occur in Kenya. The aetiological agents for CL which include _L. major_ which has been reported in Baringo; _L. tropica_ in Laikipia, Samburu, Isiolo, Nakuru and Nyandarua districts while _L. aethiopica_ has been reported in the Mt Elgon area. In Kenya, _P. duboscqi, P. guggisbergi_ have been shown to be the vectors of _L. major_ and _L. tropica_, respectively, while _P. pedifer, P. longipes_ and _P. elgonensis_ have been implicated as vectors of _L. aethiopica_. Since 1980, the Kenya Medical Research Institute (KEMRI) has spearheaded research on leishmaniases research in Kenya focusing on various aspects including characterization of _Leishmania_ species, biology, and ecology of sand fly vectors, development of biological strategies for sand fly control, identification of animal reservoirs, diagnosis, new treatment strategies, new chemotherapeutic agents, and vaccine-related studies. KEMRI, a founding partner of the Drugs for Neglected Disease Initiative (DNDi), whose overall aim is to address lack of new or improved drugs for neglected diseases (which include leishmaniases, malaria, trypanosomiasis and chagas disease) has made major contributions in leishmaniases research and control in Kenya and the eastern Africa region.


Introduction

_Leishmania spp_ are protozoan parasites of the Trypanosomatidae family that cause disease in humans and animals. In general, infections with these parasites can be divided into three main forms namely, cutaneous (CL), mucocutaneous (MCL) and visceral (VL) (or kala azar) leishmaniases [1]. The disease is prevalent in many tropical and subtropical regions of the world, where it is transmitted via the bite of an infected sand fly. Although leishmaniasis is endemic in 88 countries, 90% of CL cases have been reported in Afghanistan, Syria, Saudi Arabia, Brazil, and Peru. VL, also known as kala azar, is the most dangerous form of the disease and occurs in Bangladesh, Brazil, India, and Sudan. A new syndrome in which _Leishmania_ co-infects patients with AIDS is particularly deadly and has been reported in 33 countries including Kenya [1, 2]. The impact of leishmaniasis on humans is enormous. One tenth of the world’s population is at risk and 2 million new cases are reported each year [1]. There are 22 species that cause disease in humans or animals [3] and specific
parasite species are associated with specific types of syndrome (see Table 1). For example, VL is caused by *L. donovani* and *L. chagasi* [4] whereas CL is caused by different species in different areas of the world. For example, *L. major* causes CL in the Middle East and *L. mexicana* causes CL in Central America. In addition, lesions caused by *L. braziliensis* complex in the skin can spread to the mucous membranes resulting in a late complication known as MCL, or espundia [5].

<p>| Table 1: Spectrum of leishmaniases, aetiological agents and worldwide distribution |
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<th>Type of leishmaniasis</th>
<th>Causative organism</th>
<th>Worldwide distribution</th>
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| Visceral | *L. donovani*  
*L. infantum*  
*L. chagasi* | China, India, Iran, Sudan, Kenya, Ethiopia, Mediterranean basin, Brazil, Colombia, Venezuela, Argentina |
| Cutaneous | *L. tropica*  
*L. major*  
*L. aethiopica*  
*L. mexicana* | Mediterranean basin, Afghanistan, Middle East, W. and N. Africa, Kenya, Ethiopia, Central America and Amazon basin |
| Mucocutaneous | *L. braziliensis* complex | Brazil, Peru, Ecuador, Columbia, Venezuela |

**Epidemiology of leishmaniases in Kenya**

Leishmaniasis has been known to be endemic in parts of Kenya from as far back as early in the 20th century [6]. An outbreak of VL in the King’s African Rifles troops encamped north of Lake Turkana in southwest Ethiopia was reported in the 1940s [7]. Since then Turkana, Baringo, Kitui, Machakos, Meru, West Pokot and Elgeyo Marakwet districts have been considered to be endemic for kala-azar. Between 1950 and 1960 more than 1,052 cases of VL were reported from these districts alone [6].

A serious outbreak of VL was reported in Kitui district that began in 1952 with 303 cases being reported and peaked in 1953 with 2,142 cases. In the same year 157 cases were reported in the neighbouring Meru district [6]. Another outbreak of VL in Meru district was reported in 1966 with 1,500 cases [8]. *Phlebotomus martini* Parrot, 1936 was shown to be the vector of kala-azar during that epidemic [9, 10]. Further outbreaks of VL were reported in Machakos district in the 1970s, and again in Kitui district in the 1980s [11-13]. Baringo and the neighbouring districts such as West Pokot were first identified as leishmaniases foci in 1955 [14]. Since then, *L. donovani* transmitted by *P. martini* and *L. major* transmitted by *P. duboscqi* Neveu Lemaire, 1906 have been shown to exist in the region allopatrically, with rodents being the reservoir of CL (15-21). Other possible vectors that have been reported include *P. celiae* Minter, 1962, *P. vansomeranae* Heich, Guggisberg et Teesdale, 1956 and *Sergentomyia garnhami* [22] for VL [23, 24]. VL caused by *L. donovani*, is endemic in Baringo District, Kenya. The disease occurring in Baringo has a focal distribution in the dry, hot areas below 1500 metres and the infections may be characterized as follows: 1) asymptomatic 2) subclinical and self-limiting (not medically identifiable), and 3) clinically manifest disease (that is medically identifiable). Half of the reported VL patients are between 5 and 14 years of age and 66% of them are males. A human case of a mixed *L. donovani* and *L. major* infection has been reported in this dual focus of VL and CL [25]. Often associated with sporadic incidents of the disease rather than epidemics, as many as 305 cases of VL were reported in Baringo district alone in 1999 [26-29]. In the early 1990s, 3 Maasai children were diagnosed with VL acquired locally in Kajiado district in the Rift Valley of Kenya. *L. donovani* s.l. was isolated but a survey of other school children in the district did not reveal any more cases. *P. martini* was found to be common in the area
while *P. orientalis* Parrot, 1936 another vector for VL though present was rare and therefore transmission was attributed to *P. martini* [30]. More recently, an outbreak of VL was reported in the previously non-endemic Wajir and Mandera districts of North Eastern Kenya where during a period from May 2000 to August 2001, 904 patients were diagnosed with VL, with the patients coming from an area that spanned Wajir and Mandera districts, southern Somalia and southeast Ethiopia. Unusual rainfall patterns, malnutrition and migration of a *Leishmania*-infected population seeking food and security are thought to have contributed to this outbreak [31].

Diffuse cutaneous leishmaniasis (DCL) was first described in Kenya in 1969 with 3 patients from the indigenous communities in Bungoma district, around the Mt. Elgon area diagnosed [32]. *L. aethiopica* has since been identified as the aetiological agent, rodents as the animal reservoirs and *P. pedifer* Lewis, Mutinga et Ashford, 1972 to be the vector of DCL in the Mt. Elgon region [14, 33, 34].

Cutaneous leishmaniasis caused by *L. major*, and transmitted by *P. duboscqi* was first reported in Kitui district in the 1990s [35]. *L. major* has also been isolated from an infected monkey (*Cercopithecus aethiops* from Kiambu District, central Kenya [36]. However, no human cases have been reported from the district so far.

Meanwhile, active case detection and investigations of sand fly resting places conducted in the early 1990s, led to the identification of *L. tropica* CL in Central and Rift Valley provinces, mainly Laikipia, Samburu, Isiolo, Nakuru and Nyandarua districts [34]. Three sand fly species belonging to the subgenus *Larroussius* namely, *P. pedifer, P. aculeatus* Lewis, Minter et Ashford, 1974, *P. guggisbergi* Kirk et Lewis, 1952 and one *Paraphlebotomus* species (*P. saevus* Parrot et Martin, 1932) were found to be common in these areas [34,37-39]. *P. guggisbergi* has since been shown to be the vector for *L. tropica* in Kenya [40].

Currently, disease control strategies rely on chemotherapy to alleviate the disease, on vector suppression, and personal protection to reduce transmission [1]. To date, there are no proven vaccines against any form of leishmaniasis [41]. Since 1980, the Kenya Medical Research Institute (KEMRI) has made major contributions to leishmaniasis research and control focusing on various aspects including characterization of *Leishmania* species, biology, and ecology of sand fly vectors, development of biological strategies for sand fly control, identification of animal reservoirs, diagnosis, new treatment strategies, new chemotherapeutic agents, and vaccine-related studies.

This has been achieved through collaborations with several agencies including the UN Development Program/World Bank/World Health Organization Special Program for Research and Training in Tropical Diseases (TDR), US Army Medical Research Unit-Kenya (USAMRU-K), the Ministry of Health’s Division of Vector Borne Diseases (DVBD), International Centre for Insect Physiology and Ecology (ICIPE), the Institute for Primate Research (IPR), Médecins Sans Frontières (MSF), local and international universities and colleges. As a result of this KEMRI scientists regularly participate in the Ministry of Health’s Disease Outbreak Management Unit, (DOMU), WHO and MSF to assist in the control of Kala azar outbreaks in Kenya and in the eastern African region. The Centre for Biotechnology Research and Development (CBRD) and the Centre for Clinical Research (CCR) of KEMRI have spearheaded leishmaniasis research. The Institute is a leader in sand fly biology research and it maintains the only sand fly colony in sub-Saharan Africa. The Centre for Clinical Research (CCR), designated a Good Clinical Practice (GCP) compliant facility, has also been involved in testing new anti-leishmanial drugs. KEMRI has an animal care facility that supports laboratory research in leishmaniasis.

The following sections summarize research activities on leishmaniasis in Kenya in which KEMRI has been a major contributor.
Characterization of Leishmania species in Kenya

It is essential to know the identity of the parasite(s) in each focus, since this knowledge has implications for control and treatment of leishmaniases [42]. Therefore, isolates originating either from research, entomological and zoological activities should be identified and compared with international references stains. Cryobanks are also required for storage and for future availability. To address this need, a laboratory at CBRD of KEMRI was designated a regional reference centre for leishmaniasis taxonomy in Kenya. This facility maintains a cryobank of Leishmania isolates and is internationally referred to as Nairobi Leishmania Bank (NLB). At least 1800 Leishmania and other Leishmania-like isolates obtained from humans, other vertebrates, sand fly vectors and other arthropods from Kenya and other parts of Africa have been cryopreserved in this bank.

Through this bank it has been possible to compare the biological characteristics of the Leishmania parasites in Kenya and the neighbouring countries [43]. Zymodeme analysis of the Kenyan VL and CL isolates resulted in the identification of 11 subpopulations of the L. donovani species complex and six subpopulations of the L. tropica species complex endemic to different geographic areas of Kenya [37, 39]. A Leishmania-like isolate from the reptiles has since been identified as Sauroleishmania (RGER/KE/89/NLB-1236) and has been shown experimentally to cause L. major-like cutaneous lesions and visceral leishmaniasis in BALB/c mice [44].

Research on sand fly biology and control in Kenya

Control of phlebotomine sand flies remains a difficult problem throughout the world because of the insects' very highly specialized breeding sites. Use of insecticides remains the most effective method of sand fly control. However, resistance to insecticides has proved to be a major challenge. Use of bed nets or permethrin impregnated wall cloth, repellents and other personal protective measures have proved to be unreliable in Kenya [45]. With these shortcomings, there is need to identify new insecticides.

In general, control of leishmaniasis is hampered by the diversity of vectors, parasites, and reservoir hosts and the interventions must take into account these differences. It is therefore crucial to understand the biology of the leishmaniasis as well as that of the sand fly. The exploration of host-parasite interactions between species of Leishmania and respective vectors represents a wide and important field for basic and applied research as well. To address these needs, laboratory reared sand fly colonies have been established at KEMRI. These include P. martini and P. duboscqi Neveu-Lemaire (Diptera: Psychodidae) [17]. It is through studies done using P. duboscqi that L. major development within the sand fly was unravelled [46]. These studies have shown that it takes a period of 4-25 days, for the parasite to develop inside the sand fly and during the next blood meal the infective metacyclic stage enters the body of host through a sand fly bite [46, 47]. At least five developmental forms have also been recognized during development in the subgenus Leishmania, namely, procyclic promastigotes, nectomonad promastigotes, haptomonad promastigotes, paramastigotes, and metacyclic promastigotes [46].

Understanding of sand fly biology is also important in designing new control programmes in leishmaniases. It has also been shown that P. perniciosus can acquire and allow the development of L. infantum by feeding on L. infantum/HIV coinfected patients. Since this sand fly is an important vector of VL in southern Europe, a new natural anthroponotic cycle could be considered in the epidemiology of L. infantum/HIV coinfection [48]. This phenomenon is known as xenodiagnosis and this technique has been shown to be able to detect the presence of Leishmania parasites in a patient that other conventional diagnostic techniques failed [48]. Therefore, the design of leishmaniasis control programs and the management of coinfected individuals should take these findings into account in southern Europe [48].

Investigations on vectors of leishmaniases in Kenya started only in the early 1950’s when the VL assumed importance as a result of a
major disease epidemic outbreak [49]. Since then these investigations on vectors have resulted in identification of the main vectors for both VL and CL. *P. martini* Parrot has been confirmed as the vector for *L. donovani* the aetiological agent of VL in Kenya, southern Sudan, and Ethiopia [15, 21,50]. This sand fly species rests and breeds in termite hills, animal burrows, tree holes, and house walls [51, 52]. It feeds mainly on goats, rabbits, and humans, and to a lesser extent on dogs, cattle, and other hosts [52]. Another vector for *L. donovani* in Kenya is *P. orientalis* which occurs in Kajiado district of Kenya [30].

Among the cutaneous forms of leishmaniasis *P. duboscqi* Neveu-Lemaire (Diptera: Psychodidae) has been confirmed as the main vector of *L. major* in West Africa and the Rift Valley of Kenya [53, 54]. *P. pedifer, P. longipes* and *P. elgonensis* have been implicated as vectors of *L. aethiopica* occurring in the vicinity of Mount Elgon, Kenya [32, 34, 55, 56]. *P. guggisbergi* has been incriminated as a vector of *L. tropica* endemic in Samburu, Laikipia, Narok, Nakuru and Nyandarua districts of Kenya [37, 40].

Research on animal reservoirs of Leishmaniasis in Kenya

Extensive research has been carried out in eastern Africa for animal reservoirs of both VL and CL. The domestic dog [54] has been the only domestic animal so far implicated as a possible reservoir for visceral leishmaniasis [58]. For cutaneous leishmaniasis caused by *L. aethiopica*, the rock (*Denobrahyrax arboveus*) and tree (*Procavia johnstoni*) hyraxes and the giant rat (*Cricetomys sp*) are the proven reservoirs of the disease [33], while several species of rodents have been demonstrated to harbor *L. major* which include *Tatera robusta, Arvicanthis niloticus* and *Aethomys kaiser* [15, 18, 19]. The domestic sheep [58] and goats [59] which were initially suspected to be animal reservoirs for VL have since been proven experimentally to be non susceptible to *L. donovani* infection and therefore unlikely to be a synanthropic reservoir of this parasite [60, 61].

In Kenya, anthroponotic VL in Baringo District has shown that *Leishmania* deoxyribonucleic acid (DNA) is detectable in patients 10.5 months before diagnosis, up to 3 years after diagnosis and apparently successful treatment. Sub clinical cases have also been reported to have detectable circulating parasite DNA in their blood. These findings may indicate that sub clinical cases can be a reservoir and formerly treated VL patients can remain a reservoir for a long time. Xenodiagnosis may be important in such areas to determine whether sub clinical cases and former VL patients do have role in transmission of VL in Kenya [62].

Research on new diagnostic tests for leishmaniases

Sensitive, specific, reproducible, feasible and cheap diagnostic tests are needed if one wants to build an effective and efficient test-treatment strategy [63]. Since Leishman identified the parasite in 1901, the definitive diagnosis of VL has relied on demonstrating the organism by microscopy in smear or culture of aspirates or tissue [64,65]. However, a splenic-aspiration technique [66] which is used to acquire these tissues can hardly be recommended for rural district hospitals because of the risk of fatal haemorrhage, which subsists even with the recently introduced safer procedures [67]. Therefore, the search for a suitable alternative for splenic aspirates is thus still going on.

Over the past 20 years, several serological tests have been developed showing high sensitivity for visceral disease [68]. Enzyme linked immunosorbent assays (ELISA) for detecting leishmanial antibodies has also been established and successfully applied in clinical routine and sero-epidemiological surveys in Kenya [26, 27, 69]. Of all the available serological tests, the direct agglutination test (DAT) has proved to be the most appropriate one for field use in Kenya [29, 63, 70, 71].

Other methods that have been tested include isoenzyme analysis [72, 73]; kDNA based techniques [74, 75]. In recent years polymerase chain reaction (PCR) techniques for leishmaniases have been developed and applied to visceral disease with contradictory results [76, 77]. Apart from the fact that PCR does not eliminate the need for tissue
sampling, it is not exactly the type of appropriate technology needed in endemic areas.

**Research on new treatment strategies and chemotherapeutic agents for leishmaniases**

Neglected diseases such as leishmaniasis, trypanosomiasis, Chagas disease, and malaria have had a devastating impact on the world's poor. These treatable, infectious tropical diseases have been progressively marginalized by those in charge of making research programme decisions, both in the public and private sectors. Unfortunately, people suffering from these diseases do not constitute a market lucrative enough to attract investment in research and development for new drugs. KEMRI is a founding partner of an international effort, Drugs for Neglected Disease Initiative (DNDi), whose aim is to address lack of new or improved drugs for neglected diseases such as leishmaniasis. KEMRI’s Centre for Clinical Research (CCR) brings to DNDi a rich history of involvement in tropical diseases and expertise in clinical research for neglected diseases.

Over the last 25 years, scientists at CCR have been addressing the issue of treatment options for Kala-azar. The treatment of leishmaniasis, as currently conducted in Kenya with sodium stibogluconate, is unsatisfactory as it is expensive, resistance and relapses may occur [78]. However, it is through collaborative efforts of CCR scientists several new drugs or including AmBisome® a safer and more effective lipid formulation of Amphotericin B (second line VL treatment); sitamaquine and aminosidine, alone or combined with sodium stibogluconate, in visceral leishmaniasis, compared to treatment by stibogluconate alone have been tested [79].

Worldwide, Leishmania parasites are increasingly becoming more and more resistant to antileishmanial drugs. The increment of *in vitro* antimony resistance due to intermittent drug exposure [80-83], the isolation of antimony-resistant *Leishmania* strains from patients with unresponsive CL [84,85], and recent reports, of numerous cases of VL among patients with the human immunodeficiency virus [86-89] indicate the need for new therapeutic agents for control and management of leishmaniases. Extensive studies of new drugs with antileishmanial activities, including natural products and synthetic compounds, have been undertaken worldwide [90], but problems associated with the currently available drugs remain unresolved. In recent years, there has been growing interest in alternative therapies and use of natural products, especially those derived from plants [91]. The use of plant-based medicine for healing and prophylaxis is as ancient and universal as medicine itself. Recent research undertaken in KEMRI has led to discovery of plant-based products with antileishmanial activities. For instance, studies have shown that leaf, root and stem extracts from *Ajuga remota* and *Trichilla emetica* have antileishmanial activity when tested against *L. donovani in vitro* and *in vivo* [92]. Some of the active compounds isolated from plants include iridoid glucosides, limonoids and terpenoids [92]. KEMRI has also initiated studies aimed at testing extracts/compounds from medicinal plants used widely by the local people for treating splenomegaly related ailments in leishmaniasis endemic areas of Kenya [92]. A long term goal of this research is to develop oral drugs for leishmaniases. These drugs have an advantage of reducing treatment-related socioeconomic difficulties (inadequate health care infrastructure and the long period of patient hospitalization) prevalent in the endemic areas.

Among the products tested for antileishmanial activity in the rodent models (BALB/c mice and Syrian hamsters) at KEMRI includes metal ion chelators namely (Pristane, EGTA, and HEEDTA). Results of these studies suggests that metal ions chelators have antileishmanial activity when tested against *L. donovani in vitro* and *in vivo* [92]. Some of the active compounds isolated from plants include iridoid glucosides, limonoids and terpenoids [92]. KEMRI has also initiated studies aimed at testing extracts/compounds from medicinal plants used widely by the local people for treating splenomegaly related ailments in leishmaniasis endemic areas of Kenya [92]. A long term goal of this research is to develop oral drugs for leishmaniases. These drugs have an advantage of reducing treatment-related socioeconomic difficulties (inadequate health care infrastructure and the long period of patient hospitalization) prevalent in the endemic areas.

**Vaccine related research for leishmaniases in Kenya**

Currently there is no vaccine available for use against any form of leishmaniases worldwide [41]. In brief, vaccines based on killed promastigotes with or without *Mycobacterium bovis* BCG have shown significant protection against *L. braziliensis* [95], *L. mexicana* or *braziliensis*, *L. major* [96] and *L. donovani* [97] in humans. In experimental animal
models, several other vaccine preparations are being tested. Examples include: attenuated live parasites [98]; subunit vaccines delivered by live carriers such as BCG expressing the surface protease gp63 of *L. major* [99]; vaccinia virus expressing the glycoprotein gp46/M2/PSA-2 [100]; gp63 expressed in attenuated *Salmonella typhimurium* [101]; purified recombinant or native proteins formulated with an adjuvant such as the *Leishmania*-homologue of receptors for activated C kinase (LACK) plus IL-12 [103, 102], gp46/M2/PSA-2 or protein dp 72 plus *Corynebacterium parvum* [104], T cell epitopes plus Poloxamer 407 [104]; and vaccination with DNA encoding gp63 [105], LACK [106], or gp46/M2/PSA-2 [107]. In general, these vaccination protocols elicited partial protection against *L. major*.

Vaccine research at KEMRI is still at the rodent model stage of development in leishmaniases. So far live-attenuated *L. major* parasites [108], *L. major* culture-derived soluble exogenous antigens (SEAgs) [109], lipophosphoglycan (LPG) alone or LPG plus *Mycobacterium bovis* Bacille Calmette-Guerin (BCG) [110], and LPG plus salivary gland lysates [111] have been tested.

Transmission blocking vaccine studies in leishmaniases have also been undertaken at KEMRI. These studies have shown that LPG is an excellent candidate as a transmission blocking vaccine against *L. major* infections [112, 113]. In these studies, sand flies, which fed on BALB/c mice, immunized with *L. major*-derived LPG [114] or monoclonal antibodies raised against LPG [115] showed that parasite development was inhibited at the log phase (procyclic) of the parasite. There was also a marked reduction in the numbers of metacyclic promastigotes developing, leading to reduced transmission of *L. major* to naive BALB/c mice [113]. It has also been shown that *P. duboscqi* gut lysates and proteins present in *L. major*-derived LPG share two common proteins of molecular weights 105 kDa and 106 kDa [115]. The goal of these studies has been to develop a vaccine that can be utilized both to reduce transmissible infections within the sand fly and disease severity within the host. Some of the important findings relevant to vaccine research also include the determination of an inoculum dose required for affecting a visceral infection in rodents [116].

At the Institute for Primate Research (IPR) in Karen, Nairobi it has been shown that the vervet monkey (African Green monkey) is a good model for human cutaneous or visceral leishmaniases [117, 118]. Availability of a non-human primate model of leishmaniasis facilitates the study of different aspects of this disease and will accelerate the development of vaccines and new drugs for leishmaniases. Using this model the safety and immunopotency of the recombinant gp63 mixed with Baccille Calmette Guerin (BCG) vaccines [119], and also the adjuvant potential of two doses of IL-12 when used with a killed *L. major* vaccine [120] have been evaluated. It has also been demonstrated that high cross-reactivity between *L. donovani* and *L. major*, and that *L. donovani* protects against *L. major* infections [121]. These findings have relevance for vaccine development in leishmaniases.

**Conclusion**

Although various aspects of the transmission and control of leishmaniases have been studied in Kenya, the impact of visceral leishmaniiasis or kala azar is still enormous in Kenya. Control measures against sand flies and reservoir hosts need to be further evaluated in terms of their effect on disease incidence. Very few attempts have also been made to quantify local factors or to identify the causative mechanisms of epidemics in previously nonendemic or low endemic areas. Research to develop more effective drugs that meet the current standards of safety also remains a high priority. It is hoped that the entry of Drugs for Neglected Disease Initiative (DNDi), whose aim is to address lack of new or improved drugs for neglected diseases including leishmaniases will mobilize inter-country, international support and collaboration in terms of both finance and technical expertise towards achieving this goal. Diagnostic and vaccine-related studies are also still required to be pursued vigorously.

Many cases of leishmaniases still go unreported or undiagnosed hence the official statistics are currently not available for.
determining the actual number of cases in Kenya. Health education activities are still required to sensitize people living in endemic areas, medical and public health managers, and individuals at risk on leishmaniases. Decision makers should be sensitized on the importance of the leishmaniases as a public health problem so that they will support and defend control programmes. Notwithstanding these challenges, contributions from KEMRI and its partners towards leishmaniases control in Kenya and the eastern Africa region is commendable.

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