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Human African Trypanosomiasis in Suburban and Urban Areas: A Potential Challenge in the Fight Against the Disease

Lisette Kohagne Tongue[1,2*], Jacques François Mavoungou[3], Raceline Gounoue Kamkumo[2], Dramane Kaba[4], Guy Christian Fako Hendji[1], Richard Pamba[5], Paulette Mengue M'eyi[6], Bertrand Mbatchi[3] and Francis Louis[1,7]

[1]*Association pour la Promotion de la Lutte contre les Trypanosomiases et les Tsé-tsé (APLTT), Yaoundé, Cameroun*
[2]*Université de Yaoundé I, Faculté des Sciences, B.P. 812 Yaoundé, Cameroun*
[3]*Université des Sciences et Techniques de Masuku, Franceville, Gabon*
[4]*Institut Institut Pierre Richet – Institut National de Santé Publique, Abidjan, Côte d'Ivoire*
[5]*Institut d'Hygiène Publique et d'Assainissement (IHPA), Ministère de la Santé, Libreville, Gabon*
[6]*Programme National de Lutte contre la trypanosomiase humaine Africaine (PNLTHA), Ministère de la Santé, Libreville, Gabon*
[7]*Association against Trypanosomiasis in Africa (ATA), Château de Brives, Lavans Saint-Sulpicin, France*

Abstract

Sub-Saharan countries are facing a demographic growth of 3% per year. That increase of the population in number, associated with climate changes, has deeply modified environmental landscape and affected biodiversity. The distribution of tsetse flies or *Glossina*, vector of sleeping sickness, has been considerably modified over time. Species of *morsitans* group (*Glossina* subgenus) had disappeared from some areas, while those of *palpalis* group (*Nemorhina* subgenus) developed and adaptation in Human habitats with peridomestic behaviors. The great capacity of these species to adapt in suburban and urban areas as soon as microclimatic conditions and host availability are met has brought up a new epidemiological context of the disease: suburban and urban foci. We are reviewing that epidemiological feature in order to draw attention to that particular aspect which may impede the progress of disease elimination in sight in many *T. b. gambiense* sleeping sickness foci.

Keywords: Vector-borne disease; Human African trypanosomiasis; *Trypanosoma brucei*; Demographic growth; Urbanization; *Glossina* foci

Introduction

Sleeping sickness or human African trypanosomiasis (HAT) is a vector-borne parasitic disease that is fatal if left untreated. It is caused by a single-celled protozoa belonging to the *Trypanosoma* genus. Parasites are transmitted to humans by the bite of a tsetse fly (*Glossina* Wiedeman, 1830 genus) that has acquired the infection from human beings or from animals harboring the human pathogenic parasites. The disease takes two forms, depending on the parasite involved: the chronic form due to *Trypanosoma brucei gambiense* Dutton, 1902 found in west and central Africa which represents more than 97% of reported cases and the acute form due to *Trypanosoma brucei rhodesiense* Stephens & Fanthams, 1910 found in eastern and southern Africa [1]. Sleeping sickness is restricted to sub-Saharan Africa, in the range of the tsetse vector. Tsetse flies are specifically distributed within their area: they are closely related to vegetation which forms a screen from solar radiations and wind and which is itself dependent on the presence of surface or underground water, that increases the humidity of both atmosphere and soils [2]. In West and Central Africa, the riverine forest species, belonging to the *Glossina* (*Nemorhina*) Robineau-Desvoidy, 1830, subgenus are the more important vectors of the disease. The distribution of the parasites and consequently the disease within the vector range is focal. Thus, sleeping sickness is a public health problem where the vector, the parasite (and its reservoir hosts) and humans co-exist.

Current epidemiological situation

The epidemiology of sleeping sickness is characterized by its occurrence in foci: a focus defined as "a zone of transmission to which a geographical name is given" [3]. The impact of sleeping sickness in terms of public health lies not in the annual incidence, but in its potential for the development of explosive epidemics causing thousands of deaths. If incidence alone is considered, the disease appears as a minor health problem compared with other parasitic diseases like malaria and helminthic infections [4]. Distribution of HAT is very heterogeneous. The disease develops in areas whose size can range from a village to an entire region. Within a given area, the intensity of the disease can vary from one village to the next. In the 1990s, estimates (both forms combined) for HAT indicated that 60 million people were at risk in approximately 250 distinct foci of 36 sub-Saharan countries [4]. Prevalence of 50% had been reported in some villages in the Democratic Republic of Congo, Angola and Southern Sudan. Sleeping sickness was considered as the first or second greatest cause of mortality in those communities. Thanks to many control measures such as systematic patient screening, treatment and follow-up established in western and central Africa for the *T. b. gambiense* form and the animal reservoir and vector control implemented in eastern and southern Africa for the *T. b. rhodesiense* form, the number of new cases reported throughout the continent had substantially reduced: less than 10,000 new cases reported in 2009 for the first time in 50 years [5]; which represents a decrease of 63% since 2000 [6].

The *T. b. gambiense* form of the disease has in several foci already reached a prevalence threshold compatible with the concept "eliminated as a public health problem" [6]. In other foci, the disease remains a

***Corresponding author:** Lisette Kohagne Tongué, Université de Yaoundé I, Faculté des Sciences, B.P. 812 Yaoundé, Cameroun, Tel: 00 237 22 10 38 49; E-mail: lisetteappmv@yahoo.fr

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public health issue due to poor accessibility or security constraints [7]. The occurrence of sleeping sickness is related to the presence of the cyclical vector. But, for reasons that are so far unexplained, there are many regions where tsetse flies are found but sleeping sickness is not [8,2]. *Glossina* species are known to survive only in very specific types of habitat, where the density of canopy and underwood determines suitable environmental conditions (temperature, humidity, luminosity), easiness of flight, as well as the presence of animals which are tsetse fly feeding hosts [2]. Due to such peculiar environmental conditions, tsetse flies are mainly found in remote areas and therefore, sleeping sickness is considered as a disease affecting rural areas; a disease of poor, marginalized and rural populations who depend on their land and labor for a livelihood [9]. It is one of the seventeen Neglected Tropical diseases [10]. The transmission of the *T. b. gambiense* form to humans is principally related to close contact with the fly. Species of the *palpalis* group (*Nemorhina* subgenus), main vectors of the disease, have great capacity for adaptation to peridomestic habitats. Thus, human populations and, to a certain extent, domestic animals are important factors affecting the distribution of these vectors [11]. They are found widespread in all components of the ecosystem in infested areas, including forest, "interstitial savannas", coffee and cocoa plantations, tracks and villages [12]. This wide and close distribution of the vector to human beings (species of *palpalis* group are known to easily colonized anthropics habitats), combined with massive immigration of populations (potential human reservoir of parasites) from rural areas to towns has brought up a new epidemiological feature of the disease: suburban and urban sleeping sickness foci.

Urbanization and sleeping sickness

Urbanization is a fairly recent phenomenon in Africa. There is no global standard for the classification of urban environments, as the definition of what constitutes an urban area varies among countries and in some cases it even varies over time within a single country [13]. Some countries define their urban population as those people living within certain administrative boundaries, such as administrative centers or municipality councils. Other countries prefer to classify their urban population using population size or population density as the primary consideration and economic function as the second. Thus, places that are classified as urban in one country may be classified as rural in another. For example, In Angola, all localities with 2000 inhabitants or more are considered urban, while in Benin only localities with 10000 inhabitants or more are classified as urban and communities fewer than 10000 inhabitants are classified as rural [14]. This criterion and others such as non-agricultural activity of at least 75 percent of the population [15] are not considered in defining urban or suburban sleeping sickness foci. Besides, the geographical extent of cities changes significantly over time due to many factors in relation to human growth such that an urban HAT focus described in the 1960s may be considered as a rural focus in the 2000s.

Observations

Urban sleeping sickness focus is an old concept. It was firstly described in 1960s, both in the savanna and forest zones. The savanna HAT urban focus described was in Bamako, Mali where the transmission and the manifestation of the disease in the town were favored by a rural to urban migration of populations (human reservoir of parasite) that followed independence days and to an existence of suitable environmental conditions for survival of tsetse flies in the vicinity of the town [16,17]. In Brazzaville, the forest HAT urban focus described [18,19], that the reason of the manifestation of the disease in the town was not a direct consequence of a rural to urban migration of populations. Brazzaville is an old sleeping sickness focus. From 1906 to 1908, all HAT cases diagnosed in the hinterland (known as "Afrique Equatoriale française" which at that time joined together three countries: Gabon, Congo and Central African Republic) were brought to Brazzaville, the capital for treatment [20]. That operation favored the endemicity of the disease in an area highly infested with tsetse flies. During that period, road construction, housing estate and buildings pushed tsetse resting sites at the periphery of the town, around the Djoue stream, tributary to the Congo River and the disease in 1970s was mainly endemic only in suburbs. But in the zoological park, an area kept in its natural conditions downtown Brazzaville, *Glossina* were still present due to suitable environmental conditions and feeding hosts (primates, suids, bovids, reptiles, etc.) tamed in the area. Brazzaville was, therefore known as a suburban and urban HAT focus [21]. In the course of time, demographic concentration and human activities destabilized the ecosystem balance and, some years later, it was pointed out that a vector control activity was progressively achieving itself in downtown Brazzaville, due to urbanization and market gardening along streams and ravines [22,23]. In 1992, it was even observed that the southern limit of tsetse distribution around Brazzaville was then far from the Djoue stream, with a progressive replacement of *G. fuscipes quanzensis* by *G. palpalis palpalis* [24]. Meanwhile, the zoological park was hardly under control despite vector control activities put in place [25] up to the end of 1990, when animals tamed in the zoo were killed because of a civil unrest in Brazzaville. The absence of blood meals for tsetse compromised their survival in the area and, ten years later, an entomological survey suggested the *Glossina* disappearance from the zoo [26]. Nowadays, Brazzaville suburban and urban focus no longer exists. Nevertheless, as the Mbamou Island situated in the Stanley Pool, upstream from Brazzaville is still a tsetse infested area (Kohagne, personal communication) and there is an intense population's movements between active sleeping sickness foci (located in the hinterland) and Brazzaville, one could consider that Brazzaville human population is still at risk of HAT. More recently, *Glossina* resting sites were also described in suburbs of many others cities, such as Bangui in the Central African Republic [26], Daloa, Sinfra and Bonon in Côte d'Ivoire [27-30], Kinshasa in the Democratic Republic of Congo [31-33] and Dubréka, Boffa in Guinea [34]. Many of these areas are historical sleeping sickness foci where, currently, population's settlement has pushed tsetse flies to the periphery of the town. Although these foci exhibited the same epidemiological feature, suburban or urban foci, modalities of the disease transmission varied according to human behavior and to local environment. In Côte d'Ivoire, urban foci are mainly observed in the Center-West of the country, in areas where intensive coffee and cocoa cultivation has favored expansion of towns, due to a higher concentration of populations. Disease transmission does not occur in the city-centre; people live in town but get infected during their rural activities in tsetse infested areas located in the vicinity. Such foci are called "rural foci with urban manifestation" [29]. In suburbs of Kinshasa town, comprising a hardly altered ecosystem around a built-up area, there exists natural human-fly-human transmission cycle since *T. b. gambiense* has been identified from infected flies [33]. Kinshasa is a town located along the Congo River with many tributary streams: Djili, N'Sele, Lukaya, Lukunga, Mikonga, Kalamu and Makélélé. That township shelters about 10,000,000 inhabitants in three different

ecological parts: an urban area (city-centre), a suburban area and a rural area. Suburban and rural areas harbor 80% to 90% of the total of inhabitants who, though being civil servants, are regularly involved in rural activities (farming, fishing, etc.) because of economic crisis [32]. Environmental conditions around the Congo River and its tributary streams are suitable not only for human activities, but also for tsetse flies and during the discharge of their duties; people are exposed to bite of the flies and at risk of infection with sleeping sickness. Contrary to the suburban focus of Brazzaville where demographic pressure has annihilated tsetse resting sites and transmission of sleeping sickness, demographic concentration in Kinshasa seems to lesser effect on the endemicity of the disease in the outskirts of the town. In Libreville, Gabon, the suburban HAT focus exhibits a peculiar epidemiological characteristic. Libreville is a town opened to the Atlantic Ocean where coastal vegetation is made essentially by swamp mangrove, suitable for tsetse flies. The Gabon estuary is known to be an overflowing tsetse infested area [35,36] and the extension of the town has brought closer tsetse resting sites to urban population. In the past, that area was frequented only by fisher-men (potential human reservoir of parasites) who are incriminated to spread the disease in the coastal area of Gabon [36,37] and who have probably, favored the outbreak of the disease in that suburban location. Actually, the suburban area of Libreville town is used by all citizens for various activities including fishing, trade and tourism. The consequence of the several and regular frequentation of populations in tsetse infested area neighborhood Libreville is that, sleeping sickness is, henceforth, passively diagnosed in populations from all strata of society and from all origins, even in Europeans [38,39]. So far, only certain particular strata of society were involved in suburban or urban sleeping sickness transmission. The suburban HAT focus of Libreville is revealing other epidemiological feature.

Discussion

Urbanization occurs through three distinct channels: the rural to urban migration, the growth of the existing urban population and the reclassification of rural areas into urban or otherwise [15]. In many Sub-Saharan Africa countries, urbanization is the consequence of a rural to urban migration of populations that followed the independence period. The increase of human settlements leading to a population explosion amplified human activities and profound pressure was perceptible on the land, wildlife and forest resources. This has resulted in an overall reduction in natural tsetse habitats and wildlife hosts of several *Glossina* spp [40]. The corresponding alteration in the pattern of tsetse distribution was that tsetse species were now seeking more environmental conducive habitats with abundant hosts. Human habitats are fast becoming tsetse conducive, particularly for the riverine group species which exhibit peridomestic behaviors [41]. Urban environmental changes reduced the extent of potential tsetse biotopes, but the pattern of urban land use leads to an increase in human population density and favors man-fly contact which is an important factor in sleeping sickness transmission. Thus, urbanization did not bring about cessation of HAT transmission; rather it did result in the concentration of tsetse in the town outskirts, where environmental conditions remain conducive to survival of the flies and for man-vector contact enough for the disease transmission. In the course of time, urbanization extends through the growth of the existing urban population. The effects on land use (housing estate, road construction, etc.) in conjunction with local (or global) changes in climatic parameters become pronounced and environmental degradation contributes to tsetse disappearance and consequently, disappearance of existing suburban sleeping sickness focus, such as Bamako and Brazzaville. It is known that high population growth could eliminate tsetse flies from large areas, irrespective of control activities [42]. That phenomenon has been observed in some quarters of the suburban area of Kinshasa town, where tsetse flies disappeared without any deliberate intervention against the vector, but primarily because of the population growth and its impact on the environment [43]. The assumption is that human population density is correlated with the area of tsetse habitat cleared for cultivation or housing estate [44]. However, the risk of trypanosome transmission is not absolutely correlated to vector density, but depends also on a number of contextual factors including human mobility [45]. In many sub-Saharan countries, urbanization is rarely defined upon the basis of non-agricultural activities. People living in town, civil servants, traders or self-employees are for the most part involved in agricultural activities (cocoa, coffee, palm tree, etc.) practiced in appropriate areas located either in the neighborhood or far from the town. In sleeping sickness endemic areas, the constant presence of populations in tsetse infected areas acts in favor of an intense contact with flies and urban populations are exposed to the disease in the same way as those living in the rural tsetse infested areas. The existence of the disease in the urban area is sometimes a consequence of an intense relationship between rural and urban areas [29]. Knowledge about local epidemiology situation of HAT is necessary for the success of a control program. In many *T. b. gambiense* foci, the main strategy put in place is active mass screening (by mobile teams examining populations at risk, village by village) and treatment of all cases detected. This approach is addressing the occurrence of the disease mainly in rural areas, at the furthest extremities of the formal health system, where it is difficult for patients to access health care particularly for those in the second stage of the disease and for control campaigns to have an effective outreach [46,47]. With the spread of HAT in urban areas, one could assume that sleeping sickness control by active case-detection strategy would be reinforced by an efficient passive case-detection since affected individuals would easily come to the health centers or hospitals for examination. But, clinical signs of sleeping sickness are generally unspecific and their frequency varies between individuals and between disease foci [3]. Most patients in early stage will be missed and their presence within the populations will contribute to the spread of the disease. In urban foci where the disease transmission is related to a well implemented agricultural system, exposed populations (labor) should be screened and examined in their job place for more efficiency. Indeed, large-scale control campaigns targeting only the human reservoir can locally eliminate transmission of sleeping sickness [48]. In urban areas where exposed populations are not well defined because of that, transmission is more related to the regular presence of individuals in tsetse infested area than to a particular activity, it would be really necessary to think about an integrated approach that would take in account all elements of the transmission cycle. In some HAT endemics countries, medical profession is not always aware of extend of the disease; thus, significance should be given to the consciousness-raising of the potential incidence of HAT in urban local population. In contrast of what previously expected about a probable extinction of tsetse flies because of a population growth [42,44], urbanization has brought up an epidemiological feature which may constituted a new challenge in the fight against trypanosomiasis. Some analysis has shown that riverine species are little affected or not at all by human population growth and are thus likely to remain extant indefinitely

[49]. Indeed, in areas both infected by savanna (*morsitans* group) and riverine species, the number and the distribution of species of *morsitans* group decreased in the course of time, while those of *palpalis* group are less affected [50,51]. Moreover, beyond their peridomestic behavior, species of *palpalis* group exhibit an ability to adapt in big urban centers as soon as microclimatic conditions and host availability are met, with a possibility to transmit trypanosomosis [52] and even a biting nuisance to humans in their houses [53]. Several domestic animals such as pigs, goats and sheep are known to harbor *T. b. gambiense* [54-56]. The role of animal reservoir in the maintain and the resurgence of sleeping sickness is not well defined. However, as domestic animals close to human beings can harbor and even amplified human's trypanosomes, there is an urgent need to think about a new strategy that will interrupt the progression of the disease in urban areas.

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