EcoHealth 2, 183–194, 2005
DOI: 10.1007/s10393-005-6331-9

ECOHEALTH

Original Contributions

Sleeping Sickness in Southeastern Uganda: A Systems Approach

Lea Berrang-Ford,[1] David Waltner-Toews,[1] Dominique Charron,[2] Martin Odiit,[3] John McDermott,[4] and Barry Smit[5]

[1]*Department of Population Medicine, University of Guelph, Guelph, Ontario, N1G 2W1, Canada*
[2]*Foodborne, Waterborne and Zoonotic Infections Division, Public Health Agency of Canada, Guelph, Ontario, Canada*
[3]*Ministry of Health, Kampala, Uganda*
[4]*International Livestock Research Institute, Nairobi, Kenya*
[5]*Department of Geography, University of Guelph, Guelph, Ontario, N1G 2W1, Canada*

Abstract: Sleeping sickness continues to be a significant public health burden in southeastern Uganda. Continued spread of the disease into new areas of Uganda highlights our inability to understand and predict the distribution of infection. Multiple factors influence the distribution of sleeping sickness, including climate, land cover, cattle movements, prevention and control activities, and social conflict. We draw on a systems approach to conceptualize and characterize the multiple interacting forces and processes that influence the spatial and temporal dynamics of sleeping sickness in Uganda. This synthesis reveals a complex system of interactions among human and biophysical systems, feedback, and scale dependence. We identify some common analytical modeling approaches relative to our system characterization and identify opportunities for sleeping sickness research and improved understanding of disease dynamics in Uganda.

Key words: sleeping sickness, trypanosomiasis, Uganda, tsetse, social conflict, systems approach

INTRODUCTION

Sleeping sickness is the name used to describe the human form of African trypanosomiasis (*Trypanosoma* spp.), a protozoal parasitic disease that affects humans, livestock, and many sylvatic species in much of sub-Saharan Africa. Transmitted by the tsetse fly vector (*Glossina* spp.), trypanosomiasis is a significant constraint to livestock development in sub-Saharan Africa (Jordan, 1979, 1986; McDermott and Coleman, 2001). Southeastern Uganda has generally experienced the acute form of sleeping sickness, caused by the subspecies *Trypanosoma brucei rhodesiense*, which is predominant in eastern and southern Africa (Koerner et al., 1995; Welburn et al., 2001; Fèvre et al., 2004). A second subspecies, *T. b. gambiense*, causes a chronic form of sleeping sickness and is prevalent predominantly in western and central Africa and southern Sudan. Sleeping sickness has continued to be a significant public health burden in southeastern Uganda, with epidemics in 1901–1915, 1940–1946, and 1976–1989 (MacKichan, 1944; Hide, 1999; Fèvre et al., 2004). More recently, the spread of sleeping sickness into areas previously thought to be free from the disease has highlighted gaps in the ability of current research to explain and predict the distribution of infection (Fèvre et al., 2001).

Published online: July 12, 2005
Correspondence to: Lea Berrang-Ford, e-mail: berrangl@uoguelph.ca

The incidence and control of sleeping sickness have been subject to the interactions of multiple determinants in space and time (Ford, 1969, 1971; Jordan, 1979, 1986; Hendy and Makin, 1988; Hursey and Slingenbergh, 1995; Mills and Pender, 1996; Reid et al., 1997; Bourn et al., 2001). These include the ecology of the parasite, vector, and host species, whose distributions and interactions are affected by sociopolitical factors. In this article, we draw on a systems approach to conceptualize and characterize the multiple interacting forces and processes that influence the spatial and temporal dynamics of sleeping sickness in Uganda. On the basis of this systems characterization, we identify some research opportunities relative to several major modeling approaches used in sleeping sickness research.

Sleeping Sickness in Uganda

Uganda, located in East Africa (Fig. 1), is surrounded on the east by Kenya; on the west, by the Democratic Republic of the Congo; on the north, by Sudan; and on the south, by Tanzania and Rwanda. The country is located in a region that has experienced extreme poverty and civil unrest over the past 100 years, and these conditions have coincided with, or preceded, outbreaks of sleeping sickness in Uganda (Okiria, 1985; Mbulamberi, 1989b). References to sleeping sickness in this article refer to the acute form of the disease in humans, caused by *T. b. rhodesiense.* The epidemiology, pathology, and ecology of *T. b. rhodesiense* vary significantly from the more chronic form of sleeping sickness, caused by *T. b. gambiense* (Mbulamberi, 1994). Early symptoms of acute sleeping sickness include headache, fever, anxiety, and confusion, followed by disruption of sleeping patterns, slurred speech, mental confusion, coma, and eventual death within 6 to 12 months if untreated (Hide, 1999). Trypanosomes infect many species, including cattle and other livestock. Animal trypanosomiasis is generally considered to take an endemic form (i.e., consistent, often low-level disease). Nonetheless, there have been several epidemics of animal trypanosomiasis, particularly in cattle, over the past 100 years (Ford, 1971; Leak, 1999; Fèvre et al., 2004). In this article, we use the term *sleeping sickness* for the human infection, whereas the infection in animals, sometimes called *nagana* in cattle, will be called *animal trypanosomiasis*.

Sleeping sickness is influenced by the ecology of the parasite and its tsetse fly vectors, including the differential interactions of multiple vector species with multiple host and parasite species. The epidemic nature of the disease means that small changes in the factors influencing transmission can trigger an epidemic (Platt, 1996). These triggers include shifts in land use and agricultural activities, population movements, animal movements, and bush growth or elimination. Moreover, such changes are often driven by social upheaval (Platt, 1996), including war and movements of refugees and their livestock, cattle raiding, and economic and agricultural policy changes in the region.

Scope and Scale of Sleeping Sickness Research

The forces that influence sleeping sickness operate on different spatial and temporal scales (Rogers, 2000). Research on sleeping sickness has occurred on a variety of scales and in a range of disciplines, including ecology, geography, history, veterinary epidemiology, parasitology, medicine, and public health. Each research discipline tends to focus on processes that occur at particular spatial and temporal scales (Fig. 2). Research on the scale of the African continent, for example, may use satellite imagery to understand climate and land uses that represent preferred vector habitat (Rogers, 2000; Rogers and Randolph, 2003). Land cover as a determinant of sleeping sickness has been investigated at the more local district level (Odiit, 2003). Prediction of the effects of climatic changes on vector habitat at the continental scale (McDermott et al., 2001) is important for the understanding of long-term secular trends. It also contributes to the understanding of changes in vector distribution observed at the local and regional levels.

In another example of the importance of scale, genetic research conducted on the microscopic scale allows for the identification of trypanosome species, strains, genotypes, and isolated clusters (Hide et al., 1996; Hide, 1999). This research has contributed to the understanding of sleeping sickness patterns at the regional and national scales, revealed new information on which trypanosome species may have caused the 1900–1920 Ugandan outbreak (Hide et al., 1996; Welburn et al., 2001), and highlighted the role of cattle movements in parasite spread (Fèvre, 2001; Fèvre et al., 2001). Research, by necessity, focuses on a particular temporal and spatial scale. As the previous example of genetic research indicates, however, research findings from one discipline often have implications for research in other

Figure 1. A: Map of Africa and Uganda**. B:** Map of Uganda and southeastern Uganda.

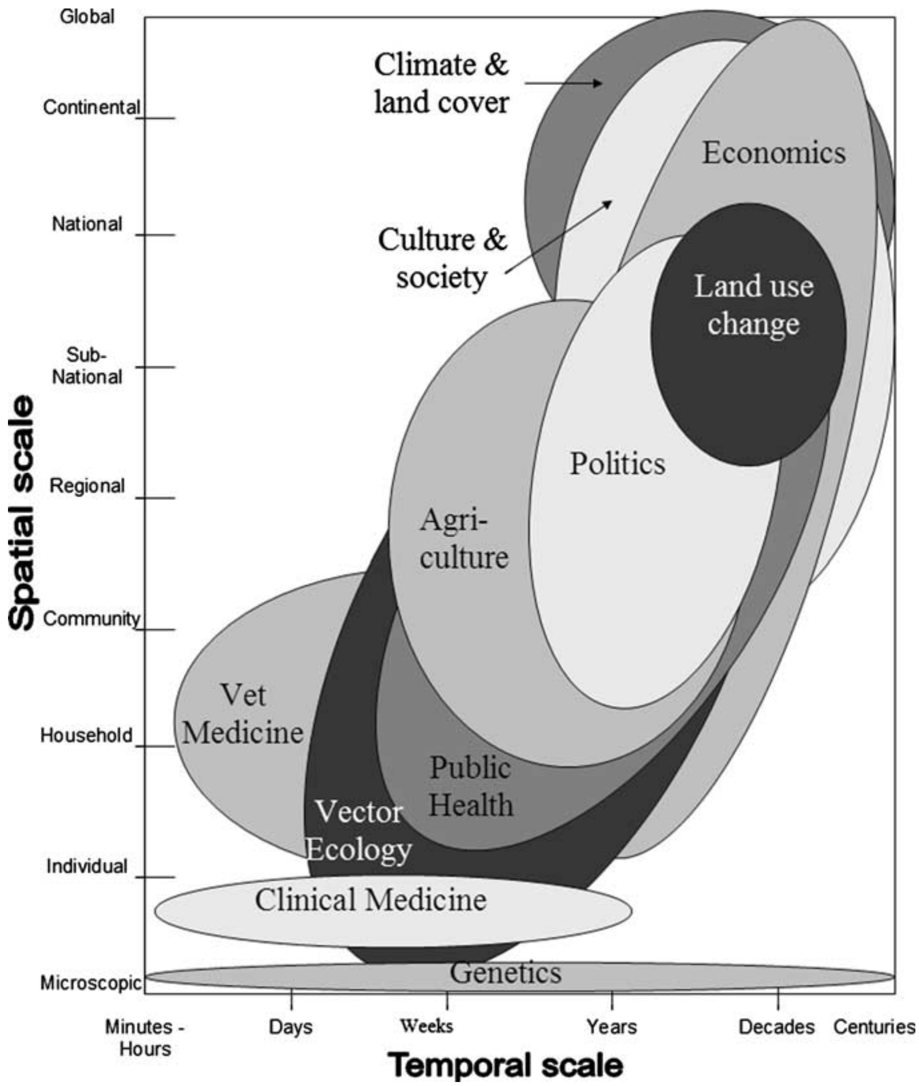

Figure 2. Spatial and temporal scales for sleeping sickness research in Uganda. Adapted from Gibson et al. (2000, p 227).

disciplines at different scales. The following discussion draws from several disciplines on research conducted at different scales (Fig. 2) as a basis for our characterization of sleeping sickness dynamics and interactions.

System Descriptions of Sleeping Sickness in Southeastern Uganda

Four system categories are used to structure our review of sleeping sickness: the parasite life-cycle system, the biophysical system, the livestock livelihood system, and the sociopolitical system. Interactions among these systems are discussed at the end of the section.

Sleeping Sickness Parasite Life-Cycle System

The life cycle of trypanosomiasis includes the parasite, the tsetse fly vector, and the human, wildlife, and livestock hosts of human-infectious trypanosome parasites. Not all trypanosome parasites are infectious to humans. Only *Trypanosoma brucei* causes sleeping sickness (Leak, 1999). Two other parasites in southeastern Uganda, *Trypanosoma congolense* and *Trypanosoma vivax*, cause infection in animals, but not in humans. Humans become infected by *T. brucei* when bitten by an infected tsetse fly; this leads to subsequent sleeping sickness symptoms. Wild animals and livestock acquire parasite infection in the same way and can act as a reservoir for human infection where tsetse are transmitting the parasites from animals to humans. The likelihood that a case of sleeping sickness generates additional or secondary cases of disease (the transmission potential) is relatively low. This inherently low transmission potential is influenced by the infectivity of *T. brucei* spp., which is lower than that of other major tsetse-transmitted trypanosomes. Transmission is favored by a large ratio of flies to humans, a relatively high prevalence of infection in flies and humans, and a high level of contact between flies and hosts (Rogers, 1988; Rogers and Williams, 1993; Hide, 1999). This low transmission potential is responsible for the typical pattern of sleeping sickness in Uganda: generally very low levels of sleeping sickness interrupted by distinct epidemics. These epidemics arise from variations in the determinants of transmission, such as ecological or social upheaval (World Health Organization, 2001). The low transmission potential of the disease has meant that control targeted at interrupting the transmission of the parasite can be very effective in reducing sleeping sickness incidence.

The sleeping sickness transmission cycle is a function of the parasite species, the vector species, and their host preferences. Each parasite is differentially able to infect and be transmitted by the three tsetse species present in southeastern Uganda: these include *Glossina pallidipes, G. fuscipes fuscipes*, and *G. brevipalpis* (Gashumba and Mwambu, 1981; Matovu, 1982). *Glossina fuscipes fuscipes*, for example, is considered the key vector for human infection by the parasite *T. brucei* in southeastern Uganda (Hide, 1999), whereas the tsetse vector, *G. pallidipes*, may also play a role in sleeping sickness transmission in some regions (Matovu, 1982; Okiria, 1985). In southeastern Uganda, *T. brucei* is generally not associated with high rates of cattle mortality, thus resulting in a larger reservoir of infected cattle (Olila et al., 2002). The extent to which low-level but persistent infections in cattle increase or decrease the potential for human infection is the subject of current studies (Coleman and Welburn, 2004). Issues of parasite detection and prevalence are further complicated by evidence of differing results due to diagnostic methods, which may significantly underdetect trypanosome prevalence (Picozzi et al., 2002).

Biophysical System

Climate and vector habitat are key components of the biophysical aspect of the sleeping sickness system. Each tsetse vector uses a particular habitat. The main vector of recent sleeping sickness in southeastern Uganda, *G. f. fuscipes* (Abaru, 1985; Okiria, 1985), is generally a riverine species found near rivers or lakes in riparian forests (Leak, 1999). Both *G. f. fuscipes* and *G. pallidipes* are vectors of cattle trypanosomiasis; the latter is generally associated with savannah ecology, as well as the distribution of available wildlife, cattle, and human hosts (Allsopp et al., 1972; Leak, 1999). Vegetation and land cover near riverine, lacustrine, and savannah zones affect the distribution of the sleeping sickness vector. For example, increased vegetation growth around homesteads and the resulting movement of tsetse flies into peridomestic environments (Okoth, 1986) likely contributed to the sleeping sickness outbreaks in Kenya in 1965 and Uganda in the 1970s and 1980s (Mbulamberi, 1989b).

Land cover, land use, and associated vector habitat are affected by human population densities. In an assessment of the effect of human population growth on tsetse vector habitat, Reid et al. (2000) and McDermott et al. (2001) suggested that population growth in the coming decades is unlikely to significantly change the range of the riverine tsetse, whereas the savannah and forest flies are expected to experience decreases in habitat. In southeastern Uganda, therefore, sleeping sickness may be relatively unaffected by population growth, whereas the economically important cattle disease may decrease in nonriverine savannah habitats. Research by Odiit (2003) on sleeping sickness cases in southeastern Uganda found that there was an association between cases and areas of low population density; despite the predicted trend of increased transmission with higher population density, areas of lower population density may still experience high rates of disease because of greater human–fly contact. This association may arise from the absence of flies in high-density urban areas (Reid et al., 2000) or increased human–fly contact caused by population growth in low-density areas.

Reduced livestock illness improves livelihoods and ability to control, prevent, and combat sleeping sickness. Reduced levels of infection in livestock may also allow for expanded livestock development, thus paradoxically increasing the potential for livestock infection and greater transmission to humans by riverine tsetse. The interactions and varying scenarios associated with land use change indicate the importance of vector habitat in the sleeping sickness system.

Climate variability and change provide an example of the influence of factors that vary across wider spatial and temporal scales. As noted by Rogers (1991), climate is a dominant factor that controls the continental pattern of tsetse distributions. The importance of climate change in relation to tsetse habitat has come under increasing scrutiny (Rogers and Packer, 1993; Robinson et al., 1997; McDermott et al., 2001; Rogers and Randolph, 2003). Although it plays a large role at the global level, climate variability and change also contribute to the manifestation of local-scale processes and background variability in sleeping sickness. For example, local populations of *G. f. fuscipes* in Uganda represent the eastern fringe of the continental distribution of the riverine vector (Ford and Katondo, 1977; Leak, 1999). Climatic changes resulting in a small shift westward in the continental distribution of the riverine fly zone could theoretically eliminate *G. f. fuscipes* from southeastern Uganda. The likelihood of such a change, however, remains unclear.

Livestock Livelihood System

Livestock—cattle in particular—underlie much economic and social activity in poor rural communities in Uganda. Given the importance of cattle as a reservoir of sleeping sickness, the livestock livelihood system plays an integral role in shaping the risk and transmission of the disease. Recent research by Fèvre et al. (2001) in the Soroti District of eastern Uganda suggests that cattle markets act as a major focus for the transmission of trypanosomiasis, thus disseminating the disease through cattle reservoirs to many groups of people. In this case, re-stocking of cattle in Soroti from infected areas is argued to have resulted in the spread of sleeping sickness to a previously unaffected district. Livestock movements were also a factor in the 1976–1989 outbreak in Uganda, when parasite spread was facilitated by political instability and the uncontrolled movement of people and livestock across the Kenyan border (Mbulamberi, 1989b). At the wider regional scale, cattle movements due to raiding and forced migration create the potential for transmission of either tsetse vectors or parasite species into new areas.

Sociopolitical System

Within Uganda, the history of conflict and political instability has had a dramatic effect on agriculture, economics, ethnic relations, language, power struggles, and livelihoods. British colonial rule at the start of the 1900s coincided with severe outbreaks of sleeping sickness (Lyons, 1991; Worboys, 1994). Social and political conditions under the colonial government were characterized by disruption of settlement and agricultural patterns, forced labor, and warfare—factors that may have contributed to the severity and extent of the outbreaks (Ford, 1971, 1979; Jordan, 1986; Musere, 1990; Worboys, 1994). Sleeping sickness outbreaks in the 1970s and 1980s in Uganda also followed a period of civil instability and conflict. Political instability under Idi Amin in the 1970s led to economic decline, social upheaval, collapse of public services, and dramatic shifts in social and ecological systems; these factors are believed to have played a key role in the increase in sleeping sickness incidence after Amin's rule (Matovu, 1982; Okiria, 1985; Mbulamberi, 1989a, b). Increased movements of human and animal hosts, for example, increased the potential for vectors or parasites to be carried to new areas. Disruption of public and health services, social infrastructure, and coping capacities inhibited prevention and control measures. Social processes play a significant role in driving sleeping sickness risk in Uganda; such processes may provide the triggers necessary to push transmission of disease above epidemic thresholds and into new areas.

Finally, diseases other than trypanosomiasis influence sleeping sickness in southeastern Uganda. Outbreaks of rinderpest at the turn of the 20th century resulted in catastrophic losses of cattle and reduction of tsetse populations (Ford, 1971). After this, it is believed that tsetse populations became reestablished because of lusher vegetation free from grazing cattle (Ford, 1971; Jahnke, 1976) or re-stocking with infected cattle (Fèvre et al., 2004). The social structure was particularly vulnerable because of livestock losses and famine (Ford, 1971, 1980; Musere, 1990), thus creating the conditions for significant outbreaks of trypanosomiasis in the early 1900s. Fèvre et al. (2004) suggest that parasite spread during the rebuilding of cattle stocks after the rinderpest outbreaks may have provoked the 1900–1920 sleeping sickness outbreaks.

The emergence of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome in recent years and related changes in the epidemiology of tuberculosis have taxed Ugandan health services and caused social and economic upheaval because of high acquired immunodeficiency syndrome and tuberculosis mortality in young adults. Although Uganda's rapid response to HIV has been relatively successful, the prevalence of HIV remains high (see Pisani [2002] for an excellent discussion of HIV in Uganda). As noted by Mbulamberi [personal communication, 2004], funding for sleeping sickness surveillance and control in Uganda has been significantly limited by the demands of controlling malaria, HIV, and tuberculosis.

System Interactions

Although the four systems described previously are helpful in structuring a review of the factors that affect sleeping sickness, they are subjective categorizations. The parasite life-cycle, biophysical, livestock livelihood, and sociopolitical systems are interconnected through the interactions of humans with the shared habitat of wildlife hosts, livestock hosts, and tsetse vectors. A change in livelihood changes the rate at which humans are bitten by tsetse vectors. Fishing and exploitation of forest resources result in higher vector–host contact than cropping, for example (Leak, 1999). Exposure to the parasite changed in the 1970s, when abandoned cropping resulted in increased forest resource extraction, such as charcoal and firewood collection [Mbulamberi, personal communication, 2004]. Within these interactions are also feedback mechanisms. For example, increased prevalence of disease drains limited health resources and worsens poor livelihoods, thus further increasing vulnerability to disease.

Sleeping sickness in southeastern Uganda is driven by processes that affect the transmission potential of the trypanosome parasite. This transmission is affected by the presence of appropriate parasite and tsetse species; these are influenced by climate and land use, which affect tsetse habitat (Ford, 1969; Rogers, 1991). Movements of people and cattle carry the parasite or vector to new regions and populations. Civil conflict can cause changes to tsetse habitat, population movements, cattle movements, and prevention and control programs, thus triggering an outbreak (Mbulamberi, 1989b). Societies and communities burdened by poverty, civil unrest, and poor health are more vulnerable to disease (Platt, 1996); disease outbreaks may be more likely to occur, spread more rapidly, and result in more damaging effects. For example, general ill health and poor nutrition in the presence of parasites and vectors increase community vulnerability to disease while reducing the community's capacity to respond. In the case of sleeping sickness, detection and early treatment of cases is central to reducing illness and death (Odiit, 2003). Both detection and treatment are inherently linked to the availability of sleeping sickness treatment centers, the quality and quantity of detection and treatment supplies, and the capacity of Uganda's health-care infrastructure (Matovu, 1982; Abaru, 1985; Okiria, 1985; Odiit, 2003). Transmission of sleeping sickness is strongly influenced by vector control (Yu et al., 1995; Odiit, 2003) and the prevalence of infection in cattle (Waiswa et al., 2003). Veterinary, public health, and vector-control activities, for example, collapsed during the Idi Amin period, and this eliminated organized control of trypanosomiasis (Mbulamberi, 1989b). The economic and political changes of this period, as discussed previously, promoted changes that increased vulnerability to disease outbreak and reduced the capacity of the health system to respond to disease.

The four systems—the parasite life-cycle system, the biophysical system, the livestock livelihood system, and the sociopolitical system—provide a summary of the range of processes, scales, and interactions among factors that influence spatial and temporal variation in sleeping sickness in southeastern Uganda. Figure 3 is a graphic summary of the conceptualization and characterization of sleeping sickness dynamics developed in the preceding sections. This systems graphic synthesizes the components, processes, and interactions that influence the spatial and temporal dynamics of sleeping sickness in southeastern Uganda.

Approaches to Modeling Sleeping Sickness in Southeastern Uganda

Descriptions of interlinked systems are useful in identifying important interactions between factors that affect sleeping sickness on various scales (Fig. 3). The components, processes, interactions, and scales shown in Figure 3 are variously considered by different approaches to analytical modeling of sleeping sickness. Common analytical approaches to vectorborne disease modeling in sleeping sickness research include statistical epidemiological regression, mathematical transmission models, and spatial prediction models.

Statistical modeling focuses on associations between the disease and a number of variables. In Uganda, for example, regression analysis was used to assess the effect on sleeping sickness incidence of human population density and proximity to several land cover classes in two southeastern districts (Odiit, 2003). Regression modeling, however, has a limited capacity to address the complex multiscale interactions identified in Fig. 3 (Rose, 1985; Schwartz et al., 1999); this type of modeling also deals poorly with infectious disease data, which often violate assumptions of independence (Koopman and Longini, 1994). Statistical modeling of spatial and temporal dependence has evolved in conjunction with developments in Geographic Information Systems (GIS) (Odiit, 2003).

Mathematical transmission models focus on quantitative estimation of infection parameters and host and vector population sizes. Modeling of trypanosomiasis transmission is based on tsetse biting rates, proportion of tsetse infected, proportion of tsetse bites resulting in a host infection, mortality rates, recovery rates, and the ratio of vectors to hosts (Rogers, 1988). Incorporation of sociopolitical determinants of risk factors (Fig. 3) is poorly developed in mathematical transmission modeling of sleeping sickness. This is largely due to the challenges of quantifying relevant variables (McDermott and Coleman, 2001).

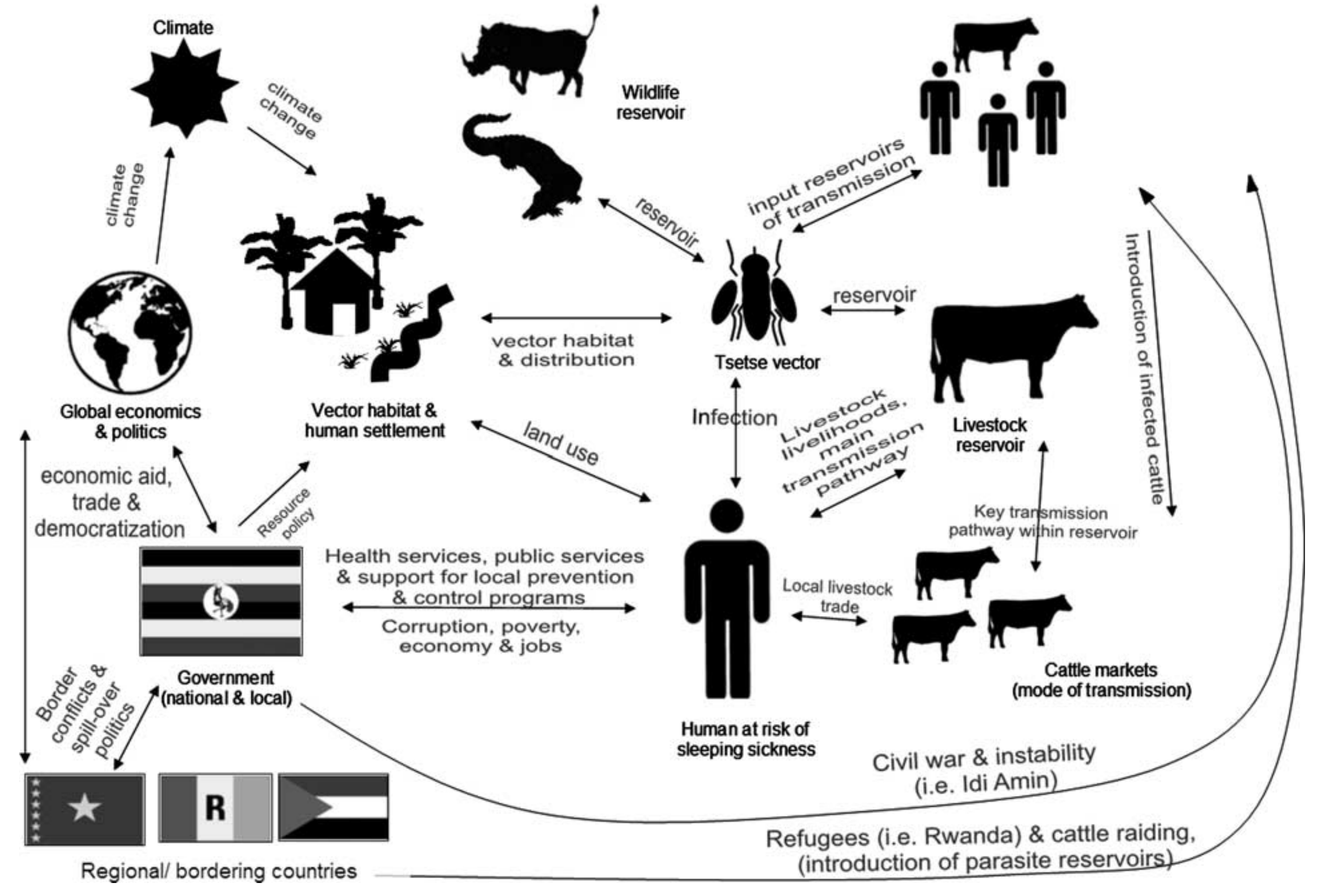

Figure 3. Rich picture of sleeping sickness in Uganda. The diagram is centered around an individual in southeastern Uganda at risk of sleeping sickness. Dominant system elements can be identified: the sleeping sickness parasite life-cycle system, the biophysical system, the livestock livelihood system, and the sociopolitical system. These four subjective categorizations are useful in grouping system processes and facilitating system descriptions.

McDermott and Coleman (2001) have extended the scope of these base models to simulate scenarios of trypanosomiasis control strategies in cattle.

More recently, developments in GIS and remote sensing have allowed for advanced spatial analyses of the determinants of vectorborne diseases (Hay et al., 2000; Rogers and Randolph, 2003). These have predominantly been at the continental or national level. Spatial models of the spread of trypanosomiasis have been used to predict the effect of human population growth on tsetse populations in Africa (Reid et al., 2000; McDermott et al., 2001). Integrated GIS have been developed to examine spatial relationships between trypanosomiasis, tsetse distribution, and land use in Togo and the Sinfra region of Côte d'Ivoire (Hendrickx et al., 2000; Lointier et al., 2001); similar databases are currently being developed for Uganda (Farming in Tsetse Conrolled Areas Project, 2004). There are spatial analyses of sleeping sickness risk at the local level for eastern Uganda (Fèvre et al., 2001; Odiit et al., 2004a). Diseases such as sleeping sickness that depend a great deal on geographic factors are particularly suited to spatial analyses such as those used in Côte d'Ivoire and elsewhere.

Models of trypanosomiasis tend to ignore sociopolitical determinants of disease. This is largely due to the difficulty of quantifying social or political factors. Our systems descriptions identified social conflict as a determinant of sleeping sickness risk because of its influences on land cover, human–fly contact rates, cattle infection rates, and prevention and control activities. Analyses of sociopolitical determinants of sleeping sickness have been largely qualitative (Musere, 1990; Lyons, 1991). Recent research in Uganda integrates quantitative and qualitative analyses to assess the significance of sociopolitical determinants of sleeping sickness. Odiit et al. (2004b) examined diagnosis and treatment delays for sleeping sickness patients in eastern Uganda between 2000 and 2002. Fèvre and associates used analysis of historical archives and retrospective data to provide context for the 1900–1920 Ugandan epidemic (Fèvre et al., 2004) and the 1998 outbreak in the Soroti District (Fèvre et al., 2001); they provide an excellent discussion of the social and environmental processes that have contributed to cattle movements and parasite spread during these events. Molecular identification of parasite genotypes in eastern Uganda is consistent with Fèvre and colleagues' findings (Hay et al., 1997; Welburn and Odiit, 2002).

Understanding of sleeping sickness risk will benefit from increased integration of spatial, statistical, mathematical, and scenario-based approaches to the assessment of sleeping sickness determinants. Mathematical transmission models such as that developed by Rogers (Rogers, 1998), for example, can be incorporated into a GIS to allow for spatial variation of population variables and infection parameters. These analyses can be integrated with scenario-based approaches, such as those used by Reid et al. (2000), McDermott et al. (2001), and McDermott and Coleman (2001). There has been recent integration of spatial analyses with statistical modeling to study sleeping sickness in Uganda (Fèvre et al., 2001; Odiit et al., 2004a). These local and regional analyses complement continued spatial research at the continental scale (Hay et al., 2000; Rogers, 2000).

Spatial and multiscale analyses are constrained by data availability. A basic transmission model of sleeping sickness in Uganda, for example, requires data for variables such as cattle populations, human populations, vector distributions, the proportion of cattle infected with human-infectious parasites, and human–fly ratios. An exploration of these factors across different regions and over time requires data from many points in time from multiple locations. Satellite imagery for multiple dates and locations is available and provides useful climatic and land cover data. These can be used as surrogates of tsetse habitat at the continental (Rogers, 1991, 1995) and district (Odiit, 2003) levels for multiple time periods and different locations. Information on the distribution and occurrence of historical sleeping sickness is limited, as are data on tsetse distributions in Uganda. The availability of these data is limited by the occurrence of civil war during southeastern Uganda's most recent epidemic and the current lack of resources for data collection and maintenance.

We have reviewed several modeling approaches to sleeping sickness research relative to our systems characterization of sleeping sickness dynamics (Fig. 3). From this comparison, we identified two areas of research opportunity related to sleeping sickness in Uganda: focus on sociopolitical determinants and comparison of analyses on multiple temporal and spatial scales.

The sociopolitical determinants of sleeping sickness have not yet been adequately explored. We suggest that a retrospective analysis of 1976–1989 historical Ugandan outbreak data with explicit consideration of sociopolitical determinants would complement both research performed on a finer spatial scale in Soroti (Fèvre et al., 2001) and retrospective research focusing on the 1900–1920 period (Fèvre et al., 2004). A review of case studies associating sleeping sickness outbreaks with social conflict across the continent would provide a useful macroanalysis of the sociopolitical conditions under which outbreaks of disease might be expected. A parallel opportunity for modeling sociopolitical determinants of sleeping sickness is the use of scenario-driven approaches. This would focus on simulating the effect of changes in social factors on disease transmission.

There has been an increase in the use of spatial and temporal tools in sleeping sickness research. Determinants of disease distributions on a particular scale, however, are not necessarily determinants of disease on other scales. Land cover, for example, is an important determinant of the continental distribution of trypanosomiasis (in both humans and animals; Ford, 1969; Jordan, 1979; Reid et al., 2000). An association between land use/cover change and sleeping sickness was also found on a more local spatial scale in two districts in eastern Uganda (Odiit, 2003) for the 1976–1989 outbreak. Between the continental and local scales, however, regional sleeping sickness distributions may be more strongly influenced by the spread of the parasite by infected hosts (Fèvre et al., 2001) than by land cover variation. Risk projection would benefit from investigation into whether land cover drives regional patterns of sleeping sickness between outbreaks and between districts. The effect of human population growth and tsetse habitat can be simulated for Uganda. Models used for global simulation can be replicated by using Uganda-specific data and variables. Comparison of these types of case-study application would indicate to what extent sleeping sickness foci will respond differently to population growth. Replication of analyses on multiple scales indicates which levels of application are appropriate for prediction and control initiatives.

Conclusions

This article has drawn on a systems approach to characterize the multiple components and processes that influence sleeping sickness in Uganda. System components and processes, including the biophysical system, life-cycle system, livestock livelihood system, and sociopolitical system, interact between and within a range of temporal and spatial scales. Statistical modeling and mathematical transmission modeling have been used in conjunction with scenario-based approaches, GIS, and historical accounts to analyze and understand the dynamics of sleeping sickness and its determinants. Our synthesis of sleeping sickness dynamics and the approaches used to examine them highlight opportunities for research. The understanding of sleeping sickness in Uganda will benefit from increased focus on the sociopolitical determinants of disease and comparison of analyses at multiple spatial and temporal scales.

Acknowledgments

This work was performed with the aid of a grant from the International Development Research Centre (IDRC), Ottawa, Canada. Information on the Centre is available on the Worldwide Web at http://www.idrc.ca. Research was also supported by funding from the National Science and Engineering Research Council of Canada and the IDRC in Project 100106: "Links between Sleeping Sickness and Natural Resources Endowments and Use: What Can Communities Do?" Special thanks go to Dr. Mbulamberi, Ministry of Health, Uganda; Dr. Maiso, World Health Organization, Kampala; the late Dr. Thomas Gitau; and James Ford.

References

Abaru DE (1985) Sleeping sickness in Busoga, Uganda, 1976-1983. *Tropical Medicine and Parasitology* 36:72–76

Allsopp R, Baldry DAT, Rodrigues C (1972) The influence of game animals on the distribution and feeding habits of *Glossina pallidipes* in the Lambwe Valley. *Bulletin of the World Health Organization* 47:795–809

Bourn D, Reid RS, Snow B, Wint W (2001) *Environmental Change and the Autonomous Control of Tsetse and Trypanosomosis in Sub-Saharan Africa,* Oxford: Environmental Research Group Oxford (ERGO) Ltd

Coleman PG, Welburn SC (2004) Are fitness costs associated with resistance to human serum in *Trypanosoma brucei rhodesiense*? *Trends in Parasitology* 20:311–315

Farming in Tsetse Conrolled Areas Project (2004) Farming in Tsetse Conrolled Areas Project. Available: http://www.deluga.cec.eu.int/en/newsletter/june04/farming.htm [accessed January 15, 2005]

Fèvre EM (2001) More thoughts on the control of trypanosomes in cattle. *Trends in Parasitology* 17:412–413

Fèvre EM, Coleman PG, Odiit M, Magona JW, Welburn SC, Woolhouse MEJ (2001) The origins of a new *Trypanosoma brucei rhodesiense* sleeping sickness outbreak in eastern Uganda. *Lancet* 358:625–628

Fèvre EM, Coleman PG, Welburn SC, Maudlin I (2004) Reanalyzing the 1900-1920 sleeping sickness epidemic in Uganda. *Emerging Infectious Diseases* 10:567–573

Ford J (1969) Control of the African trypanosomiases with special reference to land use. *Bulletin of the World Health Organization* 40:879–892

Ford J (1971) *The Role of the Trypanosomiases in African Ecology,* Oxford: Clarendon Press

Ford J (1979) Ideas which have influenced attempts to solve the problems of African trypanosomiasis. *Social Science and Medicine* 13B:269–275

Ford J (1980) Early ideas about sleeping sickness and their influence on research and control. In: *Health in Tropical Africa during the Colonial Period, Based on the Proceedings of a Symposium Held at New College, Oxford, 21-23 March 1977*, Sabben-Clare EE, Bradley DJ, Kirkwood K (editors), Oxford: Clarendon Press, pp 30–34

Ford J, Katondo KM (1977) Maps of tsetse fly (*Glossina*) distribution in Africa 1973, according to sub-generic groups on scale of 1:5,000,000. *Bulletin of Animal Health and Production in Africa* 15:188–194

Gashumba JK, Mwambu PM (1981) Sleeping sickness epidemic in Busoga, Uganda. *Tropical Doctor* 11:175–178

Gibson CC, Ostrom E, Ahn TK (2000) The concept of scale and the human dimensions of global change: a survey. *Ecological Economics* 32:217–239

Hay SI, Packer MJ, Rogers DJ (1997) A review of the impact of remote sensing on the study and control of vector-borne disease. *International Journal of Remote Sensing* 18:2899–2930

Hay SI, Randolph SE, Rogers DJ (editors) (2000) Remote Sensing and Geographical Information Systems in Epidemiology. *Advances in Parasitology, Volume 47*, New York: Academic Press

Hendrickx G, Napala A, Slingenbergh JH, DeDeken R, Vercruysse J, Rogers DJ (2000) The spatial pattern of trypanosomiasis prevalence predicted with the aid of satellite imagery. *Parasitology* 120:121–134

Hendy CRC, Makin MJ (1988) Land and development planning associated with trypanosomiasis control. *International Scientific Council for Trypanosomiasis Research and Control (ISCTRC)* 114:425–433

Hide G (1999) History of sleeping sickness in East Africa. *Clinical Microbiology Reviews* 12:112–125

Hide G, Tait A, Maudlin I, Welburn SC (1996) The origins, dynamics and generation of *Trypanosoma brucei rhodesiense* epidemics in East Africa. *Parasitology Today* 12:50–55

Hursey BS, Slingenbergh J (1995) The tsetse fly and its effects on agriculture in sub-Saharan Africa. *World Animal Review* 84/85:67–73

Jahnke HE (1976) *Tsetse Flies and Livestock Development in East Africa: A Study in Environmental Economies,* Munich: Weltforum Verlag

Jordan AM (1979) Trypanosomiasis control and land use in Africa. *Outlook on Agriculture* 10:123–129

Jordan AM (1986) *Trypanosomiasis Control and African Rural Development,* London: Longman

Koerner T, de Raadt P, Maudlin I (1995) The Uganda sleeping sickness epidemic revisited: a case of mistaken identity? *Parasitology Today* 11:303–306

Koopman JS, Longini IM (1994) The ecological effects of individual exposures and nonlinear disease dynamics in populations. *American Journal of Public Health* 84:836–842

Leak SGA (1999) *Tsetse Biology and Ecology: Their Role in the Epidemiology and Control of Trypanosomosis*, Wallingford, UK: CABI Publishing (in association with the International Livestock Research Institute, Nairobi, Kenya)

Lointier M, Truc P, Drapeau L, Nanga S, Tarek M (2001) Méthodologie de détermination de zones à risque de maladie du sommeil en Côte d'Ivoire par approche spatialisée [Methodology to determine risk zones for sleeping sickness in Cote d'Ivoire by the spatial approach]. *Medecine Tropicale* 61:390–396

Lyons M (1991) African sleeping sickness: an historical review. *International Journal of STD and AIDS* 2(Suppl 1):20–25

MacKichan IW (1944) Rhodesian sleeping sickness in Eastern Uganda. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 38:49–60

Matovu FS (1982) Rhodesian sleeping sickness in south-eastern Uganda (the present problems). *East African Medical Journal* 59:390–393

Mbulamberi DB (1989a) A review of human African trypanosomiasis (HAT) in Uganda. *East African Medical Journal* 66:743–747

Mbulamberi DB (1989b) Possible causes leading to an epidemic outbreak of sleeping sickness: facts and hypotheses. *Annales de la Société Belge de Médecine Tropicale* 69(Supp 1):173–179

Mbulamberi DB (1994) Recent advances in the diagnosis and treatment of sleeping sickness. *Postgraduate Doctor (Africa)* 16:16–19

McDermott JJ, Coleman PG (2001) Comparing apples and oranges—model-based assessment of different tsetse-transmitted trypanosomosis control strategies. *International Journal for Parasitology* 31:603–609

McDermott JJ, Kristjanson PM, Kruska RL, Reid RS, Robinson TP, Coleman PG, et al. (2001) Effects of climate, human population and socio-economic changes on tsetse-transmitted trypanosomiasis to 2050. In: *World Class Parasites, Vol 1: The African Trypanosomes*, Seed R, Black S (editors), Boston: Kluwer Academic, pp 25–38

Mills A, Pender J (1996) Environmental impact assessment of tsetse control historical quantification of land cover and land use. In: *Remote Sensing and GIS for Natural Resource Management (conference proceedings)*, Power CH, Rosenberg LJ, Downey (editors), Chatham, UK: Natural Resources Institute, pp 72–86

Musere J (1990) *African Sleeping Sickness: Political Ecology, Colonialism and Control in Uganda,* New York: Edwin Mellen

Odiit M (2003) *Epidemiology of* Trypanosoma brucei rhodesiense *Sleeping Sickness in Eastern Uganda* (PhD thesis), Edinburgh: University of Edinburgh

Odiit M, Coleman PG, McDermott JJ, Fevre EM, Welburn SC, Woolhouse MEJ (2004a) Spatial and temporal risk factors for the early detection of *Trypanosoma brucei rhodesiense* sleeping sickness patients in Tororo and Busia districts, Uganda. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 98:569–576

Odiit M, Shaw A, Welburn SC, Fevre EM, Coleman PG, McDermott JJ (2004b) Assessing the patterns of health-seeking behaviour and awareness among sleeping-sickness patients in eastern Uganda. *Annals of Tropical Medicine and Parasitology* 98:339–348

Okiria R (1985) The prevalence of human trypanosomiasis in Uganda, 1970 to 1983. *East African Medical Journal* 62:813–816

Okoth JO (1986) Peri-domestic breeding sites of *Glossina fuscipes fuscipes* Newst. in Busoga, Uganda and epidemiological implications for trypanosomiasis. *Acta Tropica* 43:283–286

Olila D, McDermott JJ, Eisler MC, Mitema ES, Patzelt RJ, Clausen P-H, et al. (2002) Drug sensitivity of trypanosome populations from cattle in a peri-urban dairy production system in Uganda. *Acta Tropica* 84:19–30

Picozzi K, Tilley A, Fèvre EM, Coleman PG, Magona JW, Odiit M, et al. (2002) The diagnosis of trypanosome infections: applications of novel technology for reducing disease risk. *African Journal of Biotechnology* 1:39–45

Pisani E (2002) Chapter 7: Kenya and Uganda. In: *HIV and AIDS: A Global View*, McElrath K (editor), Westport, CT: Greenwood Press, pp 115–136

Platt AE (1996) *Infecting Ourselves: How Environmental and Social Disruptions Trigger Disease,* Washington, DC: Worldwatch Institute

Reid RS, Wilson CJ, Kruska RL, Mulatu WA (1997) Impacts of tsetse control and land-use on vegetative structure and tree species composition in south-western Ethiopia. *Journal of Applied Ecology* 34:731–747

Reid RS, Kruska RL, Deichmann U, Thornton PK, Leak SGA (2000) Human population growth and the extinction of the tsetse fly. *Agriculture, Ecosystems, and Environment* 77:227–236

Robinson TP, Rogers DJ, Williams B (1997) Mapping tsetse habitat suitability in the common fly belt of Southern Africa using multivariate analysis of climate and remotely sensed vegetation data. *Medical and Veterinary Entomology* 11:235–245

Rogers DJ (1988) A general model for the African trypanosomiases. *Parasitology* 97:193–212

Rogers DJ (1991) Satellite imagery, tsetse and trypanosomiasis in Africa. *Preventive Veterinary Medicine* 11:201–220

Rogers DJ (1995) Remote sensing and the changing distribution of tsetse flies in Africa. In: *Insects in a Changing Environment (17th Symposium of the Royal Entomological Society, Harpenden, UK, 7-10 September 1993)*, Harrington R, Stork NE (editors), London: Academic Press, pp 177–193

Rogers DJ (2000) Satellites, space, time, and the African trypanosomiases. In: *Advances in Parasitology, Vol 47, Special Edition: Remote Sensing and Geographical Information Systems in Epidemiology*, Hay SI, Randolph SE, Rogers DJ (editors), Baker JR, Muller R, Rollinson D (series editors), San Diego: Academic Press, pp 129–171

Rogers DJ, Packer MJ (1993) Vector-borne diseases, models and global change. *Lancet* 342:1282–1284

Rogers DJ, Randolph SE (2003) Studying the global distribution of infectious diseases using GIS and RS. *Nature Reviews Microbiology* 1:231–236

Rogers DJ, Williams BG (1993) Monitoring trypanosomiasis in space and time. *Parasitology* 106(Suppl):S77–S92

Rose G (1985) Sick individuals and sick populations. *International Journal of Epidemiology* 14:32–38

Schwartz S, Susser E, Susser M (1999) A future for epidemiology? *Annual Review of Public Health* 20:15–33

Waiswa C, Olaho-Mukani W, Katunguka-Rwankishaya E (2003) Domestic animals as reservoirs for sleeping sickness in three endemic foci in south-eastern Uganda. *Annals of Tropical Medicine and Parasitology* 97:149–155

Welburn SC, Odiit M (2002) Recent developments in human African trypanosomiasis. *Current Opinion in Infectious Diseases* 15:477–484

Welburn SC, Fèvre EM, Coleman PG, Odiit M, Maudlin I (2001) Sleeping sickness: a tale of two diseases. *Trends in Parasitology* 17:19–24

Worboys M (1994) The comparative history of sleeping sickness in East and Central Africa, 1900-1914. *History of Science* 32:89–102

World Health Organization (2001) *Report on African Trypanosomiasis (Sleeping Sickness), Report of the Scientific Working Group Meeting on African Trypanosomiasis, Geneva: Special Programme for Research and Training in Tropical Diseases; 4-8 June 2001. Report No. TDR/SWG/01*. Available: http://whqlibdoc.who.int/hq/2003/TDR_SWG_01.pdf [accessed December 21, 2004]

Yu P, Habtemariam T, Oryang D, Obasa M, Nganwa D, Robnett V (1995) Integration of temporal and spatial models for examining the epidemiology of African trypanosomiasis. *Preventive Veterinary Medicine* 24:83–95