

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

F. Rodhain^{1,*}, J. P. Gonzalez², E. Mercier³, B. Helync³, B. Larouze⁴ and C. Hannoun⁵ ¹Unité d'Ecologie des Systèmes Vectoriels, formerly Unité d'Ecologie Virale, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cédex 15, France; ²Institut de Recherche Scientifique pour le Développement en Coopération (ORSTOM), Boîte Postale 892, Bangui, Central African Republic; ³Rehabilitation Health Project of South Karamoja, Tokora, Uganda; ⁴INSERM U-13/Institut de Médecine et d'Epidémiologie Africaines, Hôpital Claude Bernard, 75944 Paris Cédex 19, France; ⁵Unité d'Ecologie Virale, Institut Pasteur, 25 rue du Docteur Roux, 75724 Paris Cédex 15, France

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, Wesselsbron, West Nile, yellow fever and Zika flaviviruses (Flaviviridae); Bunyamwera, Ilesha and Tahyna bunyaviruses (Bunyaviridae); and Sicilian sandfly fever phlebovirus (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 nairovirus 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; METSELAAR *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 Gemu Goffa (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 Piau, 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 (BARME *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-

*To whom correspondence and reprint requests should be addressed.

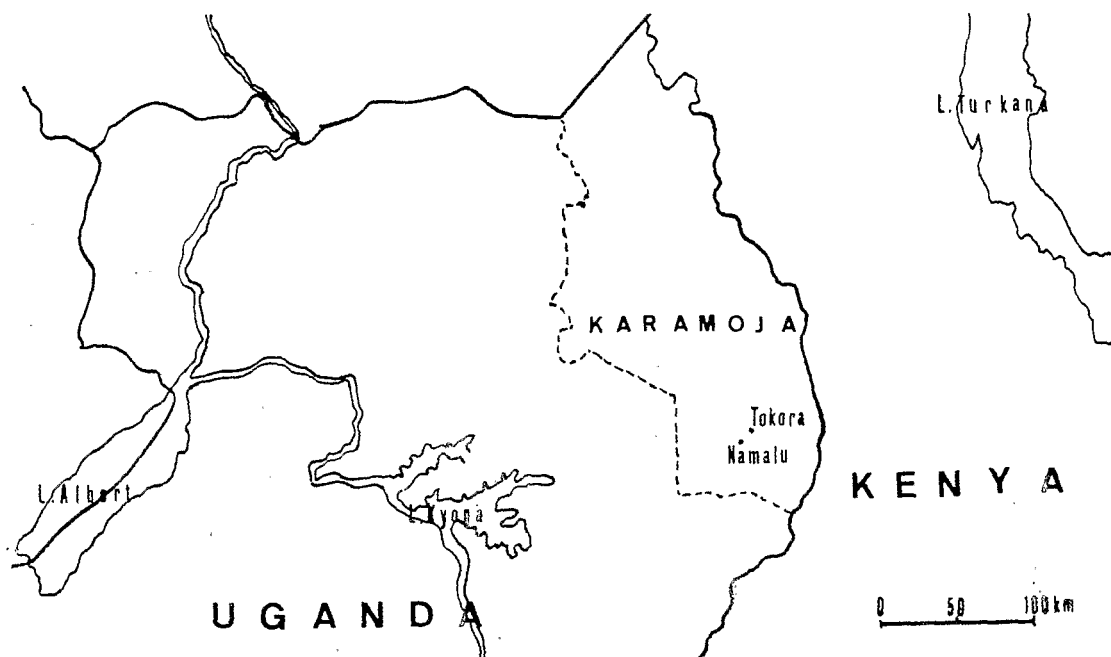


Figure. Map showing study area.

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 (54.5%) 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

Sex	Other					Total	Percentage
	Tokora	Nadip	Alamacar	Namalu	villages*		
Male	14	—	8	30	13	65	49.2
Female	13	13	11	28	2	67	50.8
Total	27	13	19	58	15	132	100

*Kokuwan: 2 (1F, 1M); Lokatapan: 3 (1F, 2M); Loregai: 1 (1M); Nakapiripirit: 4 (4M); Kalku: 1 (1M); Napenanya: 2 (2M); Nabilatuk: 1 (1M); Amaler: 1 (1M) [M=male, F=female].

Table 2. Prevalence rates of arboviral antibodies*

Village	Total								Overall positives ^c	No. sera tested		
	CHIK	SF	YF	DEN2	WN	WSL	ZIKA	flaviviruses ^b				
Tokora	12	—	—	—	1	—	1	2	2	1	14(51.8%)	27
Nadip	8	—	1	—	1	2	2	4	—	—	8(61.5%)	13
Alamacar	7	—	—	—	2	1	—	2	2	—	8(42.1%)	19
Namalu	31	1	1	1	5	6	2	8	3	4	34(58.6%)	58
Other	4	—	1	2	4	2	3	6	—	2	8(53.3%)	15
Total	62	1	3	3	13	11	8	22	7	7	72(54.5%)	132
Percentage	46.9	0.75	2.2	2.2	9.8	8.3	6	16.6	5.3	5.3		

*See text for key to abbreviations.

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

^cThe number of sera positive for at least one arbovirus.

Table 3. Prevalence rates of antibodies against haemorrhagic fever viruses^a

Village	CHF-CON	RFV	EBO-Z	EBO-S	MBG	LAS	Overall positives ^b	No. sera tested
Tokora	2	1	3	1	—	1	5(18.5%)	27
Nadip	—	—	1	1	—	—	2(15.3%)	13
Alamacar	—	—	—	—	—	2	2(10.5%)	19
Namalu	1	1	—	2	5	5	14(24.1%)	58
Other	—	1 ^c	—	—	1 ^d	—	2(13.3%)	15
Total	3	4	4	4	6	8	25(18.9%)	132
Percentage	2.2	3.0	3.0	3.0	4.5	6.0	—	—

^aSee text for key to abbreviations.

^bThe number of sera positive for at least one virus.

^cNakapiripirit village.

^dNapenanya 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 (MCCRAE *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 (MCCRAE & KIRYA, 1982). However, hu-

man 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%–81.5%) 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 Lumbo 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 Namalu) and Dugbe viruses were isolated from Karamoja (TUKEI *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 (TUKEI *et al.*, 1970), and it is not surprising that we detected antibodies in 2 of the surveyed villages. The same applies to RVF, which has also been known for a long time in Uganda (FINDLAY *et al.*, 1936) 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% for the 20-40 year age range in Turkana. The same applies to the Marburg virus: 6% of positive subjects in our study, 3.8% 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 dry areas inhabited by Nilo-Hamite cattle breeders in north Uganda and Kenya.

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