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Review

Implicating roles of animal reservoir hosts in the resurgence of Gambian trypanosomosis (Sleeping Sickness)

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Gambian trypanosomosis (Sleeping Sickness) is a complex and debilitating disease of man. For many years the disease has been ravaging in several parts of sub-saharan Africa despite decades of therapeutic control. Although animal reservoir hosts are believed to be associated with the disease, not much evidences have been established to prove the true existence of animal reservoir hosts for *Trypanosoma brucei gambiense* and the zoonotic nature of Gambian Sleeping Sickness. This paper reviews recent evidences based on molecular and other biotechnologies leading to the identification of mammalian hosts as reservoirs of *T. b. gambiense* and the roles of such hosts in transmission and resurgence of sleeping sickness in sub-Saharan Africa.

Key words: Gambian trypanosomosis, *Trypanosoma brucei gambiense*, animal reservoir hosts, biotechnologies.

Human African Trypanosomosis (HAT, Sleeping Sickness) is a complex and debilitating disease of man. The disease still ravages in several parts of sub-Saharan Africa despite decades of efforts aimed at control (WHO, 1998; Jannin, 2000; Kabayo, 2002). HAT poses as an emerging public health crisis in several countries including Nigeria (Airauhi et al., 2001; Stich et al., 2003; Waiswa et al., 2003) and a major health risk to tourists coming to tropical Africa (Sabbah et al., 1997; Conway – Klaassen et al., 2002; Jelinek et al., 2002).

HAT is caused by the parasitic protozoa of the Genus *Trypanosoma.* WHO (1998), had commented on the complex nature of the epidemiology of the human disease arising from two species of the infecting trypanosome in various parts of Africa. In East and Southern Africa, HAT described as Rhodesian sleeping sickness is caused by *Trypanosoma brucei rhodesiense,* resulting to acute disease course leading to death of infected persons within few weeks or months (WHO, 1998). In West and Central Africa, HAT is caused by *T. brucei gambiense* and is transmitted principally by tsetse flies, *Glossina palpalis* and *G. tachinoides* resulting to a devastating, chronic from of the disease described as Gambian Sleeping Sickness (Gambian trypanosomosis). Death of infected persons may not occur for several years, while the patient emaciates over many months displaying typical sleeping symptoms (WHO, 1998). Morphologically, *T. brucei rhodesiense* and *T. brucei gambiense* are undistinguishable from *T. brucei brucei* causing disease in animals (Losos, 1986).

HAT is found in sub-Saharan Africa between latitudes 14^{O}N and 29^{O}S within the geographical location of tsetse

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where about 200 endemic foci exist in 36 countries (WHO, 1998, 2000). An estimated 60 million people are believed to be at risk while about 300,000 new cases are reported each year. Higher numbers of cases are likely to occur in several countries in view of the current upsurge in both forms of sleeping sickness (WHO, 2000).

Going by WHO Statistics of 1998, Gambian trypanosomosis has a wider geographical spread than Rhodesian disease with about 77.8% of HAT endemic countries suffering from *T. brucei gambiense* (WHO, 1998).

Two forms of clinical disease are recognised. The early or haematolymphatic stage and the late or meningoencephalic stage which is characterised by Central Nervous System (CNS) disturbances following invasion by *T. brucei gambiense* (Apted, 1970; WHO, 1998). The early stage is characterised by symptoms that occur before CNS invasion by trypanosomes. These include development of a chancre at the site of tsetse bite which is followed by joint pains, muscle aches, headache, pruritis, cachexia, enlargement of lymph nodes, marked generalised oedema, moderate anaemia, fever, cardiovascular disorders and endocrinological disorders resulting to importence, reduced libido, abortions and infertility. Late stage symptoms include deep hyperaesthesia, paraesthesia, convulsions, mental disorders, insomnia, somnolence, ataxia, paresis and paralysis.

There is no single clinical diagnostic sign or symptom that can be regarded as pathognomonic for sleeping sickness. Accurate diagnosis is therefore dependent on detection of parasites and or antibodies, circulating antigens or trypanosomal DNA using both laboratory and field based techniques. Parasite detection using direct methods such as blood films (thin, thick or wet) and concentration methods such as microhaematocrit centrifugation technique, buffy coat method and *in vivo* inoculation of biological materials (e.g. cerebrospinal fluid and lymph node aspirates) from human suspects into mice, rats, guinea pigs have been documented (WHO, 1998). Other indirect methods routinely used include, card agglutination test for trypanosomiasis (CATT), enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) (WHO, 1998) . The place of other diagnostic techniques such as anion exchange cellulose chromatography (Lanham and Godfrey, 1970), miniature anion-exchange centrifugation technique (Lumsden et al., 1979), genetic identification of trypanosomes by multi-locus enzyme electrophoresis (Godfrey and Kilgour, 1976; Gibson et al., 1980) and use of kit for *in-vitro* isolation of trypanosomes (Aerts et al., 1992) in the diagnosis of both from, of HAT has recently been reviewed by Truc (2003).

Control of HAT is dependent largely on chemotherapy and tsetse control. Whereas pentamidine and suramin sodium may be effective for early stage sleeping sickness, melarsoprol, Eflornithine and Nifurtimox has been recommended for late stage sleeping sickness (WHO, 1998). HAT arising from *T. b. gambiense* constitute a major problem arising from the controversial role of animal reservoir hosts.

Although campaigns against HAT in the 1960s brought the disease below epidemic proportions, there is presently a dramatic resurgence in both forms of HAT which has been blamed on wide spread civil disturbances and wars, declining economies, reduced health financing, dismantling of disease control programes (Smith et al., 1998; Penchenier et al., 1999) and animal reservoir hosts (Magona et al., 1999; Simarro et al., 2001; Rahman, 2002). WHO estimates that over 600,000 persons are currently infected with HAT, the most of them in Central Africa (Truc, 2003). Gambian Sleeping Sickness now occurs in epidemic proportion in several parts of sub-Saharan Africa especially Sudan, Democratic Republic of Congo, Uganda and Cameroon (WHO, 2000; Truc, 2003) as well as Cote d'Ivoire (Jamonneau et al., 2003) and Equatorial Guinea (Simarro et al., 2001).

In Nigeria, although the exact sleeping sickness situation is not well known, there is increase in number of volunteer cases presented for treatment each year (Enwezor and Ukah, 2000; Airauhi et al., 2001). Apart from the old Gboko endemic focus remaining active, outbreak of sleeping sickness in the new Abraka focus presently constitute a major health risk (Airauhi et al., 2001) resulting to several deaths. During an outbreak, out of 3,583 volunteers from 24 communities scattered around this focus, 359 were seropositive and 104 parasitologically positive for *T. b. gambiense* (Edeghere et al., 1998).

Although man is the natural mammalian host for *T. b. gambiense,* several animals have been found to be susceptible to the parasite (Gibson et al., 1978). For many years, pigs have been identified as animal reservoir hosts for *T. b. gambiense* (Watson, 1962) and recently has been associated with the persistence and epidemics of sleeping sickness in Uganda (Magona et al., 1999), Equatorial Guinea (Simarro et al., 2001) and Cameroon (Nkinin et al., 2002) . It has also been associated with maintenance of old sleeping sickness endemic foci in Nigeria (Onah and Ebenebe, 2003). Use of standard procedures such as, resistance to human serum based on the blood incubation infectivity test (Rickman and Robson, 1970) and molecular characterization of *T. brucei* stocks from man and animals by isoenzyme electrophoresis (Gibson et al., 1978; Mehilitz, 1986) and polymerase chain reaction based methods (Penchenier et al., 1999) have led to the identification of more mammalian hosts as reservoirs for *T. b. gambiense*. Such hosts include dogs, sheep, cattle and a range of game animals. Identification of serum-resistance-association (SRA) gene in eight *Trypanozoon* isolates resistant to human serum has been reported by Welbourn et al. (2001) while such genes were absent in isolates sensitive to human serum. Although this

technique identified human-infective trypanosomes in cattle as reservoir in the sleeping sickness endemic foci in Uganda arising from *T. b rhodesiense,* it may similarly be used for identification of animal reservoir host in *T. b. gambiense* endemic areas.

Simo et al. (2000) using PCR methods reported 8% *T. b. gambiense* infection rate in wild animals in the Bipindi sleeping sickness focus of Cameroon which was believed to be responsible for resurgence and perpetuation of the disease in the area. High prevalence of *T. b. gambiense* was observed in rodents (*Atherurus africanus* and *Cricetomys gambianus*), monkeys (*Cercopithecus* and *Cercocebus*) and ungulates (*Cephalophus spp*). Two small carnivores (*Genetta servalina* and *Nandinia binotala*) also harboured trypanosomes infective to man. Similarly dogs, pigs, wild animals and bovids were identified as reservoir hosts in Liberia, Cote d'Ivoire and Burkina Faso based on isoenzyme electrophoresis, resistance to human serum and DNA analysis (Mehilitz, 1986). The capacity of *T. b. gambiense* to proliferate and persist in alternative hosts in the absence of symptoms with prolonged maintenance of infectivity to the vectors makes it maintain a wide range of reservoir hosts (Mehilitz, 1986) which may differ from one endemic area to another.

Adaptation of PCR technique for identification of *T. b. gambiense* and blood meals of both animal and human origins in tsetse flies (Truc et al., 1999; Waiswa et al., 2003) has paved way for determination of the roles of animal reservoir hosts in epidemics of Gambian Sleeping Sickness. Sene et al. (2000) reported the involvement of *Glossina palpalis* in cyclical transmission of sleeping sickness from pigs to man in Cote d'Ivoire. Waiswa et al. (2003) similarly reported pig-tsetse-human, cattle-tsetse-human and sheep-tsetse- human transmission cycles in three endemic foci in South-Eastern Uganda. Even though the role of animal reservoir hosts in the transmission of *T. b. gambiense* have been controversial current biotechnologies that differentiate between *T. brucei brucei*, *T. b. gambiense* and *T. b. rhodesiense* in the tsetse vector and animals confirm the true zoonosis of Gambian trypanosomosis. Going by such findings maintenance of animal- tsetse-animal *T. b. gambiense* transmission cycle is not unlikely. The zoonotic nature of the disease seem to be further enhanced by the feeding pattern of *G. palpalis* group which apart from feeding on man, feeds on domestic pigs, wild ruminants and lizards (Spath, 2000).

Animal reservoir hosts for *T. b. gambiense* has been identified as one of the principal factors associated with the persistence of Gambian trypanosomosis in endemic areas in-spite of chemotherapeutic campaigns (Simo et al., 2000). For example, the presence of pigs in Mbini focus of Equatorial Guinea is believed to be responsible for the persistence of infection despite several years of treatment (Simarro et al., 2001). This is supported by the ability of *G. palpalis* group to cyclically transmit *T. b. gambiense* from unlimited number of animal reservoir hosts, to man (Spath, 2000; Waiswa et al., 2003) and the difficulty associated with the control of trypanosomosis in game animals.

Based on observations using human serum resistance, isoenzyme electrophoresis and DNA-test for molecular characterization of *Trypanozoon* leading to more definitive identification of *T. b. gambiense* in pigs and other domestic and wild animals, the role of animals as reservoir hosts for Gambian Sleeping Sickness and resurgence of the disease can not be questioned any longer. Going by the feeding habit of *G. palpalis* group on unlimited range of animal hosts, and the ability of *T. b. gambiense* to perpetuate in such hosts without clinical symptoms supports the fact that animal reservoirs indeed constitute important complications militating against eradication of Gambian Sleeping Sickness in sub-Saharan Africa.

An Intergrated approach to the control of human and animal trypanosomosis is essential in the control of the current upsurge in human trypanosomosis and in limiting the present economic impact on Africa and tourism potentials of sleeping sickness endemic countries.

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