

LESSON 15: OTHER VECTORED DISEASES

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Other Vectored Diseases in Ethiopia

- Lymphatic Filiriasis
- Leishmaniasis
- Onchocersisis
- Trypanosomiasis
- Yellow Fever
- Other Arboviral Diseases

TRYPANOSOMIASIS

What is African trypanosomiasis?

“There are two types of African trypanosomiasis (also called sleeping sickness); each named for the region of Africa in which they are found” [1]. East African trypanosomiasis is caused by a parasite called *Trypanosoma brucei rhodesiense* which is carried by a fly vector known as tsetse fly. West African trypanosomiasis, (also known as Gambian sleeping sickness), is a vectored infection caused by the *Trypanosoma brucei gambiense* parasite which is also carried by the tsetse fly. “More than 66 million women, men and children in 36 countries of sub-Saharan Africa suffer from human African trypanosomiasis (HAT)”. [2]

Disease Ecology

The Vector:

Over 30 species and subspecies of tsetse flies are recognized under the genus *Glossina*, family *Glossinidae*, and order *Diptera*. Although not continuous the glossina population is found throughout Sub-Saharan Africa from Senegal in the West to Somalia in the east. [3]

“Tsetse populations are denser in West and Central Africa, and are found more sporadically to the East and down to the borders of the Kalahari and Namibian Deserts in Southern Africa. Although tsetse fly habitats may vary considerably, climate and altitude - through their direct effects on vegetation, rainfall, and temperature - are still the primary determinants for proliferation. Unlike other insects, there are no seasonal interruptions in the life cycles of tsetse flies. However both adult longevity and puparial duration are related to temperature, and a significant seasonal decline in tsetse populations is normal, particularly in savannah habitats during the dry season. The 3 groups of tsetse flies are generally adapted to different habitats and ecozones.” [3]

Tsetse fly species vary in their susceptibility to develop infection, and thus transmit the infection to humans or animals. Female flies are said to have higher infection rates than males tsetse flies, partially because they live longer and thus have more time to infect humans. “However it has not yet been determined whether the sex of a fly influences the infection” . [3]

Tsetse fly has a very strong negative impact on Africa’s economy. The effect of the tsetse fly has been variously described. According to the Food and Agricultural Organization FAO “African trypanosomiasis (sleeping sickness), which affects people, and livestock, lies at the heart of Africa’s struggle against poverty” [4]. In a perverse way, it is also considered a boon for the natural ecosystem, in the sense that it is “an important factor that has the effect of neutralizing human pressures and keeping land available for wildlife...”. Examples given include Kenya, Uganda and Tanzania where an estimated 40 percent of land is beyond the reach of humans due to the fly. [5]

The Parasite

The parasites - “*T. b. gambiense* and *T. b. rhodesiense* - are morphologically indistinguishable, measuring 25-40 μ m in length.” [3] Infection in the human host takes effect when the parasite is injected intradermally by the tsetse fly. The parasites quickly transform into what is known as blood-stage trypomastigotes (long, slender forms), and begin to divide by binary fission at the site of the bite wound.

“In the insect vector, the trypanosomes develop into procyclic trypomastigotes in the midgut of the fly, and continue to divide for approximately 10 days. Here they gain a fully functional cytochrome system and TCA cycle. When the division cycles are completed, the organisms migrate to the salivary glands, and transform into epimastigotes. These forms, in turn, divide and transform further into metacyclic trypanosomes, the infective stage for humans and reservoir hosts. The cycle in the insect takes 25-50 days, depending upon the species of the fly, the strain of the trypanosome, and the ambient temperature. Flies can remain infected for life (2-3 months). Tsetse flies inject over 40,000 metacyclic trypanosomes when they take a blood meal. The minimum infective dose for most hosts is 300-500 organisms, although experimental animals have been infected with a single organism. Infection can also be acquired by eating raw meat from an infected animal. In East Africa, this mode of transmission may be important in maintaining the cycle in some reservoir hosts.” [3]

If untreated, trypanosomiasis death may occur within 6 months due to cardiac failure or from *the* parasitic infection itself especially if *T. b. rhodesiense* infection is involved. The second type - *T. b. rhodesiense* - usually leads to a more chronic forms of the infection and leads to the classic "sleeping sickness" disease. General symptoms include [6]:

- Swollen, red, painful nodule at site of fly bite

- Swollen lymph nodes all over the body
- Headache
- Fever
- Sweating
- Anxiety
- Increased sleepiness
- Insomnia at night
- Mood changes
- Drowsiness
- Uncontrollable urge to sleep

Trypanosomiasis in Ethiopia.

Trypanosomiasis (*T. b. rhodesiense*, the East African type) is prevalent in the northwestern and southwestern parts of Ethiopia with the later serving as the main stronghold of tsetse-transmitted animal trypanosomiasis. “The human disease, based on case reports occurs in Oromiya Region (Illubabor and Wellega), Gambella, and Southern Nations Nationalities and Peoples Region (SNNPR)” [7] Recent population movements including resettlement, as well as climate change favoring the expansion of the tsetse habitat have brought humans and domestic animals, particularly cattle, in direct contact with the fly thereby exposing a significant number of human and animal populations in the lowlands of western and southern Ethiopia to trypanosomiasis infection.

The first confirmed human case of trypanosomiasis in Ethiopia reportedly occurred in 1967, and a major epidemic took place in 1969/70 in Gambella near the border with Sudan [7]. Available studies have helped to identify the distributional features of the disease by focusing on the ecology of the vector – tsetse fly.

“The tsetse flies in Ethiopia are confined to the southern and western regions between longitude 33⁰ and 38⁰ E and latitude 5⁰ and 12⁰ N. ...Tsetse infested areas extend from the lowlands to the valleys of the Blue Nile, Baro, Akobo, and Omo rivers...The infested area extends from the southern part of the River Valleys, around the southwestern corner of the country and along the western lowlands and escarpments north to the Blue Nile Basin. Restricting a further eastward spread are the Central Highlands and the semi-desert and Southern Highlands east of the Rift Valley. Elsewhere, there have been advances of tsetse including extension of the upper altitudinal limit of the fly from about 1600m to 2000m in certain areas, although it is not known if flies caught at high altitudes are representative of self-sustaining vector populations. Tsetse fronts in many places are unstable and the tsetse-animal interface is constantly moving. Consequently, new areas are being invaded and settled communities are being continually evicted by the advancing tsetse. Such hot-spots include areas in the Upper Didessa Valley, the northern and northeastern shores of the Lake Abaya in the Rift Valley, and upper reaches of the Omo-Ghibe and its tributaries.” [7]

ONCHOCERCIASIS

What is Onchocerciasis?

The tropical disease Onchocerciasis is caused by the filarial parasitic worm known as *Onchocerca volvulus*. It is transmitted from person to person through the bite of infected vector - blackflies of the *Simulium* species - which carry immature larval forms of the parasite.

“In the human body, the larvae form nodules in the subcutaneous tissue, where they mature to adult worms. After mating, the female adult worm can release up to 1000 microfilariae a day. These move through the body, and when they die they cause a variety of conditions, including blindness, skin rashes, lesions, intense itching and skin depigmentation.” [8]

Onchocerciasis has been controlled in a number of countries through spraying of the breeding sites of the vector blackfly with insecticide. Treatment is available to kill the microfilariae parasite, thereby alleviating symptoms and lessening transmissibility. “An international control effort aims to bring annual treatment with this drug to all populations at risk by the year 2010. When that is achieved, onchocerciasis may cease to be a public health problem”. [8]. The disease is endemic in 36 countries in Africa mainly in East Central and West Africa as well as the Arabian Peninsula and the Americas with 123 million people at risk (96% in Africa). An estimated 17-18 million people are infected. [9]

“Onchocerciasis is a major cause of blindness in many African countries. As a public health problem, the disease is most closely associated with West and Central Africa, but it is also prevalent in Yemen and six countries in Latin America. Onchocerciasis has in the past greatly reduced the economic productivity in infected areas and left vast tracts of arable land abandoned. It is estimated that there are about half a million blind people due to river blindness.” [10]

The Disease

“When the fly bites, it deposits the larvae of a parasitic worm, which matures to adulthood and produces millions of tiny worms, called microfilaria”. The *Onchocerca volvulus* parasitic worm lives for up to 14 years in the human body. “Each adult female worm, thin but more than .5 metre in length, produces millions of microfilariae (microscopic larvae) that migrate throughout the body” [11]

The microfilariae migrate throughout the body and give rise to a variety of symptoms [11]:

- Rashes
- Lesions
- Intense itching and depigmentation of the skin
- Lymphadenitis, which results in hanging groins and elephantiasis of the genitals
- General debilitation and serious visual impairment, including blindness

Manifestations of the Onchocerciasis illness begin to occur one to three years after the blackfly bite and the injection of infective larvae.

Vector Ecology

The vector's life cycle begins when eggs are laid in fresh running water, and the larvae attach themselves to nearby rocks. They then use tiny hooks located at the end of their abdomen to "...hold on to the substrate, often using silk holdfasts and lines to move or hold their place....They will pupate under water and then emerge in a bubble of air as flying adults" [11].

Today, the main vector in most parts of Africa is *Simulium damnosu*. However, in Ethiopia, Uganda, the Democratic Republic of the Congo, and Tanzania, *Simulium neavei* is more common. [12]. The female black fly feeds on blood while males feed mainly on nectar.

The Agent *Onchocerca volvulus*

Following inoculation into a human host by the black fly the agent larvae enter the subcutaneous tissue, where they migrate and lodge in nodules, and gradually mature into adult worms. New worms continue to form new nodules or find existing nodules and cluster together.

"It is thought that the smaller male worms may migrate between nodules to mate". After mating, eggs formed inside the female worm develop into microfilariae and leave the worm one by one. A female worm may produce 1000 microfilariae per day. Many thousands of microfilariae migrate in the subcutaneous tissue. When the microfilariae die, they cause skin rashes, lesions, intense itching and skin depigmentation. Microfilariae also migrate to the eye and can cause blindness" [13]

Onchocerciasis in Ethiopia

"The existence of onchocerciasis in southwest Ethiopia was first reports by Italian investigators in 1939...[as] confined to the western part of the country where there are many rivers with vegetation that provide suitable vector habitats." [7]. Subsequent reports listed former provinces of Illubabor, Wellega, Keffa, and Gamo Gofa as areas of onchocercia endemicity. Gojam, Sidamo, and Shewa were suspected to be endemic. The prevalence rates are higher near rivers where the vector blackfly breeds and decline with distance away from rivers. Altitude also plays a role. "Higher parts of the highlands and the arid lowlands of the country do not support the *Simulium* vectors, due to low temperatures in the highlands and absence of perennial, fast-flowing (well-oxygenated) rivers in the arid lowlands" [7].

The disease represents a significant public health and socio-economic challenge in Ethiopia. However, there is a scarcity of data on prevalence and other aspects. A literature-based survey featuring 12445 study subjects in 21 study articles showed the prevalence rate ranging from 85.3 percent in Teppi to 6.9 percent in Kuwara in northwestern Ethiopia with male rates higher than females. “This study clearly shows the existence and severity of onchocerciasis in many parts of Ethiopia mainly in the Southwestern Ethiopia.” [14]. (Refer to Fig. 1 in [7] to see the location of endemic areas in Ethiopia)

“A complete national survey (1997-2004) in Ethiopia determined that onchocerciasis was much more wide spread than originally believed. Nine regions were shown to be endemic, with 7.3 million people at risk and more than 3 million already infected... The endemic areas extend from the northwest part to southwest part of the country that borders the Sudan ... Manifestations of the disease in Ethiopia is mainly dermal that are characterized by the disabling itching and thickening of the skin, hanging groin etc. Blindness, a common manifestation of this disease in West Africa, is a rare complication in Ethiopia ...” [14]

The endemic areas of southern and southwestern Ethiopia have, for more than two decades, been a favored government target area for resettling famine victims and landless farmers, or those pushed off their lands by environmental degradation which rendered their areas of habitation totally unproductive. This has obviously ensured a fresh supply of human hosts, a significant percentage of whom eventually leave by entering the return migration stream, thereby helping to propagate the illness to previously unaffected locations. Seyoum et.al. summarize the current state of the disease in Ethiopia and efforts to control it as follows [7]:

“Although apparent absence or near-absence of onchocerciasis-related blindness in Ethiopia reduces the public health significance of the disease, considerable suffering as well as the large number of people affected makes onchocerciasis in Ethiopia a disease of considerable public health importance. The Federal Ministry of Health has already incorporated onchocerciasis control into the Health Sector Development Program (HSDP). This, by itself, is an important step forward in recognizing and combating this debilitating human scourge”.

A recent study of Ethiopian Falasha (Jewish) immigrants in Israel focused on blood samples drawn from 1200 individuals “...to determine whether onchocerciasis is the cause of cutaneous and ocular symptoms among recent immigrants from the Kuwara province in Ethiopia”. Beginning in 1992, approximately 9,000 immigrants had arrived in Israel from Kuwara (also spelt Quara) province of northwest Ethiopia where the prevalence of onchocerciasis is particularly high. [16] The conclusions were as follow:

“In the detailed skin examination performed in 83 patients, the most common skin finding was chronic papular onchodermatitis, found in more than 46 patients (55%); depigmentation and atrophy was found in 13 (15%) and 12 (14%), respectively. In 40 patients (48%), living microfilaria were detected in their skin snips. Of the 65 patients who underwent a through eye examination, 45 patients (66%) had ocular complaints. Corneal abnormalities were found in 55 of the 130 eyes (42%), active anterior segment intraocular inflammation and live microfilariae were found in 4 eyes (3%) and lens changes in 16 eyes (1%). Eleven eyes (9%) showed retinal or choroidal changes. CONCLUSIONS: Skin and eye manifestations associated with onchocerciasis are prevalent among symptomatic Ethiopians who immigrated to Israel from the Kuwara province”. [16]

LYMPHATIC FILARIASIS

What is Lymphatic Filariasis (LF)?

Filariasis is an infectious diseases caused by any of several round, thread-like parasitic worms. Infection with a parasitic worm that lives in the human lymph system is the most common type of filariasis. This is called lymphatic filariasis.

The disease puts at risk more than a billion people in more than 80 countries [17]. It is estimated that more than 120 million have already been affected, over 40 million seriously, with severe incapacitation and disfigurement. Approximately one-third live in India, a third in Africa, and the remainder in South Asia, the Pacific and the Americas. The disease is still on the rise with continued increases in infection rates in tropical and subtropical areas where lymphatic filariasis is well-established. A prime contributing factor is the rapid urbanization and unplanned growth of cities, "...which creates numerous breeding sites for the mosquitoes that transmit the disease" [17]. The causes, and methods of transmission are given in a WHO report as follows:

The disease is transmitted by mosquitoes that bite infected humans and pick up the microfilariae that develop, inside the mosquito, into the infective stage in a process that usually takes 7-21 days. The larvae then migrate to the mosquitoes' biting mouth-parts, ready to enter the punctured skin following the mosquito bite, thus completing the cycle. The thread-like, parasitic filarial worms *Wuchereria bancrofti* and *Brugia malayi* that cause lymphatic filariasis live almost exclusively in humans. These worms lodge in the lymphatic system, the network of nodes and vessels that maintain the delicate fluid balance between the tissues and blood and are an essential component for the body's immune defence system. They live for 4-6 years, producing millions of immature microfilariae (minute larvae) that circulate in the blood. In its most obvious manifestations, lymphatic filariasis causes enlargement of the entire leg or arm, the genitals, vulva and breasts. In endemic communities, 10-50% of men and up to 10% of women can be affected. The psychological and social stigma associated with these aspects of the disease are immense. In addition, even more common than the overt abnormalities is hidden, internal damage to the kidneys and lymphatic system caused by the filariae.

And some of the pathologic and geographical characteristics of the disease are as follows: [15]

- Lymphatic filariasis is a disease of the tropics.
- It is caused by infection with any of several round, thread-like parasitic worms.
- The parasite is spread from person to person by infected mosquitoes.
- Long-term exposure and repeated infections can cause severe damage to the lymph system and serious, debilitating complications.
- Prevention centers on controlling mosquito populations in communities and avoiding mosquito bites.

The Disease [17]:

- The parasite reproduces in, and damages the lymph system
- Most infected people around the world remain asymptomatic and will never develop clinical symptoms.
- A relatively small proportion of infected individuals will develop lymphedema: improper functioning of the lymph leading to fluid collection and swelling mostly in legs, (but can be in the arms, breasts, and genitalia). Most patients develop these symptoms following the progression of the disease into later stages years after being infected.
- The continual swelling and the diminished function of the lymph system reduces the body's ability to fight germs and infections. Patients will most likely have more bacterial infections in the skin and lymph system. This invariably leads to the hardening and thickening of the skin – a phenomenon known as, elephantiasis. Appropriate skin hygiene can help patients reduce infections in the skin.
- One of the most common outcomes is hydrocele in men, or swelling of the scrotum.
- Another aspect of the illness is filarial infection of the lungs, and hence, pulmonary tropical eosinophilia syndrome, usually found in persons living with the disease in Asia. “Symptoms of pulmonary tropical eosinophilia syndrome include cough, shortness of breath, and wheezing. The eosinophilia is often accompanied by high levels of IgE (Immunoglobulin E) and antifilarial antibodies” [17]

“The standard method for diagnosing active infection is the identification of microfilariae by microscopic examination. This is not always feasible because in most parts of the world, microfilariae are nocturnally periodic, which means that they only circulate in the blood at night. For this reason, the blood collection has to be done at night to coincide with the appearance of the microfilariae. Serologic techniques provide an alternative to microscopic detection of microfilariae for the diagnosis of lymphatic filariasis. Because lymphedema may develop many years after infection, lab tests are often negative with these patients.” [12]

The Vector

“The parasite is transmitted by the bite of infected species of various genera of mosquitoes, including *Culex*, *Aedes*, *Anopheles*, and *Mansonia*....Humans are the only definitive host for the parasite.’ [18]

Subfamilies and genera [19]

Anophelinae: Anophelines contain the genus *Anopheles* and two other genera of no medical importance. *Anopheles* species are the main transmitter of malaria and lymphatic filariasis.

Culicinae: Within the subfamily of the culicines there are about 2000 species, including the important genera *Culex*, *Aedes* and *Mansonia*.

The Parasite [20]

Distribution

W. bancrofti exists throughout the tropical regions of Africa, Asia, China, the Pacific and the Americas. Current estimates put the population infected with lymphatic filariae of all types at 100 million, and most of these cases are bancroftian filariasis.

Life Cycle:

“The third-stage infective larvae (L3i) enter the blood through the wound made by the mosquito. They then migrate to the nearest lymph gland where they mature into the thread like adult worms about 3 months to 1 year later. The average incubation time before patency is about 15 months. The mature adults can survive for 5 to 10 years and the damage of the lymphatic vessels they cause and the immune system's response to their presence (and that of microfilaria and newly inoculated L3i) can result in the various” [20]

“Once male ... and female ... nematodes mate the female viviparously produces microfilariae (first stage larvae or L1) which then move through the circulatory system and collect in arterioles of the lung during the day and emerge at night (if nocturnally periodic) when night biting mosquitoes are most active.... Once the microfilariae have entered an appropriate mosquito host through its blood meal they penetrate the insect's gut wall and move to the thoracic muscles where they mature (through two life stages) into third-stage infective larvae” [20]

Pathology

There is usually a period of vigorous immune response to the invading larvae following infection with third stage larvae. If the body is unable to clear the larvae at this stage, then the various pathologies associated with filarial infection can develop. It appears that the immune reaction accounts for much of what is going on at this stage rather than the effects of the nematodes themselves. “The most pronounced of these is the damage to the lymphatic vessels which is mediated by the immune system's response to the adult worms living in them” [20]. These immune responses (Lymphangitis) are typically manifested through the inflammation of the affected area (most often extremities, predominantly legs, and also genitals), and fever. “Repeated episodes of lymphangitis leads to the formation of fibrous and calcified tissues”[20].

Lymphatic Filariasis in Ethiopia

There is no national study of lymphatic filariasis in Ethiopia. In a 1993 study in clinical parasitology focusing on night blood surveys (there are more parasites in the blood at night than during the day) in two communities adjacent to Baro river near Gambella, Jemaneh L. and Kebebe D. showed the overall lymphatic filarial prevalence rate (using the counter chamber technique) to be 20.7 percent. This is an average of the male rate (23.7%) and the female prevalence rate (18.5) but infection densities were higher among females than males. The study covered 90 percent of the population in Tektak and Ketch. [21]

Infection densities varied between 40 and 1540 microfilariae (mf) per ml of blood among the infected, giving a geometric mean intensity of 309 mf/ml of blood which was much more pronounced in females than in males. In males, 20.3% had hydrocoele and this condition was noted above the age of 35. About 40% of those with hydrocoele had microfilaremia. Groin gland enlargement was recorded in 40.0% of the examined. No case of elephantiasis was encountered. [21]

The same researchers conducted an in-depth study focusing on the microfilarial density in the blood of two volunteer males and females from the village of Ketch (near Gambella) in southwestern Ethiopia by drawing blood ever 4 hours for a 24 hour period. [22]

In the blood of the volunteers the majority of the microfilariae appeared between 20 and 04 hours with peak at 24 hours (range at peak time + 3060-3560 mf/ml blood) depicting a nocturnal periodicity of circulating *Wuchereria bancrofti* microfilariae. This has important implications for the diagnosis, monitoring and transmission of lymphatic filariasis in the area. [22]

A similar micro study was conducted two decades earlier by Dennis D.T et.al using a method in which paired day and night blood specimens from 41 persons living in a hyperendemic *Wuchereria bancrofti* area of southwestern Ethiopia were drawn. [23]

A literature review by Asrat Hailu [24] attempted to piece together information based on the few studies on lymphatic filariasis in Ethiopia. It indicated that the first written report on the diseases relates to a patient who resided in "...an area endemic for onchocerciasis [thus], diminishing the reliability of the report". More recent studies point to the existence of the disease in the former provinces of Keffa, Illubabor, Wellega, and Gamo Gofa. They all concluded that lymphatic filariasis is endemic to western and south western Ethiopia. "This conclusion was based on the documentation of clinical cases described as Elephantiasis scrota (scrotal elephantiasis), Elephantiasis vulvae (vulval elephantiasis), Elephantiasis penis (elephantiasis of the penis), and Elephantiasis mammae (breast elephantiasis)". [24] The authors also note the absence of anti-filarial health policy in Ethiopia, and the difficulty of separating out the socio-economic consequences of filarial elephantiasis from non-filarial elephantiasis caused by podoconiosis.

Podoconiosis

A related but non-filarial illness causing similar bodily effects including elephantiasis is podoconiosis (non-filarial endemic elephantiasis of the lower legs caused by absorption of silica particles from the soil, through the feet of someone from a susceptible family.). A new cross-sectional study focusing on the knowledge, attitude and practice of the population in highly endemic podoconiosis areas of southern Ethiopia revealed widespread misconception of the causes and etiology of podoconiosis [23]. There were 438 study participants most of whom reported either having seen a patient with podoconiosis (94%) or hearing about such patients (92%). The study also found that:

The proportion of respondents holding at least one misconception about causation was 93.4% (95% CI 91.1-95.7%). More than one-half (55.8%) showed stigmatising attitudes towards social interactions with podoconiosis patients and 63.8% had unfavourable attitudes towards the condition. Just over one-half (55.2%) of respondents were wearing shoes during the interview, but shoe wearing was inconsistent and inadequate to prevent podoconiosis. In this highly endemic area, the community held significant misconceptions about causation, care, treatment and prevention of podoconiosis. [23]

What is podoconiosis?

“Podoconiosis is a non-infectious geochemical elephantiasis caused by exposure of bare feet to irritant alkalic clay soils. It is found in at least 10 countries in tropical Africa, Central America and northwest India, where such soils coexist with high altitude, high seasonal rainfall and low income. Podoconiosis develops in men and women working barefoot on irritant soils, with signs becoming apparent in most patients by the third decade of life. Colloid-sized silicate particles appear to enter through the skin, are taken up into macrophages in the lower limb lymphatics and cause endolymphangitis and obliteration of the lymphatic lumen. Genetic studies provide evidence for high heritability of susceptibility to podoconiosis. The economic burden is significant in affected areas dependent on subsistence farming. Podoconiosis is unique in being an entirely preventable non-communicable disease. Primary prevention entails promoting use of footwear in areas of irritant soil; early stages are reversible given good foot hygiene, but late stages result in considerable economic and social difficulties, and require extended periods of elevation and occasionally nodulectomy.”. [25]

LEISHMANIASIS

What is Leishmaniasis?

“In 1903, Leishman and Donovan separately described a protozoan parasite found in the splenic tissue of patients in India. Their simultaneous discovery of the protozoan now called *Leishmania donovani* first alerted the scientific community to the life threatening disease of leishmaniasis” [26].

Now a century later, hundreds of millions are at still risk of infection and millions are afflicted by Leishmania (also known as "kala-azar", "black fever" or "black sickness") [27]. It is an illness recognized for its complexity and diversity of symptoms and effects. It is endemic to most ecological regions of the world ranging from the rainforests ecosystems to desert landscapes, afflicting both rural and urban communities.

About 21 different species of Leishmaniasis have been identified, and are categorized “... under its primary syndromes; *cutaneous*, *mucocutaneous* and *visceral*, which result from parasite multiplication in macrophages in the skin, nasal-oral mucosa and internal organs, respectively” [26]. The *Leishmania donovani* protozoan agents are transmitted by over 30 species of fly vectors – the *phlebotomine* sand flies. The visceral form is particularly dangerous and often fatal. The parasites reside and reproduce in the liver, spleen and marrow. In the absence of treatment the infection results in certain death. The cutaneous form (also known as "oriental sores" or "oriental buttons") “...causes skin ulcers and sometimes lead to a total disfigurement of the face”. [27]

Vector-borne, transmission is not the only form of transmission, however. Some of the *Leishmania donovani* infections “...are congenital and parenteral (i.e. by blood transfusion, needle sharing, and laboratory accident)” [26]. Moreover, the new Human Immuno-deficiency Virus has found a highly immune-compromised population in Leishmania sufferers, and vice-versa. “Co-infection has become a significant concern for developing nations with high numbers of HIV immuno-compromised individuals” [26].

“Also, increases in travel and international migration have brought this disease to the attention of developed nations. Available treatments for leishmaniasis are expensive or have serious associated toxicities and may lead to the development of drug-resistant parasites. Prevention and control regimens focusing on vector reservoir control had not changed in decades. However international attention has now shifted towards the development of effective and cost-efficient treatment. Exciting recent advances in diagnosis, treatment, prevention make now the most interesting time to research and learn about Leishmaniasis”. [26]

The symptoms of visceral leishmaniasis include fever, fatigue, and rheumatism together with general weakness which leads to a gradual but complete destruction of the liver and spleen. If treatment is not sought, the patient will die in 6 to 24 months. [27]

The Vector

“Sandflies of the *Phlebotomus* genus transmit the disease between humans, between animals, and from animals to humans or vice versa.” [27]. Phlebotomine sand flies are mosquito-like insects found in the tropics and subtropics. They are notorious vectors for the agents of several deadly diseases. Hosts for the blood-feeding females insects include donkeys, horses and humans. [28]

The Parasite [29]

Leishmania commonly infects rodents and humans and currently affects 12 million people in 88 countries. “Leishmania cells have two morphological forms: promastigote (with an anterior flagellum)^[6] in the insect host, and amastigote (without flagella) in the vertebrate host”. “Old World” species include *L. donovani*, *L. major*, *L. tropica*, and *L. aethiopica*. [29].

Leishmaniasis in Ethiopia

All four species of *Leishmania* mentioned above are thought to exist in Ethiopia [30] with several species of the phlebotomine vector involved its transmission, but the agent *L. donovani* which causes visceral leishmaniasis (VL), or Kala azar “...is known to be of significant clinical and public health importance” [30].

The phlebotomine vector species that are known, or implicated in the transmission of the different forms of leishmaniasis in Ethiopia include: *Phlebotomus martitni*, *P. celiae*, *P. orientalis*, *P. pedifer* and *P. longpipe*, and *P. duboscqi*. [30].

There are no national studies on leishmaniasis in Ethiopia. Therefore, knowledge about the disease and form of transmission is far from complete, and the morbidity and mortality from VL remains largely undetermined. The following facts on leishmaniasis in Ethiopia are obtained from the literature survey of past works on the subject by Asrat Hailu et. al. [30]

Visceral leishmaniasis (VL)

Visceral leishmaniasis (VL – the most dangerous form of leishmaniasis) is found throughout the lowland areas of Ethiopia including the Lake Abaya area, Segen Valley in Konso Wereda, the Omo River plains, and the Humera plains in the northwest with varying degrees of endemicity.

The search for the VL vector in southwestern Ethiopia identified eight vector species of which *P. orientalis* (long known to be an important man-biter) appears to be the most dominant.

Active research in the lowlands of Humera (bordering endemic areas in the Sudan where significant VL epidemic deaths occurred) has identified VL as a major public health issue affecting major settlements and the transient seasonal-migrant population. This also has a strong gender component in the sense that the proportion of affected males is higher than females by a ratio of roughly 4 to 1.

“In the vast lowlands of the northeastern Rift Valley of Ethiopia (Awash Valley), VL occurs only sporadically and in association with HIV co-infection...” in spite of the high rates of positive leishmanin skin tests (as high as 95% among some of the Afar pastoralist groups, for instance).

Cataneous leishmaniasis (CL)

Cutaneous leishmaniasis in Ethiopia is caused mainly by the parasite *L. aethiopica*. “The disease, as well as the sand fly vector are widespread over much of the highlands of Ethiopia, mainly between 1,700 and 2,700m altitude...”. Lack of treatment for the illness insures that the disease remains a major public health challenge in the affected communities.

Studies have shown positive serological tests in a range localities including Meta-Abo, Sebeta, Ochollo (Gamo highlands), Kutaber (Wello), Soddo, and Addis Ababa.

YELLOW FEVER

And Other Arboviral Diseases

Unlike the vectored diseases discussed so far whose agents are parasitic protozoa, Yellow Fever is caused by a virus, and hence, cannot be cured. It can be prevented with a vaccine, however. What are arboviral diseases? “Arboviral (short for arthropod-borne) infections are caused by any number of viruses transmitted by arthropods such as mosquitoes and ticks. These infections generally occur during warm weather months, when mosquitoes and ticks are active.” [31]. Infected mosquitoes are vectors in most arboviral transmissions. Fortunately, a limited species of mosquitoes are capable of transmitting diseases and at any given time only a small proportion of the mosquitoes vectors will actually be carrying a virus. It has been known for years that, migrating birds have the ability to carry viruses from one region of a country to another but birds cannot directly infect humans. Mosquitoes who feed on those birds do. Some arboviral infections are transmitted by infected ticks.

What is Yellow Fever?

Yellow fever is a viral disease is transmitted to humans through the bite of infected mosquitoes. “The mosquito can also pass the virus via infected eggs to its offspring (vertical transmission)” [32]. It is found in the tropical regions of Africa and the Americas. The illness “...ranges in severity from an influenza-like syndrome to severe hepatitis and hemorrhagic fever” [33]. The Yellow fever virus (YFV) is maintained in nature through vector-borne transmission between nonhuman primates (jungle Yellow Fever). Vector-borne transmission from one human to another also occurs during epidemics of “urban yellow fever.”

The virus is constantly present with low levels of infection (i.e. endemic) in some tropical areas of Africa and the Americas. This viral presence can amplify into regular epidemics. Until the start of this century, yellow fever outbreaks also occurred in Europe, the Caribbean islands and Central and North America. Even though the virus is not felt to be present in these areas now, they must still be considered at risk for yellow fever epidemics....Thirty-three countries, with a combined population of 508 million, are at risk in Africa. These lie within a band from 15°N to 10°S of the equator. In the Americas, yellow fever is endemic in nine South American countries and in several Caribbean islands. Bolivia, Brazil, Colombia, Ecuador and Peru are considered at greatest risk. [32]

Disease Ecology [32]

Three types of transmission cycle are recognized for yellow fever: sylvatic, intermediate and urban. All three cycles exist in Africa, but in South America, only the latter two occur.

- *“Sylvatic (or jungle) yellow fever:* In tropical rainforests, yellow fever occurs in monkeys that are infected by wild mosquitoes. The infected monkeys can then pass the virus onto other mosquitoes that feed on them. These infected wild mosquitoes bite humans entering the forest resulting in sporadic cases of yellow fever. The majority of cases are young men working in the forest (logging, etc). On occasion, the virus spreads beyond the affected individual.
- *Intermediate yellow fever:* In humid or semi-humid savannahs of Africa, small-scale epidemics occur. These behave differently from urban epidemics; many separate villages in an area suffer cases simultaneously, but fewer people die from infection. Semi-domestic mosquitoes infect both monkey and human hosts. This area is often called the “zone of emergence”, where increased contact between man and infected mosquito leads to disease. This is the most common type of outbreak seen in recent decades in Africa. It can shift to a more severe urban-type epidemic if the infection is carried into a suitable environment (with the presence of domestic mosquitoes and unvaccinated humans).
- *Urban yellow fever:* Large epidemics can occur when migrants introduce the virus into areas with high human population density. Domestic mosquitoes (of one species, *Aedes aegypti*) carry the virus from person to person; no monkeys are involved in transmission. These outbreaks tend to spread outwards from one source to cover a wide area.” [32]

The Vector

The virus is transmitted from person to person or from one animal to another (horizontal transmission) by a biting mosquito (the vector). The agent also has the advantage of a generational transmission, in that it can pass the virus via infected eggs to its offsprings (vertical transmission). Moreover, "...the eggs produced are resistant to drying and lie dormant through dry conditions, hatching when the rainy season begins. Therefore, the mosquito is the true reservoir of the virus, ensuring transmission from one year to the next." [32]

Several species of the *Aedes* mosquito and *Haemogogus* (S. America only) carry and transmit the yellow fever virus. These include domestic mosquitoes (i.e. they breed around houses), and wild (jungle-breed), or semi-domestic types (display a mixture of habits). Any region, tropical or subtropical populated with these mosquitoes can potentially harbour the disease. Successful mosquito control programmes have eradicated mosquito habitats in the the developed world and much of South America. "However, these programmes have lapsed over the last 30 years and mosquito populations have increased. This favours epidemics of yellow fever." [32]

The Parasite

Yellow fever is caused by a virus belonging to the *flavivirus* group. "In Africa there are two distinct genetic types (called topotypes) associated with East and West Africa." [32]. Flavivirus is a family of viruses transmitted from person to person by mosquitos and tick bites. They cause many important diseases, including dengue, yellow fever, tick-borne encephalitis virus, and West Nile fever. "The flaviviruses are positive-strand RNA viruses containing three structural proteins and a host-derived lipid bilayer." [35]. A key feature of flaviviruses survival and transmission is its ability to reproduce in the vector. "Without the ability to replicate in the vector, they would not remain viable to be passed from one host to the next." [36]

Yellow Fever in Ethiopia

Sporadic cases of Yellow fever were identified annually in East Africa until the year 1959, when an epidemic outbreak was noted in the Blue Nile region of Sudan "...and subsequently in the neighboring region of Ethiopia" [38]. The largest outbreak to date occurred from 1960 to 1962, in southwestern Ethiopia. Additional serologic studies conducted since then confirmed that "...yellow fever activity was widespread in Uganda, Somalia, Ethiopia, and Kenya". [38]

The first recorded cases in Ethiopia came in 1959 from the Asosa area in the then Wellega province (now in Benishangul Gumuz), and was centered in "...the lowlands between Asosa and Kurmuk towns". About 100 people were said to have died in the outbreak [39]. A yellow fever epidemic hit "...the lower Omo Valley near Dime in the former Gamo Gofa region" a year later, and was characterized in a literature survey done by Mekonnen and Kloos as "the most severe yellow fever epidemic ever reported from Africa..." [39]

"This epidemic lasted for 18 months and affected an area of 100,000 sq. km. With a total population of about 1 million largely devoid of protective antibodies ...But within this area, yellow fever cases were seen only in the low lands below 1,600 m although sera with neutralizing antibodies were found in villages up to 1950 m. Most cases were reported from Gamo Gofa, Kefa, and Sidamo and a few cases from the Didesa River Valley in Wellega. There is indirect evidence that the epidemic also affected Illubabir...All age groups and both sexes were affected, although there were more males than females and slightly more adults than children infected. The severity of the epidemic was indicated by a total morbidity of around 100,000 persons and mortality rates ranging from less than 30% up to 85% in some localities...The epidemic is believed to have originated in endemic yellow fever centers in southern Sudan. Caravans and monkeys are suspected of having carried the virus to the Omo Valley" [39]

The last reported yellow fever epidemic in Ethiopia occurred near Lake Ababya and around Akobo town in Illubabor in 1966 [39]. This involved a total of 2200 cases, and led to 450 deaths.

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