Arbovirus infections and viral haemorrhagic fevers in Uganda: a serological survey in Karamoja district, 1984

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Abstract
Sera collected in May 1984 from 132 adult residents of Karamoja district, Uganda, were examined by haemagglutination inhibition tests for antibodies against selected arboviruses, namely Chikungunya and Semliki Forest alphaviruses (Togaviridae); dengue type 2, Wesselbron, West Nile, yellow fever and Zika flaviviruses (Flaviviridae); Bunyamwera, Ilheus and Tahyna bunyaviruses (Bunyaviridae); and Sicilian sandfly fever phleboviruses (Bunyaviridae); and by immunofluorescence tests against certain haemorrhagic fever viruses, Lassa fever arenavirus ( Arenaviridae), Ebola-Sudan, Ebola-Zaire and Marburg filoviruses (Filoviridae), Crimean-Congo haemorrhagic fever nairoviruses and Rift Valley fever phlebovirus (Bunyaviridae). Antibodies against Chikungunya virus were the most prevalent (47%), followed by flavivirus antibodies (16%), which were probably due mainly to West Nile virus. No evidence of yellow fever or dengue virus circulation was observed. A few individuals had antibodies against Crimean-Congo haemorrhagic fever, Lassa, Ebola and Marburg viruses, suggesting that these viruses all circulate in the area.

Introduction
After the epidemics of yellow fever in Ethiopia in the 1960s and 1970s, epidemiological surveillance of arbovirus infections was carried out in the regions affected by the disease and in neighbouring regions: in northern Kenya, to the east of Lake Turkana (Lake Rudolf) (HENDERSON et al., 1968, 1970a; METSE-LAAR et al., 1970) and to the west of the lake, among the Turkana people (HENDERSON et al., 1968; RODHAIN et al., 1975); in south-west Ethiopia, in the province of Genu Gofa (SERIE et al., 1968; RODHAIN et al., 1972, 1975); in northern Uganda, in the province of Karamoja (HENDERSON et al., 1968, 1970b); and in southern Sudan, in Sannar district (SALIM & PORTERFIELD, 1973).

Few data have been obtained in this part of Africa during the last decade. We took advantage of the fact that 2 of us (B.H. and E.M.) were in the region to determine whether the socio-economic changes which have occurred in recent years have had an effect on the epidemiology of arbovirus infections. In addition, the emergence of certain viral haemorrhagic fevers, especially in the Sudan, prompted us to include the main African agents of these diseases in the survey.

Study region
The sera were collected in the villages of Tokora and Namalu and in the neighbouring villages in the province of Karamoja, northern Uganda (Figure; Table 1). Limited to the south by the small range of Kadam mountains and to the east by the Rift valley escarpment, the southern Karamoja region is at an average altitude of 1100 m and is covered with shrubby or grassy savannah. There are 2 rainy seasons: March to June and October to November.

The inhabitants belong to the Karamajong, of Nilotic origin like their close relatives the Turkana of Kenya (GULLIVER & GULLIVER, 1968). The territorial group predominating in the surveyed villages was the Piatu, with a few Bokora. They are basically livestock farmers breeding mainly cattle, and lead a semi-nomadic life-style regulated by the search for pasture. However, modifications in the climate, the subsequent major loss of cattle, and the permanent insecurity of recent years practically enforced a sedentary life-style, and many of the cattle breeders became farmers. The traditional social structures have thus been completely altered.

Methods
The subjects involved were all the adults of both sexes, aged from 20 to 40 years and in good apparent health, who attended the Tokora health centre during the first week in May 1984; subjects with fever or recent history of fever were excluded. It was considered unlikely that the selected subjects had ever been vaccinated against yellow fever. The following information was obtained for each of them: surname, first name, sex, age, surnames of father and mother, village of residence (Table 1).

Sterile blood samples were collected in Vacutainers® and the sera decanted within a few hours and frozen at -20°C until use in Paris. 132 sera were tested for arbovirus antibodies by haemagglutination inhibition using a micromethod with 96-well plates according to the usual technique (BARE et al., 1969-1970). After kaolin or acetone treatment (sera which were positive for viruses from different groups after kaolin treatment were treated with acetone), each serum was tested against a batch containing the following antigens: Chikungunya (CHIK) and Semliki forest (SF) alphaviruses (Toga-
viridae); Bunyamwera (BUN), Ilesha (ILE), Tahyna (TAH) bunyaviruses, sandfly fever Sicily type (SFS), and phlebovirus (Bunyaviridae); yellow fever (YF), dengue type 2 (DEN2), West Nile (WN), Wesselsbron (WSL), and Zika (ZIKA) flaviviruses (Flaviviridae). A titre of 1:10 was considered positive.

Antibodies against haemorrhagic fevers were searched for using a classical immunofluorescent assay with antigen-infected Vero cells (WULFF & LANGE, 1975). Sera were screened on polyvalent slides with multiple antigen-infected cells and then titrated on monovalent slides (JOHNSON et al., 1981). The following antigens were used, belonging to several virus strains which had been recorded previously from the Central African Republic (GONZALEZ et al., 1983): Crimean-Congo haemorrhagic fever nairovirus (CHF-CON) and Rift Valley fever phlebovirus (RVF) (Bunyaviridae); Ebola Zaire (EBO-Z), Ebola-Sudan (EBO-S), and Marburg (MBG) filoviruses (Filoviridae); and Lassa fever arenavirus (LAS) (Arenaviridae).

Results

Arboviruses. Seventy-two sera (54.3%) showed antibodies against at least one arbovirus (Table 2). All positive sera had low titres, at the most 1:80. No sera were found with antibodies to BUN or SFS.

Haemorrhagic fever viruses. Twenty-five sera (18.9%) showed antibodies against at least one of the tested antigens (Table 3). The titres observed did not exceed 1:128. No serum reacted with either Marburg or Ebola antigens.

No difference according to sex was observed in the prevalence rates of antibodies to either arbovirus or haemorrhagic fever viruses.

Table 1. Origin of sera studied

<table>
<thead>
<tr>
<th>Village</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tokora</td>
<td>14</td>
<td>8</td>
<td>22</td>
</tr>
<tr>
<td>Nadip</td>
<td>13</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Alamarac</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Namalu</td>
<td>27</td>
<td>19</td>
<td>46</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>58</td>
<td>120</td>
</tr>
</tbody>
</table>

Table 2. Prevalence rates of arboviral antibodies

<table>
<thead>
<tr>
<th>Village</th>
<th>CHIK</th>
<th>SF</th>
<th>YF</th>
<th>DEN2</th>
<th>WN</th>
<th>WSL</th>
<th>ZIKA</th>
<th>Total flaviviruses</th>
<th>ILE</th>
<th>TAH</th>
<th>Overall positives</th>
<th>No. sera tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tokora</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Nadip</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>8(61.5%)</td>
<td>13</td>
</tr>
<tr>
<td>Alamarac</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>8(42.1%)</td>
<td>19</td>
</tr>
<tr>
<td>Namalu</td>
<td>31</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td>3</td>
<td>4</td>
<td>34(58.6%)</td>
<td>58</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>8(53.3%)</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
<td>3</td>
<td>3</td>
<td>13</td>
<td>11</td>
<td>8</td>
<td>6</td>
<td>22</td>
<td>7</td>
<td>7</td>
<td>72(54.5%)</td>
<td>132</td>
</tr>
</tbody>
</table>

*See text for key to abbreviations.

The number of sera positive for at least one virus in this group.

The number of sera positive for at least one arbovirus.
Table 3. Prevalence rates of antibodies against haemorrhagic fever viruses\(^a\)

<table>
<thead>
<tr>
<th>Village</th>
<th>CHF-CON</th>
<th>RFV</th>
<th>EBO-Z</th>
<th>EBO-S</th>
<th>MBG</th>
<th>LAS</th>
<th>Overall positives(^b)</th>
<th>No. sera tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tokora</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>5 (18.5%)</td>
<td>27</td>
</tr>
<tr>
<td>Nadip</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>2 (10.5%)</td>
<td>13</td>
</tr>
<tr>
<td>Alamacar</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>5 (24.5%)</td>
<td>19</td>
</tr>
<tr>
<td>Namali</td>
<td>1</td>
<td>1(^c)</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>14 (24.5%)</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>-</td>
<td>-</td>
<td>1(^d)</td>
<td>-</td>
<td>-</td>
<td>1(^d)</td>
<td>2 (13.3%)</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>25 (18.9%)</td>
<td>132</td>
</tr>
</tbody>
</table>

\(^a\)See text for key to abbreviations.
\(^b\)The number of sera positive for at least one virus.
\(^c\)Namalu village.
\(^d\)Napenanya village.

Discussion

The arbovirus prevalence rates showed only moderate differences between villages (42-61%). Because of the relatively similar results obtained from ecologically comparable regions, the discussion will deal with the overall findings.

The overall positive rate for arboviruses (54.5%) is comparable to that observed in 1971 in the Kibish river region (Ethiopian-Sudanese border), about 300 km to the north (RODHAIN et al., 1972).

Antibodies against the Chikungunya virus were by far the most frequent in all villages, with an overall prevalence rate of 46-9% and titres ranging from 1:10 to 1:40. In 1967-1969 HENDERSON et al. (1970b) observed a prevalence rate of only 9.9% among 182 subjects aged over 15 years. It is possible that some of the antibodies detected were the result of infection with O'Nyong Nyong virus (ONN), which is closely related to CHIK. CHIK virus is present in man and monkeys throughout Uganda and epidemics of CHIK and ONN occur periodically in Uganda. Epidemics of CHIK occurred in the Zika forest in 1968 (MCRAE et al., 1971) and in Mukono (Kampala region) in 1982 (KALUNDA et al., 1985). Such an epidemic probably occurred in south Karamoja in recent years, but as no children's sera were included in our survey it was not possible to date this event.

The prevalence rate of 16% for flaviviruses which we detected is much higher than the 1-6% reported by HENDERSON et al. (1970b), with high titres mainly for WN virus and no YF antibodies (though prevalence rates up to 69% were observed in other parts of Uganda). Qualitatively, however, our results are comparable: no trace of YF or DEN2 circulation was observed, since positive sera had only low titres and were also slightly positive for antibodies to other viruses belonging to the same group; isolated WN antibodies were detected in 7 subjects (with titres up to 1:80), in all the villages, and WSL and ZIKA antibodies in 3 and 4 subjects respectively. These results indicate that WN virus is present throughout the region, and that WSL and ZIKA are probably not so common. These results are comparable to those we found in 1972 in Turkana district (RODHAIN et al., 1975).

This region therefore seems to be free of yellow fever, and has been for 20 years, although the virus circulates actively in west and central Uganda in forest monkeys (MCRAE & KIRYA, 1982). However, human cases are extremely rare in these enzootic areas (low anthropophilia of potential vectors?). Furthermore, the Zika virus is no longer considered to interfere with the circulation of yellow fever virus (HENDERSON et al., 1970a; CORNET et al., 1979).

Although there was no trace of BUN in our study, 5-3% of the subjects were carriers of ILE antibodies. In the surveys carried out in 1967-1969, considerable differences (0-4%–81%) in the prevalence rates of BUN antibodies (the only one tested for) were observed according to the region of Uganda, with 3-3% in Karamoja (HENDERSON et al., 1970b). Our studies in 1971 and 1972 found a marked circulation of ILE (0-9 to 6-1%) and practically no BUN in Turkana or in the lower Omo valley (Ethiopia).

Finally, we found a relatively high frequency (5-3%) of TAH antibodies, which could indicate activity of Lombo virus. We found no trace of it in Turkana in 1972.

There are many other arboviruses in this region, amongst which the Kadam (prototype isolated in Namala) and Dugbe viruses were isolated from Karamoja (TUKEL et al., 1970), and antibodies against the Dugbe and Bhanja viruses are regularly found in cattle (UGANDA, 1975).

Antibodies against all 6 viral haemorrhagic fever antigens used were found, and sera from all the villages were positive for at least one of these viruses. The prevalence rates were moderate, however, comparable to those observed in other African countries.

CHF-CON has been known to be present for a long time in Uganda, both in man and animals (especially cattle). One of its usual vectors, Amblyomma variegatum, is common on cattle in Karamoja (TUKEL et al., 1970), and it is not surprising that we detected antibodies in 2 of the surveyed villages. The same applies to RFV, which has also been known for a long time in Uganda (FINDLAY et al., 1956) and caused enzootics in Sudan in 1976. In the Turkana, at Lodwar, antibodies have been found in 90% of examined subjects (JOHNSON et al., 1983).

To our knowledge, LAS virus has not previously been found in Uganda, but our results need to be backed up by a larger survey. However, antibodies have apparently been found in west Sudan. The positive results which we detected may imply that another, related, virus is present in the region, with little or no pathogenicity for man.

We have observed a similar frequency (3%) of
antibodies against both types of Ebola viruses. This agrees with the results of Johnson et al. (1983), who found 7.8% of EBO-Z antibody carriers at Lodwar, and those reported by the World Health Organization (WHO, 1984). 4.6% of the population aged 10-40 years in Turkana. The same applies to the Marburg virus: 6.5% of positive subjects in our study, 5.8% at Lodwar (Johnson et al., 1983), and 2.3% in Turkana (WHO, 1984). Although the number of subjects was low, we noted, as did the authors working previously in Kenya and Zaire, the marked preponderance of EBO antibodies in females (6 of 8). By contrast, for MBG 5 of the 6 positive subjects were male. These results, together with those of Johnson et al. (1982, 1983) in man and monkeys, suggest that EBO, MBG and RFV are present, at least temporarily, in Kenya and Zaire.

We thank Mrs M. T. Douret and M. Rouseau for their excellent technical assistance and J. Alik and G. Ten Have for translating and typing the manuscript.

References


Received 8 September 1987; revised 2 May 1989; accepted for publication 2 May 1989.