Reviewer's report

Title: Analysis of risk factors for T. brucei rhodesiense sleeping sickness within villages in SE-Uganda

Version: 2 Date: 17 October 2007

Reviewer: Vincent Jamonneau

Reviewer's report:

General comments

This manuscript by Zoller et al. deals with spatial and behavioral risk factors in Human African Trypanosomosis at the within-village scale, a topic that has yet been poorly investigated for the T. b. rhodesiense acute form of the disease. Such work is necessary to better understand the distribution of HAT cases in endemic area and thus propose new control measures. For these reasons, data presented in this paper will be of valuable interest to the community working in HAT epidemiology.

1. However the paper suffers from methodological problems, mainly concerning the multivariate analysis of behavioral and socio-demographic risk factors. To my point of view the main risk factor evidenced by the study (familial aggregation of HAT) is also poorly discussed in the view of the data presented. Authors should develop this point more in detail since it is the major finding of this study.

2. The manuscript does not provide any data, any figure and any information on the vector nor on the cattle distribution while considered as “the main determinant of transmission (Background section)”.

3. There seems to be no clear link between the study on the behavioral and the spatial risk factors while they should be studied together.

This paper should be considered for publication as long as authors answer the points raised below and modify their manuscript accordingly.

Major revisions

Background

4. “If left untreated, it is invariably fatal”. Authors have to moderate this since no data are available on the “natural evolution” of the disease. Long term asymptomatic carriers have been described (see Sternberg 2004 Parasite Immunol. 26, 469-476), spontaneous cures and human “trypanotolerance” are suspected (see Garcia et al., 2006, Trends Parasitol).

6. “Whereas in West-African HAT humans are the reservoir for the parasites…”.
While its epidemiological significance is still under debate, the existence of an animal reservoir of T. b. gambiense has been proven.

Results:

Study population

7- It is said in this part that “There were only slight differences between women and man with regard to occupation and activities involving potential risks for HAT infection (see Table 2)”. Examining table 2 shows that they differ significantly for almost all activities presented (P=0.001; P=0.007; P<0.001) except for visiting the cattle market. This is in total contradiction with the sentence above. Furthermore, it appears that in this area (given the data in LIRI) males are more affected than females (62% versus 38%). This deserves to be discussed in the discussion part.

Behavioral and socio-demographic risk factors

8- This part is presented in two sections: univariate analysis and multivariate analysis. Description of the variable included in the analysis is given in the multivariate part. This should rather be done in the first part and focus in the second part on only those variables which remain significant in the multivariate analysis.

9- Table 3: Presentation of this table is not satisfactory and authors should find a way of making it more readable (studied variable should be written on only one line); 0.053 and 0.05 are not <0.05.

10- In their analysis authors included all variables in the multivariate analysis by conditional logistic regression (22 variables). This number is far too high, especially since the number of individual included in the study is low and can cause statistic instability. In order to calculate more accurate OD ratio and provide a better model authors have to conduct a stepwise conditional logistic regression analysis were only variable with suggestive P values (<0.2) in the univariate analysis are selected and entered one by one in the model until no significant increase in the likelihood of the model is observed.

Discussion

11- Authors should read their discussion and rewrite it to make it fit to the data presented in the result section. For example, in the second paragraph: “In our case-control study, having a family member with history of HAT was the strongest risk factor associated with HAT infection, followed by the need for regularly leaving the village for work outside the village” No mention is made here about cassava crops (P=0.021) whereas regular work outside the village is only borderline significant (P=0.049).

12- As stated by the authors the main finding of this study is the presence of
familial aggregation of HAT cases, “an established feature in HAT”. The fact that in their work author make this observation in the frame of a study of environmental and behavioral risk factor should allow them to better discuss this point. In fact in this study, no such factor were able to explain the familial aggregation (having a previous case of HAT in the family remains the most significant factor even after introducing other environmental and behavioral risk factors in the multivariate model). Thus either this familial aggregation is due to none evaluated environmental risk factors or it could be due to factors from the host itself, i.e. genetic factors of resistance/susceptibility. Familial aggregation is a common feature in many infectious diseases (malaria, tuberculosis, leprosy, leishmaniasis, schistosomiasis…). For these diseases it could be demonstrated that it was not only due to shared environmental factors but to the genetic background of the host. Considering this point authors should note that although few work has been carried out on host genetic factors in THA, several studies indicate their importance in human whereas it has been clearly demonstrated in animal models such as mice and bovine (see review in Garcia et al., 2006, Trends Parasitol).

“The poorest villages, and within those the poorest inhabitants, are therefore most at risk of contracting sleeping sickness.” The authors evoke some socio-economic factors while no mention of such factors is made in the methods nor in the results section.

Minor revisions:

1. “by Okia et al. in 1994”, add [17]

References

2. Reference 14 is not essential and should be removed.