Original Article

SLEEPING SICKNESS IN LIBERIA – A HISTORICAL REVIEW

Mehlitz, Dieter¹ and Gangpala, Lincoln²

¹Institute for Parasitology and Tropical Veterinary Medicine, Department of Veterinary Medicine, Freie Universitaet Berlin, Robert-von-Ostertag-Strasse 7-13, D-14163 Berlin, Germany

²Public Health and Medical Research, National Public Health Institute of Liberia, Charlesville, Liberia

ABSTRACT

Sleeping sickness or Human African Trypanosomiasis (HAT) caused by Trypanosoma brucei gambiense is a vector-borne protozoan disease occurring in central and western Africa. HAT caused devastating epidemics during the last century. Due to sustained efforts of surveillance and control measures the disease incidence dropped dramatically during recent years. HAT is now targeted for elimination for the year 2020. The epidemiological significance of ancient HAT foci not being surveyed or the non-provision of data recording for long periods, due to war riots and civil unrest like in Liberia is not clear. Its assessment, however, is essential for the implementation of future control strategies. The review compiles the history of HAT of Liberia with results of known but partly unpublished details of active and passive surveillance of ancient foci (Lofa and Bong Counties). Forty-three HAT cases mainly of Bong County are listed for the years 1967 to 1989; no cases were diagnosed in the ancient Kissi focus. An experimentally prooven antelope-Glossina palpalis gambiensis-antelope cycle of T. b. gambiense emphasizes the epidemiological role of animal reservoir hosts in the Liberian rainforest with implication for the resurgence of the disease.

Keywords: Sleeping sickness; Liberia; history; wild animals; reservoir hosts

*Corresponding author Email: d.mehlitz@gmx.de Phone: +49 30 8618739
INTRODUCTION

Human African Trypanosomiasis (HAT) is a vector-borne protozoan disease caused by the species *Trypanosoma brucei* transmitted by the bites of tsetse flies (*Glossina* spp.) which have acquired their infection from human beings or animals harbouring human pathogenic trypanosomes. HAT occurs in 36 sub-Saharan African countries. People most exposed to tsetse flies and therefore the disease live in rural areas and depend on agriculture, fishing, animal husbandry or hunting (WHO, 2017). The disease occurs in two forms, the chronic Gambian form caused by *T. b. gambiense* found in Central and West Africa, and the acute form of the zoonotic disease caused by *T. b. rhodesiense* found in eastern and southern Africa. Generally, both forms of the disease are fatal if untreated although for Gambian HAT healthy parasite carriers and self-cure were described (Jamonneau et al., 2012). The disease caused devastating epidemics during the last century (Büscher et al., 2017). Due to sustained efforts of surveillance and control measures launched in 2007 and put in place 2011 (WHO, 2012), the disease incidence dropped dramatically to 2804 new reported cases in 2015 (Büscher et al., 2017), of which 2733 were caused by *T. b. gambiense*. HAT is now targeted for elimination for the year 2020 (fewer than 2000 cases per year) and for the elimination of transmission for 2030 (Franco et al., 2017). For Gambian HAT, 55 million people are still estimated to be at risk of infection (period 2010–2014), with 1.2 million at very high risk and high risk (most of them in the Democratic Republic of Congo followed by the Central African Republic), and 9 million at moderate risk living in areas where Gambian HAT is considered being still a public health problem. In West Africa, only Guinea, Ivory Coast and Nigeria are still reporting significant levels of the disease (Franco et al., 2017). For countries with long-lasting civil wars in the past, civil unrest or outbreaks of Ebola virus disease like Guinea, Sierra Leone and Liberia, the reported cases (if at all) and the actual incidence might differ considerably (Büscher et al., 2017). From Liberia with its known ancient Gambian HAT foci (Hutchinson, 1962; Hutchinson et al., 1964) no cases and no surveillance activities have been reported to WHO since decades (Courtin et al., 2008; Franco et al., 2017).

In the context of reduced incidence of Gambian HAT in sub-Saharan Africa and the efforts towards the targeted elimination of the disease it has been strongly advised to re-consider the epidemiological relevance of old classical foci not being surveyed for long periods which might be still active or the source for the resurgence of the disease (Büscher et al., 2017). To meet this recommendation this paper aims at contributing knowledge on the occurrence and distribution of sleeping sickness cases in the West African rainforest region by reviewing the trypanosomiasis history of Liberia, by filling the gap of information on unpublished HAT cases diagnosed during the pre-civil-war period 1981 to 1989 (Annual Reports of the Liberia Research Unit (LRU) of the Tropical Institute Hamburg, Bong Mine, Liberia, unpublished, in: BNI Archive, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany) and by looking at the post-civil-war period.

LOOKING BACK TO THE BEGINNING

Sleeping sickness in Liberia became noticeable early in the 20th century. The Vai tribe in the western part of the country had a local name („konje kira“) for the disease which may be translated as „ball sickness“ or „gland sickness“ (Johnston, 1906). However, it was not before 1926 when the first authentic record of human trypanosomiasis was made by the Harvard Expedition in five patients in a cluster of villages (Nyalai, Betala, Paiata and Bakratown) near the St. Paul River, northwest of Suakoko, Bong County (former Central Province) when trypanosomes were detected in gland punctures (Strong, 1930).

Before 1930, sedentary life prevailed among tribes of the interior, few people ever leaving the confines of the clan or tribe. At that time, trypanosomiasis might have been restricted to a few endemic areas such as those discovered by the Harvard Expedition
in the hinterland near the banks of the St. Paul river. The development of roads and plantations by the end of the 1930th produced new social and economic conditions which eventually led to the increase of HAT. Travel became prevalent custom to and from market places or over long distances for transport of food supply (rice) from the north (Kissi tribe) to the coastal towns. Recruited labour moved to and from the plantations (rubber) (Bequaert, 1946).

After 1930, trypanosomiasis was diagnosed at the Ganta Hospital, Nimba County (Harley, 1933). Few cases were reported along the Cavalla river, Maryland, in 1937-1938. These cases were thought to be imported by Liberian workers returning from the islands of the Gulf of Guinea (Sao Tomé and Fernando Poo, now Bioko) - regions with historical HAT foci - into the coastal region of Liberia (González Vicente, 1948, Veatch, 1946).

THE KISSI HAT FOCUS

A systematic active surveillance of trypanosomiasis in Liberia commenced in the northern part of the country in 1941, an area which is inhabited by the tribes of the Kissi and Buzzi, because alarming high infection rates of more than 20% were reported from neighbouring countries Sierra Leone (Hutchinson, 1954) and French Guinea (Vaucel et al., 1963) during the years 1939-1941. The Kissi tribe occupied and still lives today in the triangle along the borders in the northern savannah zone of the three countries. They are known as successful rice cultivators, their traditional attitude towards production of rice has contributed considerably to the national rural development of the country during the last half of the 20th century (World Bank, 1982), assisting farmers to improve and develop up-land rice, rainfed and irrigated swamp rice resulting in intensification and diversification of farming practices. Between 1941 and 1943 the first systematic surveillance was carried out in the Kissi and Gbandi chieftoms. 13 481 sleeping cases were diagnosed parasitologically out of 90.980 persons (15%) examined on the Liberian side of the border (Veatch et al., 1946). With these findings and with those in the neighbouring countries Sierra Leone and Guinea, the classical Kissi sleeping focus became known.

The epidemiology of trypanosomiasis in this part of West Africa was associated with the habits and movements of the Kissi people. They knew no international boundaries and moved freely from one country to another to visit relatives and markets. From this focus the spread of the disease was favoured when new roads were built resulting in a prevalence of 2% of the disease in the Voinjama-Zorzor-area (Lofa County) in 1944 and of 1% at the Harbel Firestone Plantation (Montserrado County, now Margibi County) in 1943 (Veatch, 1946).

Due to the treatment of patients (antrypol, tryparsamide) in northern Liberia, the incidence dropped to 2.5% in the Kissi focus (Liberia) in 1944. Between 1944 and 1951 no further control measures were instituted, although a considerable number were reported to the Holy Cross Mission at Bolahun (Hutchinson, 1962). Between 1951 and 1953, again mass campaign of diagnosis, treatment and mass prophylaxis (lomidine) was performed and a small diagnostic team was kept operative in the area. A full survey was then carried out in the Kissi, Gbandi, Mende, Mandingo and Loma chieftoms along the border with Sierra Leone and Guinea in 1959-1960, revealing a drop of incidence to 0.15% (Hutchinson, 1962). Similar findings reported Vaucel et al. (1963) and Hutchinson et al. (1964) from the other sides of the borders.

Although the overall incidence in northern Liberia was then low, Hutchinson (1962) found a marked focal concentration around the river Mano in central and northern Kissi. Thirty-nine new cases were diagnosed, with a prevalence of 10.8% in one village (Koindu Pompo). Hutchinson concluded that this was an active new focus. Around the river Mano transitional savannah is found, patches of savannah being interspersed with residual forest or thicket along the streams being narrow but well defined due to the Kissi cultivation esp. swamp rice farms. Conditions of close man-fly contact existed,
furthermore the abundance of various domestic animal species (cattle, pigs, goats, sheep, dogs, fowls) might have influenced the dynamic of the disease transmission in this area (Foster, 1963). When this locality was re-examined by Lucasse (1961), only 7 new cases were diagnosed.

To our knowledge, Lucasse’s activities were the last performed on the Liberian side of the Kissi focus before the Liberia Research Unit (LRU) of the Tropical Institute Hamburg, Bong Mine, Bong County, started its work on the transmission dynamics of HAT in 1976 (Mehlitz, 1977). During it studies on the potential role of domestic animals as reservoir hosts in Kissi-villages described by Lucasse (1961), a serological screening (Card Agglutination Trypanosomiasis Test – CATT, Magnus et al., 1978) of 1933 persons in 12 villages followed by parasitological examination (miniature - Anion Exchange Centrifugation Test – m-AECT, Lumsden et al., 1979) of seropositive cases (7.3%) did not reveal any positive HAT cases (Mehlitz et al., 1986). The CATT positive reactors formed a group which was followed up serologically, parasitologically and clinically over a period of 6-12 months without diagnosing any HAT cases. Further, the CATT results (Kissi area) were compared with those obtained from individuals (n=696) of an endemic village (Gbonota) in Bong County (0.6% parasitologically proven cases). No significant difference (p>0.05) of the CATT results were seen between individuals of Lofa County (Kissi) (8.7%) and Bong County (11.2%) (Mehlitz, 1990). It remains to speculation whether CATT positive reactors were false positives or not and whether positive tested individuals were healthy parasite carriers and could act as a human reservoir if left untreated (Büscher et al., 2017). Further and in contrast to Bong and Nimba Counties, T. brucei infections were not diagnosed in domestic animals (n=628) in the same villages surveyed in the Kissi area (pigs, goats, sheep, cattle, dogs) although most sensitive parasitological methods were employed (m-AECT, Mastomy natalensis subinoculation, Mehlitz, 1978). Tsetse fly surveys carried out in parallel with these studies revealed a very low fly density (AD=Apparent Density - Number of flies/day/trap < 0.5%). The detected distribution pattern of Glossina in the Kissi area (G. p. gambiensis) differed from those examined in other parts of the country as to fly density and to species (Mehlitz et al., 1986; Sachs and Mehlitz, 1988). It was observed that the tsetse density was closely dependent on pigs density: after removal of pigs from a village surveyed (“pigs cause too much damage to our rice farms” town chief of the village Kpandu-Kenema), the fly density dropped from 18.4 AD to 0.1 AD within 2 1/2 months. It was concluded that HAT was absent in the ancient Kissi focus as well as T brucei infections in animals and Glossina (Mehlitz, 1990). Inquiries in the district hospitals (Phebe and Ganta hospital, Nimba County) during 1975 brought no evidence that HAT patients were recorded in local health centres.

The reasons for the change of the epidemiological situation was explained by the profound alteration of the environment, large-scale bush clearing, followed by extensive cultivation of swamp and upland rice led to decreasing living conditions for tsetse. Intensive agricultural development (land use) resulted in the radical diminishing of the game and domestic animals, particularly pigs, the favourable vector host (Mehlitz, 1990). Thus, the natural reservoir of T. brucei was reduced. Considering additionally the low susceptibility of G. palpalis. s.l. for T. brucei infections in general, it was assumed that the host-fly-host cycle was interrupted in the absence of other Glossina species (G. pallicera, G. nigrofusca) in this region, in other words, the equilibrium host-T. brucei-host was disturbed. This pattern did not apply for T. congolense and T. vivax, as G. palpalis s.l. is more susceptible to these trypanosomes species. These cycles can obviously sustain with low fly densities and a reduced number of hosts (Rogers, 1988).

HAT OUTSIDE THE KISSI FOCUS SINCE 1944

From 1944 till 1953, 10% of the out-patients of the Ganta Hospital (Nimba County) were treated for a HAT (Harley and Miller, 1955). By the number of parasitological proven cases (43% of all treated...
patients), it was concluded that the average incidence during the nine-year period was 1.5% among the population northeast of Ganta (Nimba County), between the borders of Guinea and Ivory Coast. From the same area and from Bong County sporadic cases were reported by Young (1953). A new sleeping sickness focus with 124 cases (prevalence 0.45%) was described by Lucasse (1962) in Bong County in the area between the district capital Gbarnga and the St. John River in the South. Laboratory records of the Ganta and Phebe hospitals between 1967 and 1977 brought evidence that HAT continued to occur at least sporadically. Fourteen passive case detections were registered during this period, except one all from Bong County (Phebe and Ganta Hospital Records, unpublished).

Eighteen years passed until Lucasse's focus was rediscovered and still found active with a prevalence of 1.0% (Sachs, 1983; Mehlitz, 1986). Surprisingly, also one case of a 3-year-old girl from Gbonata was reported in 1981, a village close to the St. Paul river, near the cluster of villages from where the first authentic HAT cases in Liberia were recorded 50 years earlier by Strong (1930). During a follow-up survey (active case detection) of 216 inhabitants including the villages Bellemue No 1 and Layie, two more cases were detected. Another passive case detection of the Gbonata village at the Phebe Hospital in 1987, followed by a survey (active case detection) of 570 inhabitants of Gbonota (serological screening using the CATT, positive reactors and clinically suspicious persons were subjected to the m-AECT), revealed three more cases (Zillmann and Albiez, 1986; Sachs et al., 1988). During the years 1988 and 1989, further five cases (passive case detection) were diagnosed at the LRU of the Tropical Institute Hamburg, Bong Mine, or the Bong Mining Company Hospital, sums up to 29 cases between 1980 and 1989, all but one (Nimba) from Bong County (LRU Annual Reports 1988; 1989, unpublished). During the civil wars (1989-1996 and 1999-2003) and the post-war period until these days, no active surveillance on HAT has been carried out and no new cases have been reported with one exception of a patient from Harper (Maryland County) (Hussaain et al., 2012). History, however, revealed extensive travelling of the patient to other African countries (including Guinea, Ivory Coast and Ghana). It remains unclear whether this was an autochthonous Liberian case or not. The numbers of HAT cases diagnosed between 1967 and 2012 are summarized in Table 1.

Table 1: Number of HAT cases diagnosed at the Ganta or Phebe Hospital in Bong County, Liberia (passive case detection) during 1967-1977 and by the Liberia Research Unit of the Tropical Institute Hamburg, Bong Mine, during 1980-1989 (mostly active case detection); during the years not listed after 1989, no passive case detection or active surveillance was carried out; no surveillance took place during the post-civil war period and thereafter till 2017.
THE ANIMAL RESERVOIR OF T. B. GAMBIENSE

*T. b. gambiense* group 1 (Gibson, 2001) have been found in various domestic (pigs, sheep, dogs, goats) and wild animals (mammals and reptiles) in West and Central Africa; relevant investigations were summarized and discussed most recently as to their epidemiological significance for HAT (Franco et al., 2017; Büscher et al., 2017). Non-human hosts have been assumed as one of the principal factors associated with the persistence of Gambian HAT in endemic areas in spite of chemotherapeutic campaigns. Using the concept of a next generation matrix (NGM) to understand the transmission dynamics of the disease, Funk et al. (2013) found indications for an independent transmission cycle in wild animals and assumed that reintroduction of HAT would usually occur shortly after elimination of the infection from human populations. The proof of maintenance of *T. b. gambiense* in separate transmission cycles in wild animals would have important implications for elimination strategies (Franco et al., 2017). In this context, we recall experimental studies carried out with autochthonous antelopes in Liberia. It was shown that human-derived *T. b. gambiense* multiplied and persisted in antelopes with low and intermittent parasitaemias over long periods without showing any clinical symptoms in the experimental animals (Mehlitz, 1986): Black-backed duikers (*Cephalophus dorsalis*) were infected cyclically through *G. p. gambiensis* with the *T. b. gambiense* stock TH Gamey Dolo/A, group 1 according to Gibson (2001), isolated in Gbao, Bong County, and analysed by combined use of restriction endonuclease digestion, gel electrophoresis and molecular hybridization (Paindavoine et al., 1986). Parasites were detected for up to 718 days post expositionem (daily examination with the m-AECT) with low parasitaemias hardly exceeding 50 trypanosomes/ml blood with aparasitaemic intervals of more than 200 days. Further, it was shown that *T. b. gambiense* was transmissible through *G. p. gambiensis* in the antelope-fly-antelope cycle and that the characteristics of human infectivity of group 1 *gambiense* remained stable after cyclical re-isolation under experimental conditions for several years (Mehlitz, 1986). Further, infections rates of 3.6 % with *T. brucei* spp. in wild ungulates (n = 140) were observed in the endemic HAT rainforest region of Bong County (*Cephalophus dorsalis, Cephalophus niger, Philantomba maxwellii, Tragelaphus scriptus*) diagnosed parasitologically (m-AECT) (Mehlitz, 1984). Studies on the bio-ecology of the vector (*G. palpalis* s.l.) of HAT in Bong County showed that 31 % of flies feed on humans, 30 % on reptiles and 24 % on wild ungulates, 15 % on others (domestic ruminants, dogs, birds, pigs) (Kaminsky, 1987; Mehlitz, 1990). These transmission experiments, the field studies on infections rates in antelopes and the host preference of the vector of HAT described strongly point to the existence of separate transmission cycles *G. palpalis* s.l. - wild animals - *G. palpalis* s.l. of *T. b. gambiense* and highlight the significance of animal reservoir hosts responsible at least to a certain degree for the maintenance of HAT in persistent foci or the resurgence of the disease.

CONCLUSIONS

Liberia has not been listed in the maps (atlas) for the distribution of population at risk of the HAT for decades where any level of risk has been identified until 2014 (Franco et al., 2017). This brief review is intended to draw attention to ancient HAT foci in the West African rainforest areas where no surveillance could be carried due to war riots, outbreaks of fatal epidemics like Ebola virus infection or another priority setting of national health stakeholders during recent decades. Recalling and summarizing HAT case findings for the period 1967-1977 (passive case detection) and for the pre-civil-war period 1981-1989 (active case detection) give evidence that Gambian HAT was endemic in Bong County of Liberia and has survived over decades in restricted areas of the country. Only a surveillance uptake of humans and animals (domestic and wild) can clarify whether HAT is still present in this focus. The absence of HAT in the old Kissi focus (Lofa County), however, might be the results of demographic and landscape changes over time. The most important trajectories
of land use have been associated with loss of forest cover: 15 % of the 1975 forest cover compared to 2013 have been lost. The most significant losses occurred in the Upper Guinean rainforest (Lofa County with the Kissi chiefdoms) which has been replaced by degraded forest, thickets savannah and slash-and-burning agriculture. The concerns of desertification due to high levels of deforestation are obvious (USGS, 2015). Climatic changes, particularly the decrease in rainfall to 1300 mm in the forest-savannah boundary region in the north of the country associated with increased human density, intensification of land use particularly upland and swamp rice farming along with the decline of pig farming, change of tsetse habitat not favorable for G. palpalis, the decrease of wild animals, as well as the possible changes of vector competence or human-vector contact, might have contributed to the disappearance of the disease in this region (Courtin et al., 2008). The observations and results for Liberia - so far missing and not discussed in most recent publications on the occurrence and distribution of HAT in West Africa - might foster the discussions on the changes of the reparation of Gambian HAT (Courtin et al., 2008). The experimentally proofed transmission cycle antelope-G.p.gambiensis-antelope with human-derived T. b. gambiense supports the epidemiological significance of animal reservoir hosts of the HAT in West and Central Africa being potential sources for the resurgence of the disease.

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