Follow-up of Card Agglutination Trypanosomiasis Test (CATT) positive but apparently aparasitaemic individuals in Côte d'Ivoire: evidence for a complex and heterogeneous population

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Summary
The aetiological diagnosis of human African trypanosomiasis (HAT) is based on the detection of the parasite, but currently available parasitological tests have low sensitivity and are hampered by fluctuating parasitaemia. The identification of seropositive individuals on whom to focus parasitological examination is based on antibody detection by means of the Card Agglutination Trypanosomiasis Test (CATT/T. b. gambiense). A complicating phenomenon is the occurrence of serologically positive but parasitologically unconfirmed results (isolated CATT positivity). This work presents a two-year longitudinal serological, parasitological and molecular follow-up of CATT-positive individuals including repeated examinations of each individual, to study the evolution over time of seropositivity at both the population and the individual levels. At the population level, the rate of seropositivity decreased during the first months of the survey, and afterwards showed remarkable stability. At the individual level, the results reveal the extreme heterogeneity of this population, with subjects showing fluctuating results, others with a short transient CATT positivity, and subjects that maintain their seropositivity over time. The stability of seropositivity and the pattern of results obtained with both immunological and parasitological examinations support the view that individual factors, such as immune response to infection, might be involved in the isolated CATT positivity phenomenon.

Keywords Trypanosomiasis, CATT, Individual susceptibility, Trypanosoma brucei gambiense

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Introduction
Human African Trypanosomiasis (HAT), or sleeping sickness, remains an important public health problem in sub-Saharan Africa. An estimated 55 million people are exposed to the risk of HAT, while only 4–5 million are under surveillance (WHO 1998). A chronic form of HAT, usually caused by Trypanosoma brucei gambiense (T. b. g.), prevails in West and Central Africa, whereas an acute form, caused by Trypanosoma brucei rhodesiense, occurs in East Africa. The control of the disease is based on medical surveillance, consisting of early detection and treatment of patients, and vector control. As most of the drugs currently available for treatment of sleeping sickness are toxic, a reliable diagnosis is required prior to treatment. The aetiological diagnosis of sleeping sickness is based on the detection of trypanosomes in lymph node aspirates, blood or cerebrospinal fluid, but currently available parasitological tests have low sensitivity and are hampered by fluctuating parasitaemia (Truc et al. 1994; Kanmogne et al. 1996). Antibody detection tests are currently used in mass-screening for the identification of seropositive individuals on whom to focus parasitological examinations. The most commonly used test in the field is the Card Agglutination Test for Trypanosomiasis (CATT), developed for T. b. gambiense specific antibody detection (Magnus et al. 1978).

The existence of seropositive but parasitologically unconfirmed subjects (aparasitaemic individuals, or isolated
seropositivity) (CATT+/-T-) raises the question of overt HAT cases, and may have epidemiological implications, since some of them might develop the disease and contribute to the persistence of disease foci. Presently the treatment of seropositive aparasitaemic individuals is not recommended even though it is sometimes suggested as a possible control strategy in areas with a high prevalence of HAT.

The meaning of the isolated seropositivity phenomenon remains unclear since the respective roles of trypanosome and host have not been examined extensively. First of all it is important to eliminate false seropositivity due to cross-reactivity (animal trypanosome strains or other infectious diseases), or false negativity of parasite detection tests due to subpatent parasitaemia, which may last several months in some individuals (Noireau et al. 1988). Lastly, the possibility of an efficient immune response capable of suppressing or even eliminating the trypanosomes, has also to be considered. An individual susceptibility to infection has already been described for both parasitological and bacterial infections (Abel et al. 1991; Hill et al. 1991; Garcia et al. 1998a,b). Our aim was a longitudinal survey with repeated serological and parasitological examinations, using several laboratory techniques, to study the evolution of the status of seropositive but parasitologically unconfirmed individuals. Since little is known about behavioural, environmental and individual factors potentially influencing seropositivity, our second goal was to investigate such factors.

Materials and methods

Area and population

The study took place between February 1997 and January 1999, in the Western-Central part of Côte d’Ivoire, in Sinfra focus, where a control program was conducted from 1995 to 1997. Between 1994 and 1995, more than 70 000 individuals were registered in this area. During mass-screening 50 375 individuals were tested by CATT on whole blood but were apparently aparasitaemic at least once during a previous control program. Our study population consisted of a subgroup of 90 individuals > 8 years whose seropositivity remained strong (≥ + +) in both diluted blood (1/4 dilution) and CATT with 5 µl of plasma. The purpose of the study was explained and informed consent obtained from the study subjects. If a sleeping sickness case appeared in this population, treatment was started immediately.

Biological samples and tests

The selected population was visited by a special team on six occasions in February, March, May and November 1997, and in January and June 1998. During each of these six visits, blood was collected for serological and parasitological tests in the field and serum was prepared and frozen (in liquid nitrogen) for further investigations. A last visit was performed in January 99, to collect blood for PCR analysis. In addition to these visits, the study population was regularly supervised by primary health care agents and, if health problems appeared, seropositive individuals were referred to Sinfra laboratory for HAT control.

For each subject, three CATT tests were performed (on whole blood, on a 1/4 blood dilution in PBS and on 5 µl of plasma) and parasitological examination was carried out by means of both the Mini Anion Exchange Centrifugation Technique (mAECT) (Lumsden et al. 1981) and the Quantitative Buffy Coat technique (QBCT) (Bailey & Smith 1992). In addition, a vial of the Kit for In Vitro Isolation (KIVI) (Aerts et al. 1992; Truc et al. 1992) was inoculated with 5 ml of the blood of each subject and followed up as prescribed. Immune trypanolysis tests (TL) were performed on serum according to Van Meirvenne et al. (1995) with LiTat 1.3, 1.5 and 1.6 variable antigen types of T.b. gambiense. Serum and cerebrospinal fluid IgM concentration was estimated by titration in the LATEX/IgM (Lejon et al. 1998).

PCR was performed on the samples collected in May 1997, January and June 1998, and in January 1999 according to the protocol described by Penchenier et al. (1996) using two PCR primers, both specific for T. brucei ssp. (Moser et al. 1989), TBR1 and TBR2.

Variable of interest

At each examination, a binary variable denoted as Elementary Serological Status (ESS) was defined for each sampled individual. If CATT on 1/4 diluted blood and CATT on plasma were strongly positive (≥ + +), the ESS was coded as 1, and conversely in case of weak positivity or obvious negativity of diluted CATT and/or CATT on plasma, ESS was coded as 0. In this work we were also interested in studying the individual serological status and, in order to obtain a unique variable accounting for the overall degree of seropositivity during the follow-up, a binary variable denoted as Individual Serological Status (ISS) was defined as follows. If a subject had all ESSs equal to 1 (all CATT strongly positive) the ISS was coded as 1. If at least one ESS was equal to 0 (at least one CATT weakly positive or negative), the ISS was coded as 0. The first group of individuals (all ESS = 1; ISS = 1) were referred to as seropositive; the second group (at least one ESS = 0; ISS = 0) as seronegative.
Strategy of analysis and statistical methods

Elementary serological status was used for studying the evolution, by visit, of seropositivity in the population and the stability over time of seropositivity within individuals. Individual serological status was used to test the effect of covariates on seropositivity, as well as to assess the association and agreement with other biological data, essentially IgM level, Trypanolysis (TL) and PCR results.

To assess the individual stability of ESS, the following method was used (Garcia et al., 1995) (Table 1): Let $P_j$ be the observed probability of having a positive CATT in the total number of measurements ($P_j = \frac{\text{number of positive CATTs}}{\text{total number of CATTs}}$). According to the hypothesis that a positive CATT occurs at random within individuals (i.e. all measurements are independent), the probability for an individual who had $j$ measurements that all his CATTs are positive is given by $P_j^j$, the expected number of such individuals (sampled $j$ times and being always positive) is $n_j P_j^j$, where $n$ is the number of subjects sampled $j$ times. These expected numbers were compared with the observed ones by a chi-square test for individuals with more than two measurements.

Table 1: Observed and expected number of subjects with at least three ESS measurements equal to 1*

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<table>
<thead>
<tr>
<th>No. of measurements</th>
<th>No. of all subjects with</th>
<th>Expected no. of subjects</th>
<th>Observed no. of subjects</th>
<th>ESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>j</td>
<td>$P_j$</td>
<td>with all their ESS = 1</td>
<td>with all their ESS = 1</td>
<td>ESS</td>
</tr>
<tr>
<td>3</td>
<td>0.20</td>
<td>7</td>
<td>1.40</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>0.12</td>
<td>9</td>
<td>1.10</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>0.07</td>
<td>22</td>
<td>1.57</td>
<td>8</td>
</tr>
<tr>
<td>6</td>
<td>0.04</td>
<td>31</td>
<td>1.31</td>
<td>11</td>
</tr>
</tbody>
</table>
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*Expected numbers are computed under the hypothesis that a positive ESS occurs at random with the probability $P_j$ (defined in methods), which is equal to 0.59 in this study.

For example, for three measurements this probability is $0.59^3 = 0.20$, $P < 10^{-6}$ by Pearson chi-square test.

Univariate analysis to test the effect of categorical variables on ISS was performed by means of Pearson chi-square tests. The McNemar test of symmetry was used to compare results of different tests performed on the same individual. For quantitative variables such as age and IgM titre (after a log transformation), analysis of variance was used. Multivariate analysis was performed by means of linear regression models. All computations were done using BMDP statistical software (University of California, Los Angeles, CA).

Results

Population

Of the 90 individuals selected at the beginning of the study, 77 were sampled at least twice and represent the population under study. The remaining 13 individuals who refused to continue after the first sampling did not differ significantly on individual variables from the 77 included subjects. The mean age of the latter population was 31.25 years (range = 8–83) with a male:female ratio of 1.4. Concerning SWL, 23.3% of the population has a collective system of land occupation, with important mixing of population; 53.4% lived in Sin faç town with less important forest contact. The remaining 23.3% lived in the forest with the same kind of agricultural activities as the first group, but with a different social organization. Natives of the area represented 31.5% of the included individuals and 28.8% of the population originated from Northern areas or countries with absence or very low level of trypanosomiasis endemicity; sleeping sickness cases in the family; number of years people had lived in the area; and occupation and activity divided into three categories: fieldworkers spending most of their time in the forest and the plantations, schoolchildren and teachers with low forest contact, and colleagues (city dwellers).
HAT infection in Côte d'Ivoire

Table 2 Variation, by date of visit, of the proportion of sampled population and of the proportion of positive Elementary Serological status

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of visited subjects</td>
<td>58 (0.75)*</td>
<td>68 (0.88)</td>
<td>66 (0.86)</td>
<td>58 (0.75)</td>
<td>57 (0.74)</td>
<td>59 (0.77)</td>
<td>366</td>
</tr>
<tr>
<td>ESS = 0</td>
<td>14 (0.26)</td>
<td>20 (0.31)</td>
<td>29 (0.44)</td>
<td>28 (0.42)</td>
<td>31 (0.46)</td>
<td>27 (0.49)</td>
<td>149</td>
</tr>
<tr>
<td>ESS = 1</td>
<td>44 (0.71)</td>
<td>48 (0.66)</td>
<td>37 (0.56)</td>
<td>30 (0.52)</td>
<td>26 (0.54)</td>
<td>32 (0.51)</td>
<td>217</td>
</tr>
</tbody>
</table>

* proportion of the whole population P < 0.005.

from Northern areas. The remaining 39.7% represented allogenic people from Côte d'Ivoire. Only 9.8% of the studied population declared having HAT in their family. Fieldworkers represented 32.9% and 36.8% of the population had school-related activities.

Not all individuals were present at each visit and the mean number of examinations per individual was 4.9 (range = 2–6), but no effect of the number of examinations on ISS was detected (P = 0.07).

Long-term stability of ESS

Table 2 shows the variation by date of visit of both the percentage of the total population sampled and the proportion of positive ESS. The rate of positivity (i.e., ESS = 1), decreased significantly (P < 0.005), and seemed to stabilize around 50% after the third examination (Figure 1). The probability P of having a positive ESS in the total number of measurements was 0.59. Table 1 shows, by number of measurements, the number of individuals having all ESSs positive and the expected numbers computed under the hypothesis of independence as described in the methods. The test result was highly significant (P < 10⁻⁵), leading to a strong rejection of the hypothesis of random occurrence of a positive ESS within individuals. Even though the rate of positive ESS decreased significantly in the whole population, for some individuals the probability of having all their ESSs positive was higher than under independence-hypothesis. Such subjects who maintained their ESS positivity over time were defined, in this study, as seropositive individuals (ISS = 1; n = 38), and the question was then: did they have an increased risk of developing the disease?

Factors influencing the ISS

Univariate analysis showed that there was no significant effect of gender (P > 0.20), SWL (P > 0.20) or ethnic group (P > 0.30) on the ISS. Neither the presence of a sleeping sickness case in the family (P > 0.30) nor forest-related activities (P > 0.7) have a significant influence on ISS. Mean age (SEM) did not differ significantly (P > 0.80) between the seropositive and seronegative populations, 32.2 years (3.34) and 31.5 years (3.10), respectively. Mean time (SEM) seropositive subjects lived in the area was 25.9 years (3.92) whereas the seronegative population was present in the area for 23.4 years (3.30) (P > 0.60).

Parasite detection

During follow-up no trypanosomes were found in blood by mAECT or by QBC® techniques. No KIVI was found positive. In January 1998 one seropositive subject was found with strong mental confusion without any other clinical sign. No trypanosomes were found in the blood but a lumbar puncture (LP) detected one trypanosome after double centrifugation of cerebrospinal fluid (CSF). This subject was seropositive (ISS = 1 with 5 positive ESS; 5 TL positive; high IgM titre: 8000 (normal = 1000)). Taking this result into account, lumbar puncture and CSF examination was performed on all subjects (n = 17) with the same pattern of results (i.e., ISS = 1;...
Table 3 Results of immune trypanolysis tests according to individual serological status

<table>
<thead>
<tr>
<th></th>
<th>SSI = 0</th>
<th>SSI = 1</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TL -</td>
<td>33</td>
<td>19</td>
<td>52</td>
</tr>
<tr>
<td>(0.47)*</td>
<td>(0.27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TL +</td>
<td>6</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>(0.086)</td>
<td>(0.17)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>31</td>
<td>70</td>
</tr>
</tbody>
</table>

*proportion of the whole population.

TL positive and high IgM titre). No-trypanosomes were found after double centrifugation of CSF. Unfortunately white blood cell counts could not be performed for technical reasons. As an alternative, IgM in CSF was titrated with the LATEX/lgM but none of the samples showed abnormal IgM concentrations.

Table 3 shows the TL test results according to ISS. Of the seropositive individuals 27% were TL negative and 8.6% of the seronegative subjects, for whom TL results were available, were TL positive (n = 6). These proportions differed significantly (McNemar test = 6.76; P < 0.01), suggesting that the response to these two serological tests differed in the study population. High serum IgM levels are current in infectious diseases and can be caused by any kind of infection. The mean serum IgM titre was significantly (P < 0.05) higher in seropositive individuals, 3678.6 (SEM = 445.6), than in seronegative ones, 2481.5 (355.5), and in TL positive subjects than in TL negative ones, 5000.0 (218.2) and 2459.5 (283.7), respectively. However, when multivariate analysis was performed to test the effect of both TL and ISS on the serum IgM titre, TL remained the only relevant factor influencing IgM in this population (P < 0.05).

PCR results

Table 4 shows the number of positive PCR obtained in May 1997, January and June 1998 and January 1999. The overall percentage of positivity was 14.5%, and the positivity rate did not change significantly during follow-up (P > 0.50). The percentage of PCR positivity was significantly higher (P < 0.02) for seronegative individuals (SSI = 0) than for seropositive ones (SSI = 1), 28% and 16%, respectively. Of 32 seropositive individuals sampled for PCR tests, five subjects had at least one positive PCR; of these, three had all PCRs positive (2/2, 2/2 and 3/3), whereas of 38 seronegative people sampled for PCR examination, 11 had at least one PCR positive, one of them with all its PCRs positive (4/4). Considering TL results, and disregarding other tests, the percentage of PCR positivity did not differ significantly (P > 0.2) between TL-positive subjects (37% of individuals with at least one PCR positive) and TL-negative ones, 32%. However, the four individuals who maintained positivity at PCR results were TL positive, and one of them was the subject who developed sleeping sickness.

Discussion

This work presents a two-year longitudinal serological, parasitological, and molecular survey of CATT-positive individuals including repeated examinations of each individual and studying the long-term stability of seropositivity, at both the population and the individual level. At the population level, the rate of positivity decreased during the first months of the survey, and afterwards showed a remarkable stability. At the individual level, our results confirm the extreme heterogeneity of this population, with subjects that maintained their seropositivity over time, others showing important variability and lastly, subjects with a short transient CATT positivity. Evidence exists that T. congolense or T. brucei-brucei infection in animals can induce CATT seropositivity (Noireau et al. 1986). T. congolense has been suggested to be human serum resistant (Joshua 1989) and recently Truc et al. (1998) described a mixed infection with T. b. gambiense and T. congolense in a patient in Côte d'Ivoire. This patient was only slightly positive in CATT and turned CATT negative shortly after treatment. Although we do not know how long T. congolense or T. b. brucei can persist in a human being, this period may be long enough to induce a transient CATT positivity. Cohabitation of man and domestic animals harbouring non T. b. gambiense trypanosomes could play a role in transient, fluctuating or even long-lasting CATT seropositivity in...
the human population. Eight seropositive adults accepted
daily parasitological examination during one week by means
of QBC® and mAECT. All remained parasitologically nega-
tive (data not shown). Although active surveillance of the
study population stopped in June 1998 for parasitological
tests and in January 1999 for PCR, all individuals are still
under medical surveillance and so far no new case of sleeping
sickness has appeared.

This extreme heterogeneity emphasizes the difficulty of
determining a simple and standardized control strategy for
seropositive though apparently aparasitaemic subjects. The
main problem is determining the epidemiological significance
of this population, since some of these persons may indeed
be infected, and sooner or later play a role in the transmission
of disease. Within our study and its 2 years' follow-up
(February 1997 - January 1999), one trypanosomiasis case
occurred among 77 included individuals, representing an esti-
minated incidence of 0.65 new cases per 100 person-years.

According to Van Meirvenne et al. (1995), the immune try-
panolysis test is highly specific and immune trypanolysis-
positive individuals can be considered as being or having been
infected with trypanosomes. If we consider that the only sub-
jects really at risk in our study are those who are trypanolysis
positive (n = 17 disregarding all other tests), the estimated
incidence would be much higher (2.3 new cases per 100 per-
son-years). However, our population is highly selected and no
quantitative information can be easily derived from it.

Furthermore, it is important to note that 8.6% of those sub-
jects were trypanolysis positive but had a negative individual
serological status derived from several CATT results. For two
of them, CATT was never positive, (six measurements) during
the follow-up. The mean level of trypanolytic antibody titre
did not differ between seropositive and seronegative TL-
positive individuals. Use of the IgM titre as a cut-off point to
determine a higher risk of developing the disease cannot be
proposed without reservation, since our results suggested that
observed IgM titre differences are better explained by try-
panolysis than by CATT alone. Simarro et al. (1999) recently
showed that treatment of all CATT positives with an end titre
> 1/8, can be proposed as a control strategy in high preva-
ience areas. However, our study took place in a different
endemic area and with a strongly selected population that
could be compared at the beginning of our work to the one
selected at the end of Simarro's study. Although treatment of
CATT-positive aparasitaemic people is not a recommended
control strategy, it could help in some high prevalence areas
at least at the beginning of a control program when the trans-
mision rate is still high. Nevertheless, previous results show
that the complexity of this question needs further, both prag-
matic and explicative, investigations.

In this survey, primers specific for Trypanosoma brucei s.l.
(TBR1 and TBR2) were used for PCR, and extractions were
performed as described by Penchenier et al. (1996). The
14.5% overall rate of PCR positivity in our study is higher
than the one recently published by Simo et al. (1999), using
the same method of extraction and the same primers in three
foci of Cameroon. These authors found 51 positive PCR
(3.8%) in 1343 seropositive individuals apparently negative in
QBC®, mAECT or lymph node puncture, with an important
variability according to the focus: 2.9% in Bipindi, 0.5% in
Cambo and 5.5% in Fontem. Kamnoge et al. (1996) re-
ported discordant results in Cameroon since their overall
PCR positivity rate was 22.4% (13/58) using phenol extrac-
tion (Van der Ploeg et al. 1982), but only 3.4% (2/58) using
differential lysis methods (Masiga 1994). All 58 tested indi-
viduals were strongly positive in CATT and appeared apar-
asitaemic when blood samples from them were examined after
haematocrit centrifugation, mAECT, thick blood films and in
vitro culture. However, from the 13 PCR-positive subjects,
eight presented clinical signs of enlarged glands, facial
oedema, headache, tremor, abnormal behaviour, etc., and two
of them had positive gland puncture. The same discrepancy
according to the focus was denoted by Kamnoge, since 30% of
seropositives tested from Fontem were PCR positive
whereas this rate decreased to 14.3% in Mbam. Extraction
method differences can explain discordant results between
these studies as illustrated in Kannmoge's study (Masiga
1994; Weiss 1995), and Smits & Hartskeerl (1993) clearly
showed that the quality of DNA limits the efficiency of PCR
reaction. Similar differences in sensitivity and specificity
occurred in PCR diagnosis of Plasmodium infections (Gyang

Differences in these results could not only be explained by
extraction methods but probably also by parasite intrinsic
properties: Dukes et al. (1992) showed that in Cameroon
some isolates of trypanosomes do not express LI/Tat 1.3 anti-
gen. Such parasites could be responsible for CATT-negative
infections, with subpatent parasitaemia, detected by PCR.
However, an important distinction between all these studies is
the definition of seropositive and apparently aparasitaemic
individuals. Our longitudinal follow-up shows that, with a
very strict definition of seropositive vs. seronegative indi-
viduals, PCR positivity is more frequent within the sero-
negative than within the seropositive population, suggesting
that, in a cross-sectional study, a positive PCR might appear
randomly in a population living in an endemic area. Dis-
regarding the longitudinal aspect of our work, the rate of
PCR positivity on CATT-negative individuals decreases sig-
ificantly from 67% to 33% between the first and the third
examination (no CATT was performed in January 1999),
emphasizing the importance of repeated analyses. This result
can be, at least in part, explained by the lack of specificity of
the primers used in all these studies, since TBR1 and TBR2
primers are not specific of T. brucei gambiensc and can reveal
DNA from *T. brucei brucei* originating from abortive inoculation by tsetse flies. The true value of PCR methods in diagnosis of sleeping sickness remains to be further evaluated, and development of *T. b. gambiense* specific primers would be of great interest.

Sleeping sickness treatment centres in Côte d’Ivoire are rather close to the study area and are involved in the control program established in the region covered by this study, suggesting that the included seropositive individuals probably have never been treated. However, the probability that one of our subjects was a treated sleeping sickness case cannot be totally excluded and, moreover, uncontrolled treatment using traditional medicines could also explain this phenomenon.

Our results are strongly consistent with an important heterogeneity of the CATT-seropositive population. Some trypanolysis-positive individuals with high IgM titre have probably been infected by *T. brucei gambiense* or a related subspecies of trypanosomes. Even though a rather chronic infection course is quite common, the complete absence of disease after 32 months of follow-up seems to require extra explanation, such as a strongly suited and very efficient immune response. This pattern of individual susceptibility to infection-and disease has been described for other bacterial (Abel & Demeunis 1988) and parasitic (García et al. 1999a,b; García et al. 1999) infections. While there is evidence for genetic control of either disease resistance/susceptibility (Hill et al. 1991; Marquet et al. 1996) or immune response (Hill et al. 1992), the nature of this control in human infections remains unclear (Beck et al. 1995; Migot et al. 1995). To our knowledge, in human African trypanosomiasis, although classical epidemiological studies reported some indirect arguments for familial dependencies, shared environment rather than genetic susceptibility has been put forward (Kholde et al. 1997). However, involvement of the immune system in pathogenesis, and interactions between the trypanosome and macrophages have been described in animal models (Asksn 1985; Gison et al. 1989; Sleghem et al. 1989) and humans (Okomo-Assoumou et al. 1995; Sterkling 1996). Furthermore, Kemp et al. (1999) recently identified genes involved in resistance control to trypanosomiasis in mice.

In conclusion, our study emphasizes heterogeneity of the CATT-positive but apparently aparaisitaemic population. Further analyses need to explore every element of this complex phenomenon; focusing not only on testing intrinsic qualities, but also on the interactions between the parasite and the host. All these factors will probably be of great interest for defining a strategy for taking into account this population in control programs.

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