Spread and distribution of human T-cell leukaemia virus type I-reactive antibody among baboons and monkeys in the northern and eastern Transvaal

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Summary

Antibodies which probably indicate infection with human T-cell leukaemia virus type I (HTLV-I) were determined in three species of non-human primates from several localities. A significant prevalence among chacma baboons was confirmed. According to sero-epidemiological evidence that HTLV-I infection is predominantly sexually transmitted between adult animals, comparison of prevalence rates between localities or species should therefore take sexual maturity into account. It appears unlikely that transmission from non-human primates to humans is frequent.

The two recently recognized infectious diseases, adult T-cell leukaemia (ATL) and acquired immunodeficiency syndrome (AIDS) have much in common. There is a close relationship with regard to the viral aetiology and a resemblance in the pathogenesis, involving derangement of the T-cell compartment of the immunological system with early death as the usual clinical outcome. There are other interesting, if less alarming, common features. These retroviral infections occur in humans and non-human primates, as disease or as carrier states, and both are found in Africa despite the fact that the main concentrations of these diseases among humans occur in other parts of the world and there is no overlapping as regards geography and ethnicity. It has been suggested that these viral diseases may have originated in Africa and spread from there across the world.

The prevalence pattern of antibody to the causative agent of ATL, i.e. human T-cell leukaemia virus type I (HTLV-I), as determined among human communities and free-ranging non-human primate troops in a well-controlled and reasonably accurately documented African environment, provides supportive evidence of another link, i.e. that sexual behaviour is an important factor, not only in the natural spread of this virus, as it is in the transmission of the AIDS virus, HTLV-III, but also in establishing the prevalence of infection. In this context we report our observations on non-human primates in the field or soon after capture. Data on human populations from the same area are reported elsewhere in this issue.

Subjects and methods

Three species of non-human primate occur free in the northern and eastern Transvaal. Chacma baboons (Papio ursinus orientalis in the eastern and P. ursinus occidentalis in the northern parts) and vervet monkeys (Cercopithecus pygerythrus) are widespread in rural areas where they may be in more or less close association with human habitats. In the Kruger National Park both species are found over a wide range; in addition, a race of baboons (P. ursinus griseipes) which shows some affinity with the more northern yellow baboon (subspecies P. cynocephalus) is found at Pafuri in the extreme north of the Park as a spill-over from Zimbabwe and Mozambique at the southern-most limit of its range. The rarer samango monkey (C. albogularis syn. mitis erythraceus) is present naturally in a few localities, including the northern border mountains of Venda between the Transvaal and Zimbabwe.

Sera were collected mainly from chacma baboons, since these were more easily studied in the wild and were relatively easily captured. A total of 331 samples were obtained from baboons from several sites: stored frozen sera were available from animals captured or killed at Skukuza, Thabazimbi, Loskop Dam, Koedoeskop and Hoedspruit and fresh sera were obtained from baboons at various localities throughout the Kruger National Park, Vaalwater and Pilanesberg Nature Reserve. Analysis of sex and maturity were based on samples from three separate localities: the Kruger National Park, the Pilanesberg Game Reserve and Vaalwater. In addition sera were obtained from 50 vervet monkeys and from 16 samango monkeys.

Laboratory studies

HTLV-I antibody was sought initially by indirect immunofluorescence assay (IFA) with the virus-carrying cell line MT-2, the samples being tested in Japan; during the study the transformed cell line OCH was provided by Professor Y. Hinuma, Institute for Virus Research, Kyoto University, and some confirmatory tests were undertaken at the Medical University of Southern Africa. At a later stage of the study an enzyme-linked immunosorbent assay (ELISA) using purified p24 HTLV-I antigen (Litton Bionetics, Kensington, Md, USA) was also used at MEDUNSA for screening and for comparison. Positive and negative results obtained by the two methods were largely in concordance but discrepancies did occur. Specimens which are IFA-positive and ELISA-negative are more common, and differences in titre are general. This report is based on results of IFA and/or ELISA tests.

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Results

HTLV-I antibodies were found among baboons (19 - 25%) and vervet monkeys (24%), but not among samango monkeys (Table I). Analysis of the data available for chacma baboons showed variation in prevalence according to sex and locality (Table II); when chacmas were subdivided on the basis of weight, the prevalence correlated strikingly with increasing maturity (Table III).

Discussion

Among wild chacma baboons increasing body weight is a dependable criterion of age in the earlier stages of physical development and sexual maturation. The age-dependent increase in anti-HTLV-I seropositivity has been reported previously from Japan among humans and monkeys (Macaca fuscata). A relatively low prevalence of antibody among younger individuals, represented among our sample by a frequency of 0 - 10% in four classes of males and female juveniles and subadults respectively, may be ascribed to transmission of HTLV-I from mothers to infants. This has been demonstrated at birth in humans and is considered to be either due to vertical transmission (via germinal cells or intrauterine infection, which may be transplacental or ascending) or due to horizontal infection via milk or intrapartum exposure. Unless the increasing prevalence of antibody which accompanies growth and maturation is due to latent infection becoming overt, it must be due to horizontal infection in later life. This mode of transmission has been demonstrated in adult Japanese monkeys by experimental selected matings, and it has been suggested that sexual contact is a likely explanation for the relatively high anti-HTLV-I seropositivity rate among spouses of patients with ATL.

Close scrutiny of the prevalence data in Table III, in conjunction with what is known of the social structure and behaviour of chacma baboons, suggest that sexual transmission of HTLV-I infection is an important epidemiological factor among non-human primates. In South Africa the troop size of chacma baboons varies from 10 to 100, with a fairly constant average of 40-80. All activities of the troop are centred on the dominance hierarchy of full-grown males. The mating pattern is based on promiscuity regulated by the dominance relationships between adult males, and depends on the biological cycle of the female. In the initial stages of oestrus she may copulate with subdominant males and juveniles. The dominant males, or co-dominant males in a large troop, copulate exclusively with females in full oestrus with turgescent skin indicating the follicular phase of the cycle. At this period the female and a dominant male form a consort pair which may remain exclusively associated for several hours or, more often, some days, during which time a series of copulations take place. It is exceptional, however, for one male to monopolize a female during the entire period of full oestrus. Thus, while sex is one of the prerogatives of male dominance, subdominant males are not generally banned from the mating system; rather, sexual dominance is shown by the number of copulations and their effective timing in relation to impregnation.

Physically fully developed, sexually dominant chacma males will have greater exposure to sexually transmitted infection in

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<td>Males</td>
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terms of the number of sexual partners and number of copula-
tions than will subdominant adult males, who in turn outrank
subadults and larger juveniles in the sexual hierarchy. This
may explain the disparate prevalence of HTLV-I antibody
shown for different classes of mature males in Table II, with
virtually 40% of the very large males being seropositive. At
the same time the steep increase in antibody prevalence among
females through the stages of juveniles, subadults and adults
also correlates with sexual activity. In this context HTLV-I
infection among chacma baboons is in line with the spread of
HTLV-III infection in human societies of male homosexuals
and females, among whom the number of partners and the
duration of exposure are correlates of prevalence.

It is noted that vervet monkeys have the same terrestrial
habit as baboons, and therefore require the security of a
cohesive troop structure maintained by male dominance. In
contrast, samango monkeys, among whom we have not found
evidence of HTLV infection, are almost entirely arboreal and
without the close-bound social organization of the other species.

In considering the origin of HTLV-I, it has been suggested
that Old World primates may have been exposed to an ancestral
form of lymphotrophic retrovirus of the HTLV family (of
which members occur in different avian and non-primate
mammalian species) with consequent evolution of HTLV-I in primates.
Whether call HTLV-I-type retroviruses and monkeys and that in humans are structurally identical remains
to be determined. Our unpublished experimental transmission
studies do show that blood from human HTLV-I carriers is
highly infective for juvenile chacma baboons. However, two or
more closely related mutants of HTLV do not necessarily
exclude transmission of one or more of these viruses between
human and non-human primates. An African setting for these
events has been postulated because of widespread infection
among blacks and the proximity of Old World non-human
primates as a source of infection. It is further suggested that
HTLV-I was carried by travellers from Africa to Japan in the
16th century. Historical evidence of localized Portuguese and
Dutch activity is quoted to explain the geographical
concentration of human infection on the coast and islands in the
south-west of Japan.

We submit that the alternative possibility, i.e. that HTLV-I
infection of both monkey and man in the Orient is of consider-
able length of time, is equally probable. The HTLV-I prevalence
rate among human populations in Africa generally, as well as in the northern and eastern Transvaal, is not uniform (unpublished data). It is zero, or virtually zero, in some reasonably adequate population samples. From West Africa, where HTLV-I infection is endemic,
thousands of people settled in North America, South America and the Caribbean during the 17th century. At that time non-human primates were also introduced from Africa: C. mona (mona monkey) and C. sabaeus (green monkey) to the West Indies. 15 HTLV-I became established in the New World giving rise to
demic and non-endemic areas. It is not uniformly distributed
even among people whose ancestors came from Africa in the
17th century. The higher prevalence among Caribbean blacks
is in contrast to the sporadic infection of blacks in the USA,
although their ancestors presumably started off on an equal
footing as regards HTLV-I. The distribution pattern is gene-
ally not uniform wherever HTLV-I occurs and in this respect the situation is basically similar in Africa, the New World and Japan. Therefore it may be that the primate retrovirus has existed in the East for approximately as long as it has in Africa.

Presumably, frequency and spread of HTLV-I are deter-
mined by an interdependence of epidemiological factors, of
which some may be broadly identifiable. Climate may be one,
since temperate and warm regions are favoured. Living condi-
tions may be another, since the sporadic cases in non-endemic
areas of Japan 6 and the USA 4 tend to occur in rural communi-
ties. We found the same in our unpublished study. Genetics
may be another, in view of the predilection of HTLV-I for
certain ethnic groups in man, and for certain genera and
species in non-human primates. Among the latter, their social
organization, and their sexual behaviour in particular, may be
the most important factor in determining the species affected.

With regard to the natural history of HTLV-I infections we
have mentioned that there is at present no reported evidence of
HTLV-I transmission from non-human primates in their
natural state to man. Similarly, animal workers in primate
centres in Europe were reported to be seronegative. In an
investigation of three animal centres, we found 1 individual
with HTLV-I antibodies demonstrable in peripheral blood
mononuclear cells among 22 blacks and 17 whites who are
frequently in close contact with captive baboons and monkeys.
This black man, aged 50 years, has handled primates for many
years; however, he was born in an area where HTLV-I
antibody occurs sporadically in the population. Whatever the
source of his infection, he shows no haematological or immuno-
logical abnormality apart from infected circulating leucocytes.

From the USA it is reported that monkeys in captivity
occasionally develop malignant lymphoma or lymphoprolifera-
tive disease. In closed breeding colonies in the USA there
have been a few instances of multiple cases over a limited
time, which suggests a transmitted agent. In a recent report
there a significantly higher prevalence of antibody to an
HTLV-I-carrying cell line and spontaneous lymphoid mali-
nant lesions was found among captive maquois compared
with healthy animals both in captivity and in the natural
state. 16 We have not studied baboons or monkeys from captive
breeding colonies. In three animal centres to which we have
access the animals are housed occasionally as captive parent-
child pairs for a short period, or singly on a regular basis for
periods which may last for years. Among long-term captives
(not included in Tables I-III) antibody prevalence is of the
same order as in the wild. Lymphoproliferative disease is said
to be rare or unknown among monkeys and baboons in the
animal centres about which we have personal information.
This is in keeping with observations made in the wild. The
research section of the National Parks Board maintains a
scientific wild-life management programme in the Kruger
National Park. This includes postmortem examination, often
undertaken by qualified veterinary scientists backed by ade-
quate laboratory investigation, of animals put down because of
illness or of carcasses found in the field when the cause of death
is unknown. Lymphoma or leukaemia has not been identified
among these animals.

The distribution of HTLV-I among non-human primates in
different localities will continue to receive attention in
different localities. The proper comparison of frequency must
be based on results obtained in sexually mature individuals.
This applies to studies in the field as well as among captive
animals. It is our experience that proportions of different age
classes and sex vary in random samples. Because of this, the
geographical variations which we discerned initially in this
study were less marked and we cannot confirm some earlier
reports of a female preponderance for HTLV-I among non-
human primates. 13 In our study the prevalence for mature
male and female baboons was 26% (17 of 65) and 25,5% (13 of
51) respectively.

We acknowledge the material assistance and encouragement
extended to us by the warden and staff of the Kruger National
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Distribution and possible spread of human T-cell leukaemia virus type I in human communities in the northern and eastern Transvaal

M. C. BOTHA, M. JONES, W. A. DE KLERK, N. YAMAMOTO

Summary

The prevalence of serum antibodies which probably indicate infection with a human T-cell leukaemia virus type I was determined among random population samples of more than 100 healthy black individuals in several localities in Transvaal. The percentage of seropositive subjects increases northwards and eastwards, where geoclimatic conditions are similar to those of endemic areas elsewhere in the world. The comparatively higher prevalence among females in the Kruger National Park suggests that this is predominantly a sexually transmitted disease.

Elsewhere in this issue we reported on the prevalence of antibody to human T-cell leukaemia virus type I (HTLV-I) among non-human primates in the northern and eastern Transvaal and commented on sexual contact as an epidemiological factor in the infection of chacma baboons.1 In the course of the field work undertaken for that study, blood samples were collected from human communities in these regions and tested in the same way.

Subjects and methods

Localities where samples were taken are shown in Fig. 1. Ga-Rankuwa is an industrialized, semi-urbanized area on the northern Transvaal highveld. Black male factory workers and female antenatal patients attending clinics in this area are drawn predominantly from the highveld region. Themba, Malamulele and Shongwe are on the eastern Transvaal lowveld, outside but near the eastern and southern borders of the Kruger National Park; antenatal patients attending these hospitals are from the local communities. The Kruger National Park is bordered on the north by Zimbabwe and by Mozambique in the west. Several residential camps for tourists and personnel are distributed throughout the Park. Black staff are recruited from surrounding areas, including Mozambique. Blood was obtained from 680 volunteers among black staff throughout the Park and from 52 white personnel at Skukuza rest camp.