Comparative Seroepidemiology of HTLV-I and HTLV-III in the French West Indies and Some African Countries


Laboratory of Epidemiology and Immunovirology of Tumors, Faculty of Medicine A. Carrel, 69372 Lyon, Cedex 08, France (G. de-Thé, A. G., L. G., G. N., A. C.); Tumor Cell Biology, National Cancer Institute, Bethesda, Maryland (M. R-G., G. N.); National Institute of Hygiene, Warsaw, Poland (G. N.); Hopital Compagnie Sûclière, Kwilu Nongo, Zaïre (P. M.); Shiritori Hospital, Private Bag, Musoma, Tanzania (G. B.); Hopital Militaire Avicenne, Service d’Immunologie, Marrakech, Maroc (A. B.); Centre Hospitalier Lyon-Sud, Unité d’Hygiène et Épidémiologie, 69360 Pierre-Bénite, France (F. F.); D. O. A. S., 19, rue Schoeleier, 97300 Cayenne (M. S.); Institut Pasteur Ngongo, Zaire (P. M.); Shirati Hospital, Private Bag, Musoma, Tanzania (G. B.); Hopital Militaire Avicenne, Service d’Immunologie, Marrakech, Maroc (A. B.); Centre Pasteur de la Guynne Française, 97306 Cayenne Cedex [Y. R.]; and Government Laboratory of Health Service, Island of Dominica (G. R.)

Abstract

The prevalence of antibodies detected by ELISA against human T-lymphotropic viruses, type I (HTLV-I) and type III (HTLV-III-LAV), is described in a comparative serosurvey in the French West Indies and African countries. The data confirm that the Caribbean basin is endemic for HTLV-I. In this region, HTLV-I antibody prevalence varied from 3.4% to 5.2% among blood donors and increased with age to reach a value of 33% among elderly people from the Dominica Island. In French Guyana, a South American country bordering the Caribbean sea, differences in antibody distribution across three ethnic groups (black Bonis, Indian Wayanas, and Hmongs from Asia) provide clues for investigation of the mode of HTLV-I transmission. Africa appears to be an endemic continent for HTLV-I and HTLV-III. For both viruses, the antibody prevalence exhibited an increasing gradient from northern to equatorial through Sudanic areas. These preliminary data by showing that Africa represents an endemic reservoir of HTLVs and, possibly, of other human retroviruses should stimulate further investigations on the natural history and the geographical origin of these viruses.

Introduction

A new chapter in human viral oncology was opened by Gallo in 1980 (see Ref. 1 and for review, Ref. 2). This was made possible thanks to the previous findings and characterization of T-cell growth factor by the same group (3). Within a short period of time, three human retroviruses were characterized. They were referred to as HTLV.² HTLV-I, endemic in southwest Japan (4, 5), the Caribbean (6, 22), and central Africa (7), was found to be associated with an aggressive form of T-cell leukemia-lymphoma in Japan as described by Takatsuki et al. (8) and it was also observed in the West Indies by Blattner et al. (6), by Catovsky et al. (9), and by Gessain et al. (10). In addition, HTLV-I was associated with a much more specific immunodeficiency in endemic areas of Japan, the Caribbean, and equatorial Africa, as first evidenced by Essex et al. (11–17), who showed that in Kyushu Island, 42% of the adults with various infectious diseases had HTLV-I MA antibodies as compared to 12–14% in normal population groups and to 23% for patients with tumors other than aggressive T-cell leukemia-lymphoma. HTLV-II, isolated from a hairy cell leukemia on the West Coast of the USA (12), is clearly different from HTLV-I, but its geographical distributions and disease association still remain to be determined.

The third member of the human retroviruses has been the subject of intensive investigations in the last 2 yr. This virus, labeled as LAV (lymphadenopathy-associated virus) in 1983 by Barré-Sinoussi et al. (13) and as HTLV-III in 1984 by Popovic et al. (14), appears to represent the prime cause of AIDS. The number of infected persons in North America and Europe increases steadily and creates a new and critical public health situation.

It is therefore urgent to study comparatively the epidemiological characteristics of these viruses in the endemic and epidemic areas of the world, to establish their mode of transmission, to characterize the immune response leading to protective antibodies, and to comprehend the etiopathogenesis of the associated diseases. The development of these diseases among infected individuals in endemic as well as in epidemic situations is most probably linked to genetic and environmental cofactors which deserve investigation in different parts of the world. We are reporting here preliminary seroepidemiological data on both HTLV-I and HTLV-III in the French West Indies and some African countries. These data should help to answer some questions regarding the natural history and the geographical origin of these viruses.

Table 1

<table>
<thead>
<tr>
<th>Ethnic groups</th>
<th>Age range (yr)</th>
<th>No. tested</th>
<th>No. positive</th>
<th>% positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carib Indians (Dominica)</td>
<td>18–59</td>
<td>90</td>
<td>3</td>
<td>3.3</td>
</tr>
<tr>
<td>Haitians (French Guyana)</td>
<td>18–59</td>
<td>211</td>
<td>8</td>
<td>3.8</td>
</tr>
<tr>
<td>Dominican prostitutes  (French Guyana)</td>
<td>18–59</td>
<td>82</td>
<td>6</td>
<td>7.3</td>
</tr>
<tr>
<td>Bovi blacks (French Guyana)</td>
<td>18–59</td>
<td>97</td>
<td>13 (13.4)</td>
<td></td>
</tr>
<tr>
<td>Wayana Indians (French Guyana)</td>
<td>18–59</td>
<td>57</td>
<td>2 (3.5)</td>
<td></td>
</tr>
<tr>
<td>Hmgon residents (French Guyana)</td>
<td>18–59</td>
<td>57</td>
<td>4 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Hmgon newcomers (French Guyana)</td>
<td>18–59</td>
<td>28</td>
<td>1 (3.6)</td>
<td></td>
</tr>
</tbody>
</table>

*Presented at the HTLV Symposium, December 6 and 7, 1984, Bethesda, MD. This study was made possible through financial help from Centre National de la Recherche Scientifique; Association pour la Recherche sur le Cancer, Villejuif; and Fondation pour la Recherche Médicale, Paris, France.

The abbreviations used are: HTLV, human T-lymphotropic viruses; MA, membrane antigen; AIDS, acquired immunodeficiency syndrome; ELISA, enzyme-linked immunosorbent assay; DASS, direction of social and health affairs.
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Table 2
HTLV-I antibodies in some African countries

Antibodies were detected by ELISA using semipurified HTLV-I virions as prepared by Biotech, Inc., Rockville, MD.

<table>
<thead>
<tr>
<th>Age groups (yr)</th>
<th>South Zaire</th>
<th>Northwest Tanzania</th>
<th>Ivory Coast</th>
<th>Northeast Uganda</th>
<th>South Sudan</th>
<th>Upper Volta</th>
<th>Morocco</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>0/3</td>
<td>10/58</td>
<td>0/7</td>
<td>0/7</td>
<td>0/7</td>
<td>0/7</td>
<td>0/7</td>
</tr>
<tr>
<td>5–9</td>
<td>0/29</td>
<td>19/113</td>
<td>0/14</td>
<td>3/22</td>
<td>3/36</td>
<td>2/22</td>
<td>3/22</td>
</tr>
<tr>
<td>10–14</td>
<td>2/29</td>
<td>23/92</td>
<td>4/14</td>
<td>0/3</td>
<td>0/7</td>
<td>0/7</td>
<td>0/7</td>
</tr>
<tr>
<td>40–49</td>
<td>5/23</td>
<td>6/40</td>
<td>0/7</td>
<td>0/7</td>
<td>0/10</td>
<td>0/7</td>
<td>0/7</td>
</tr>
<tr>
<td>50+</td>
<td>6/28</td>
<td>9/70</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27/187 (14.4%)</td>
<td>79/468 (16.9%)</td>
<td>16/100 (16.0%)</td>
<td>8/101 (8.0%)</td>
<td>7/76 (9.2%)</td>
<td>2/43 (4.6%)</td>
<td>4/677</td>
</tr>
</tbody>
</table>

Materials and Methods

In the West Indies, sera were obtained from blood donors thanks to Dr. Monplaisir in Fort de France (Martinique) and to Dr. Eutrope in Cayenne (French Guyana). Sera from the various ethnic groups living in French Guyana or Dominica were obtained either through existing serum banks or through collection of sera, made for other purposes, under the responsibility of the DASS (Dr. Lefait-Robin, Dr. Lefait) and of the Pasteur Institute in Cayenne.

African sera were similarly obtained either from established serum banks or from recent collections. Ugandan sera, collected in 1972–1974 during the International Agency for Research on Cancer’s Burkitt’s lymphoma study (15), were made available through the courtesy of Dr. G. Lenoir. The Ivorian sera were also collected in the early 1970s and kindly provided by Dr. Tuyns of the International Agency for Research on Cancer. Sera from the other countries were collected in the last 12 months either for the purpose of this study or in the framework of other projects, as for the case of Upper Volta, by Dr. C. Desgranges.

Antibodies to HTLV-I were tested with an ELISA technique (16), using semipurified HTLV-I virions coated on 96-well microtiter plates provided by Biotech, Inc. (Rockville, MD). Assays were done in duplicate. Results are expressed as a ratio (R) of the absorbance value of the tested sera to the average absorbance value of four readings of a standard reference normal serum.

Antibodies to HTLV-III were tested by ELISA using semi-purified virions produced by the infected H9 line (14). Different levels of positivity were set at the National Cancer Institute and in Lyon. At the National Cancer Institute, sera with an R ≥ 3 were then confirmed by Western blotting using the same semipurified HTLV-III viral preparations. In Lyon, an absorbance ratio of 5 was the mark set for confirmation by Western blotting.

While some series of African sera presented here were confirmed by Western blotting, others were not. Thus in this preliminary report, we are presenting HTLV-III data obtained by ELISA giving both the proportions of sera with R ≥ 3 and with R ≥ 5, with the knowledge that about half of the African sera with R ≥ 5 could be confirmed by Western blotting, in contrast to European or American sera which, in such circumstances, would all be confirmed.

Results

HTLV-I Antibody Prevalence. Table 1 gives the prevalence of HTLV-I antibodies in various groups in the French West Indies and in the island of Dominica. It can be seen that the background prevalence in blood donors is around 4% by the ELISA test (up to 13% by the MA test (23)). When we compared blood donors aged 18–59 yr with normal people 60–90 yr of age, a sharp increase in prevalence of antibodies ranging from 13–33% was observed.

Among the various ethnic groups living in French Guyana, significant differences of HTLV-I prevalence were observed, the highest being noted among the black Boni with 13% of them having ELISA antibodies, mostly with high titers (8 ≤ R ≤ 15), while other groups exhibited low HTLV-I antibodies (5 ≤ R ≤ 7) in only 3% of the sera. The Boni have been an isolated ethnic group since the 18th century when they escaped slavery in Surinam and migrated southward along the Maroni River in the tropical forest.

Other interesting results concerned the Dominican prostitutes with very high antibody levels as measured by Western blotting and the Hmong refugees from Campuchea. When comparing resident and recently immigrant Hmong (see Table 1), it appeared that the Hmong were infected by HTLV-I soon after their migration to Guyana.

Table 2 gives the prevalence of HTLV-I antibodies in some African countries. The results suggest the existence of an increasing gradient of infection from the mostly negative North African region to equatorial Africa, where up to 14–16% of the sera were found positive. Sudanic regions, reflected here by sera obtained from south Sudan and northwest Uganda, seem to show an intermediate gradient for infection by HTLV-I.

HTLV-III Antibody Prevalence. Table 3 gives the prevalence of HTLV-III antibodies in selected groups from the French West Indies. All the sera were first screened by ELISA, and the proportion of sera with both R ≥ 3 and R ≥ 5 is given. The latter were then tested by Western immunoblotting, and all were confirmed, as well as a few sera with 3 < R < 5. When compared with Table 1, it can be seen that HTLV-I infection is clearly more prevalent in the Caribbean region than HTLV-III. As discussed below, such an observation is confirmed by the rarity of typical AIDS detected in Martinique and French Guyana, in spite of careful search.

Table 4 presents HTLV-III antibody prevalence in some African countries. Since Western blotting was carried out for only the Zairian sera and part of the others, the results are presented with the proportion of sera with R ≥ 3 and with R ≥ 5. Besides north Africa where very few sera were found positive, the proportion of sera with R ≥ 5 exhibited significant geographical differences: from 44.8% in Uganda in 1972–1974 to 9.3% presently in south Sudan. When confirmation of positivity by Western blotting is completed, even more variations might appear.

3 F. Barin and M. Essex, unpublished data.
4 L. Gazzolo et al., Intern. J. Cancer, in press.
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Table 3
HTLV-III antibody prevalence in French West Indies
Antibodies detected by ELISA using semipurified virion sera with R 3 and confirmed by Western blotting were considered as positive.

<table>
<thead>
<tr>
<th>Group</th>
<th>Country</th>
<th>No. tested</th>
<th>West- R $&gt;3$</th>
<th>West- R $&gt;5$</th>
<th>No. of confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood donors</td>
<td>Martinique</td>
<td>108</td>
<td>11</td>
<td>1</td>
<td>1 (0.9)$^a$</td>
</tr>
<tr>
<td></td>
<td>French Guyana</td>
<td>108</td>
<td>7</td>
<td>2</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Haitians (20–39 yr)</td>
<td>French Guyana</td>
<td>455</td>
<td>20</td>
<td>12</td>
<td>14 (3.1)</td>
</tr>
<tr>
<td>Haitians (40 yr)</td>
<td>French Guyana</td>
<td>78</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dominican prostitutes</td>
<td>French Guyana</td>
<td>82</td>
<td>6</td>
<td>0</td>
<td>ND$^b$</td>
</tr>
<tr>
<td>Boni blacks</td>
<td>French Guyana</td>
<td>87</td>
<td>13</td>
<td>2</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Wayana Indians</td>
<td>French Guyana</td>
<td>78</td>
<td>21</td>
<td>2</td>
<td>2 (2.6)</td>
</tr>
</tbody>
</table>

$^a$ Numbers in parentheses, percentage.

Discussion

The preliminary results of the comparative surveys that we conducted in the Caribbean region and in Africa for both the HTLV-I and HTLV-III indicate that these two viruses exhibit similarities but also significant differences in their epidemiological characteristics. HTLV-I is endemic all through the Caribbean region where 3–4% of the population has ELISA-related antibodies, whereas in Africa, the antibody prevalence exhibits a gradient from north Africa to equatorial Africa similar to that observed in the Kyushu island (11). In the endemic Caribbean region, HTLV-I-associated adult T-cell lymphomas were observed among residents in both Jamaica (6) and Martinique (10) and among emigrant Caribbeans in Europe (9, 18). To our knowledge, similar HTLV-I-associated aggressive forms of T-cell cancers were not, until now, frequently described in equatorial Africa nor among African immigrants in France or in England. If confirmed, this result either could reflect HTLV-I strain differences between geographical areas or would suggest that cofactors, besides HTLV-I, play a role in such leukemogenesis. The example of Epstein-Barr virus-related cancers merits mention here. Epstein-Barr virus represents a causal factor for the high endemic Burkitt’s lymphoma in equatorial Africa, but not for the nonendemic tumors observed in the western countries (19).

The data concerning the Boni in French Guyana (see Table 1) bring support to the hypothesized African origin of HTLV-I, since they lived in isolation since the 18th century soon after their migration to the Caribbean region from Africa (20). Furthermore, the prevalence in the neighboring Wayana Indians, together with the infection pattern among the emigrant population, such as the Hmong, provides a unique situation to investigate the role of genetic and environmental factors in the transmission of these viruses. The HTLV-III prevalence was found to be very different from that of HTLV-I. In the surveyed area of the Caribbean region, only Haitians were found to be infected at a level significantly lower than that of any group from intertropical Africa. If HTLV-III infection appears as a recent phenomenon in the Caribbean region, is it an ancient one in Africa? Recent results by Saxinger et al. (21) and those presented here on Ugandan adult sera collected in 1972–1974 provide evidence that 10 yr ago a large part of the population of the west Nile district of Uganda was infected by HTLV-III. Obvious epidemics of deadly infectious syndromes were not observed at that time.$^5$ Laboratory tests

$^5$ E. H. Williams, personal communication.
which enabled AIDS to be defined were not available at that time in those areas, thus making assessments of the prevalence of AIDS at that time in Uganda difficult. As for HTLV-I, a gradient of infection appears to exist from north to equatorial Africa. The Sudanic African belt appears to represent the frontier of the endemic HTLV-I and HTLV-III infections. It would be of paramount interest to have cross-sectional African data to further delineate boundaries, the age-specific prevalence, disease association, and information on transmission of infection and animal reservoir.

Acknowledgments

The authors wish to thank S. Areto for her editorial assistance. HTLV-III semipurified visions used for the ELISA and the Western blots were kindly provided by Dr. R. C. Gallo.

References


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*Cancer Res* 1985;45:4633s-4636s.

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