n°5

ISSN= 0035-9203

Haemorrhagic fever virus activity in equatorial Africa: distribution and prevalence of filovirus reactive antibody in the Central African Republic

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Abstract
Seroepidemiological surveys were conducted to determine the frequency and distribution of haemorrhagic fever virus (HFV) activity in the Central African Republic. Human serum specimens (4295) were collected from 5 ecologically distinct zones. Serological evidence of HFV activity was found in all the zones. The filovirus antibody prevalence (24·4%, 1051/4295) was greater than the combined prevalence for Lassa virus, Rift Valley fever virus and Crimean-Congo HFV antibody (1·1%, 45/4295; $P<0·01$). Evidence of filovirus activity was found in all zones: 21·3% (914/4295) of the population were seropositive for Ebola virus antibody while only 3·2% (137/4295) were seroreactive with Marburg viral antigens. Age and sex were important host-related factors influencing filovirus activity, particularly in dry grassland and moist forest communities. These communities shared many factors, but differences, such as agricultural practices and ethnic backgrounds, may also affect the risk of infection. Filovirus infections appear to occur without apparent disease. Continued investigations are needed to evaluate the true pathogenicity of the African filoviruses and the likelihood that unidentified serologically cross-reacting and non-pathogenic members of the filovirus family are active in equatorial Africa.

Introduction

The haemorrhagic fever viruses (HFV), which cause severe systemic illness with haemorrhagic diathesis, plague Africa, causing widely scattered but sporadic epidemics of fatal disease. In many instances, highly pathogenic HFVs such as Lassa virus, Rift Valley fever virus, and Crimean-Congo haemorrhagic fever virus circulate undetected in nature, presumably as enzootic infections, until conditions change favouring their spread to the human population.

The filoviruses (Marburg and Ebola viruses) are the most recently described members of the African HFV group. They were identified when severe epidemics occurred in Europe and Africa during the late 1960s and 1970s. Marburg virus was first isolated during an epidemic in which 30 serious haemorrhagic fever cases, 7 fatal, occurred in (West) Germany and Yugoslavia (SIEGERT, 1970). The outbreak was associated with the processing of virus-contaminated tissues from African green monkeys (*Cercopithecus aethiops*) captured in the Lake Kyoga region of Uganda (HENDERSON et al., 1971), presumably during epidemic and epizootic virus activity (SMITH, M. W., 1982). The first recognized Ebola virus epidemics in Sudan and Zaire were more devastating; hundreds were infected and 60–90% of cases were fatal (JOHNSON, 1978; SMITH, D. I. H., 1978). The filoviruses are now considered in the differential diagnosis of unexplained fevers occurring in sub-Saharan travellers. However, routinely available diagnostic tests and effective therapeutic procedures do not exist, and the natural history of the filoviruses is unknown.

In 1984 an attempt was made to define the natural threat posed by the filoviruses in equatorial Africa. Negative-pressure flexible plastic isolators were installed in containment facilities constructed at the Institut Pasteur, Bangui, Central African Republic, and the Kenya Medical Research Institute, Nairobi, Kenya, to reduce the risk among investigators routinely handling potentially infectious clinical and environmental specimens (VAN DER GROEN, 1982). Subsequently, cross-sectional and prospective epidemiological and clinical surveillance studies were conducted in which 12 245 serosurvey samples and 3473 clinical specimens from fever cases of unknown aetiology were assessed for evidence of select HFV (Ebola, Marburg, Lassa, Rift Valley fever, and Congo-Crimean haemorrhagic fever viruses) activity. The earlier findings, from studies which suggested frequent filovirus exposure in central Africa, have been presented elsewhere (MEUNIER et al., 1987).

This paper reports the distribution and prevalence of endemic HFV activity, as measured by virus reactive antibody, and describes epidemiological factors influencing filovirus infection in human populations in distinct central African environments. The Central African Republic was selected for our study based upon early Institut Pasteur reports indicating potential virus activity there (SALUZZO et al., 1982), its close proximity and ecological similarity to Sudan and Zaire, and the continued interest of local public health officials in investigating the viral haemorrhagic fevers.

Materials and Methods
Survey areas

The Central African Republic occupies 620 000 km² between arid Saharan and moist equatorial Africa in the geographical centre of the continent. Sixty-one per cent of the 2·7 million inhabitants live in rural villages. The economy is predominantly agricultural; four-fifths of the population are involved in farming. The remaining one-fifth are hunter-gatherers who inhabit the tropical forest of the south-west. The annual rainfall occurs in 2 seasons, April to May and August to November, and ranges from approximately 1800 mm³ in Salo south of Nola to 800 mm³ in Birao (Figure). The local vegetation varies from moist tropical rain forest in the south to semi-desert in the north. Based on climate and vegetation, the territory is easily separated into 5 ecologically distinct zones:
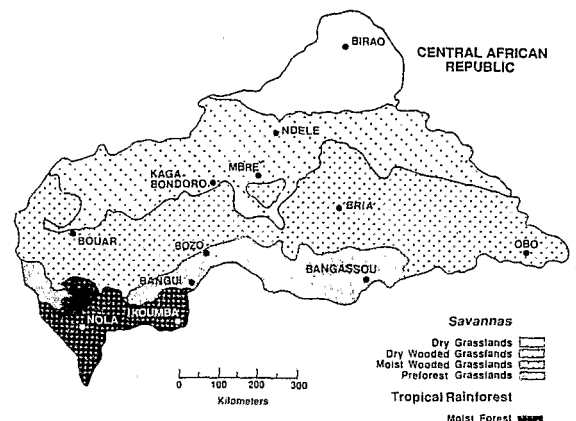

Figure. Map of the Central African Republic showing the main vegetation areas.

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dry grassland; dry wooded grassland; moist wooded grassland; pre-forest grassland; and moist forest (BOUL-VERT, 1980; GONZALEZ, 1986).

Survey populations

Blood samples were obtained from residents of each ecological zone. Detailed sero-surveys were conducted in the moist forest areas of Nola and Ikaumba, the pre-forest grassland of Bozo and Bangassou, the moist wooded grassland of Bouar and Obo, the dry wooded grassland near Mbre, and the dry grassland of Birao. Single villages were selected in areas such as Bozo and Bangassou where ethnic cultures have been amalgamated. Additional villages were surveyed, however, in areas of greater population heterogeneity, such as Nola, Ikaumba, and Birao, where multiple ethnic groups co-exist.

Survey villages were selected on the basis of accessibility. All village residents were informed of the motive and purpose of the research and only those who agreed to participate were included. If the residents of a chosen village refused, the participation of the nearest neighbouring village was solicited.

Sample collection

Study volunteers were interviewed and a form was completed documenting the individual's name, identification number, estimated age, sex, village of residence, length of residence, ethnic group, occupation, father's name, mother's name and husband's/wife's name. Venous blood was drawn aseptically from the antecubital fossa and allowed to clot overnight at 4°C. Serum was separated by centrifugation, dispensed into cryotubes and frozen in liquid nitrogen. After transport to the laboratory, the specimens were thawed, separated into aliquots, and refrozen at −20°C until re-thawed, diluted, and screened for virus reactive antibody.

Africa haemorrhagic fever viruses

The Mayinga strain (Zaïre isolate) and Boniface strain (Sudan isolate) of Ebola virus (EBOV), the Musoki strain (Kenya isolate) of Marburg virus (MBGV), the Josiah strain (Sierra Leone isolate) of Lassa virus (LV), the 10200 strain (Uganda isolate) of Crimean-Congo haemorrhagic fever virus (CCHFV), and the ZH501 strain (Egypt isolate) of Rift Valley fever virus (RVFV) were used to prepare serological reagents. Except for CCHFV and RVFV, working virus stocks were prepared as clari-fied Vero cell culture supernatant; CCHFV and RVFV were prepared as clarified, suckling mouse brain homogenates.

Immunofluorescent antibody test

An indirect immunofluorescent antibody test (IFAT), using inactivated monovalent and polyvalent spot slides of acetone-fixed virus and sham-infected or similarly prepared uninfected material, was used to detect and measure HFV reactive antibody activity (JOHNSON et al., 1981). Monovalent slides were prepared by mixing uninfected cells at a 10 to 1 ratio with cells infected with a single HFV. Polyvalent slides were produced by mixing equivalent numbers of sham-infected and HFV-infected cells.

Each serum batch contained coded known HFV antibody-positive samples and was tested 'double-blind'; neither the technician who performed the test nor the one worker who evaluated the fluorescent reactions had prior knowledge of the test specimens. The survey specimens were screened for HFV reactive antibody diluted 1:16, on polyvalent slides using fluorescein isothiocyanate-conjugated goat anti-human γ-globulin (PEDERSEN et al., 1983). Virus specificity was determined by re-screening each IFAT positive serum on a monovalent slide. Sera that reacted with infected but not uninfected monovalent cell preparations at a 1:16 or greater dilution were considered positive. The antibody level was determined by titrating the IFAT reactions on monovalent slides using 2-fold serial dilutions. Antibody titres were recorded as the reciprocal of the last clearly positive dilution. Questionable reactions were re-examined by the reviewer and technician and/or an outside observer. The tests were repeated when a consensus could not be reached. The few sera that produced inconclusive reactions on retesting were considered non-specific reactors.

Statistical analysis

The significance of differences between HFV antibody prevalence rate was determined by the χ^2 test (SNEDECOR & COCHRAN, 1969).

Results

A total of 4295 human specimens was collected from the 5 ecological zones of the Central African Republic. Completed interview forms were available for 94·4% (4074/4295) of the population surveyed. As expected from the latest available census records (1975), the ma-

Table 1. Distribution of Ebola virus and Marburg virus reactions among residents of the Central African Republic with anti-filovirus antibody

Ecological zone	Survey population No. with anti-filovirus antibody	No. positive by IFAT[a]				
		Strain specific			EBOV group	Family
		EBOVZ	EBOVS	MBGV	(EBOVZ/EBOVS)	(EBOV/MBGV)
Dry grassland	509	35 (7·0)	96 (19·1)	26 (4·2)	323 (64·0)	29 (5·7)
Dry wooded grassland	37	2 (5·4)	8 (21·6)	3 (8·1)	23 (62·2)	1 (2·7)
Moist wooded grassland	156	5 (3·2)	42 (27·2)	16 (10·3)	56 (35·4)	37 (23·4)
Pre-forest grassland	73	1 (1·4)	19 (26·4)	2 (2·7)	36 (50·0)	15 (20·8)
Moist forest	187	16 (8·6)	40 (21·4)	1 (0·5)	123 (67·9)	7 (0·6)
Total	962	59 (6·2)	205 (21·3)	48 (5·0)	561 (58·8)	89 (9·3)

[a]Indirect fluorescent antibody test: titres 1:16–1:4096. Virus strain-specific reactions, specimens which reacted with only one filovirus; EBOV group-specific reactions, specimens which reacted with both Ebola virus strains (EBOZ and EBOS); filovirus family-specific reactions, specimens which reacted with both Ebola virus (EBOV) and Marburg virus (MBVG). Numbers in parentheses represent precentages of seropositives demonstrating virus strain-specific or cross-reacting IFAT antibody.

Table 2. The distribution of filovirus-specific antibody titres in the indirect fluorescent antibody test (Central African Republic)

Test antigens[a]	IFAT reactions No. positive	Reciprocal antibody titres[b] 32–64	128–256	512–1024	2048–4096
Filovirus stain specific[c]					
EBOVZ	59	50 (84·7)	7 (11·9)	2 (3·4)	0 (–)
EBOVS	206	176 (85·4)	29 (14·1)	1 (0·5)	0 (–)
MGBV	48	32 (66·7)	13 (27·1)	2 (4·7)	1 (2·1)
Ebola virus group specific[c]					
EBOVZ	562	332 (59·0)	193 (34·3)	26 (4·6)	11 (2·0)
EBOVS	562	309 (54·9)	214 (38·1)	28 (5·0)	11 (2·0)
Filovirus family specific[c]					
EBOVZ	60	49 (81·7)	9 (15·0)	2 (3·3)	0 (–)
EBOVS	85	66 (77·6)	16 (18·8)	3 (3·5)	0 (–)
MBGV	89	89 (100)	0 (–)	0 (–)	0 (–)

[a]EBOVZ and EBOVS=Ebola virus strains Z and S; MGBV=Marburg virus.
[b]Numbers in parentheses are percentages.
[c]Specificities are described in Table 1, note a.

jority of residents tested were ≤20 years old. Few volunteers reported serious febrile illnesses or haemorrhagic disease in their villages. Reports of suspicious disease activity were vigorously investigated, but clinical HFV activity was not documented.

HFV antibody prevalence

Serological evidence of HFV activity was found in all ecological zones with only a minimal number of non-specific IFAT reactions (4·6%, 201/4295). The filovirus antibody prevalence (24·4%, 1051/4295) was greater than the combined prevalence for the other HFVs tested (1·1, 45/4295; $P<0·01$). The IFAT antibody prevalences for the non-filovirus African HFVs varied from <0·1 to 0·7%, and included 33 RVFV, 8 LV and 4 CCHFV antibody seropositives.

As a group, EBOVs seemed to be active in all ecological zones, with the highest activity in the dry grasslands (21·2%, 483/2284), moist wooded grasslands (26·8%, 140/522), and moist forest (23·0%, 186/807). Evidence of lower activity was found in the dry wooded (13%, 33/256) and pre-forest (16·4%, 71/426) grasslands. MBGV activity seemed to be limited, however, to the moist wooded and pre-forest grasslands (7·4%, 70/948; $P<0·01$). Lower activity was observed in the dry grasslands (2·4%, 55/2284), dry wooded grasslands (1·5%, 4/256), and moist forest (1·0%, 8/807).

Filovirus antibody prevalence

The majority of filovirus seroreactive specimens (86%, 825/962) reacted with EBOV and not with MBGV antigens (Table 1). Sixty-eight percent (561/825) of the EBOV reactive samples reacted with both EBOVZ and EBOVS viral antigens and were considered seropositive for EBOV group specific antibody. The percentages of EBOV group reactives in the dry grasslands and moist forest were higher than in any other zone ($P<0·01$). Broad filovirus family (EBOV and MBGV) reactions were observed in 9·3% of the seropositive samples.

Filovirus strain (EBOVZ, EBOVS, or MBGV) specific responses were also observed (Table 1). Previously, EBOVS specific serological reactions in field surveys have been rare, with strain specific reactions having been against EBOVZ antigens exclusively (BLACKBURN et al., 1982; IVANOFF et al., 1982). The EBOV strain-specific responses were not restricted to a single ecological zone.

The frequency of MBGV specific IFAT reactions in different ecological zones ranged from 0·5% in the moist forest to 10·3% in the moist wooded grassland zone. The low frequency of MBGV reactive antibody in the moister forest and pre-forest areas suggested that MBGV activity may be rare in the tropical forests of central Africa. Similarly, in eastern and southern Africa fatal human MBGV

infections have occurred predominantly in dry wooded grassland habitats (SMITH, D. I. H. et al., 1982; SWANEPOEL, 1987; JOHNSON, E. D. et al., 1993).

The distribution of filovirus IFAT titres (Table 2) was similar to that in areas of Central and West Africa where HFV activity was confirmed by virus isolation from clinical cases (McCORMICK et al., 1987). Two-thirds (1099/1671) of the positive serological reactions had relatively low titres (≤64), but the remainder often reached 2048. The distribution of antibody titre differed for the 3 filovirus reaction patterns; 43% (487/1124) of the EBOV group but only 15·5% (85/547) of the strain and family specific reactions had high titres ($P<0·01$). The endpoint dilutions for EBOVZ and EBOVS reactions in the EBOV group-specific specimens were within-2- to 4-fold dilutions. Monospecific MBGV sera tended to have high titres; 33% (16/48) of the monospecific MBGV sera had titres ≥128.

Age and sex were important host-related factors influencing filovirus antibody prevalences, particularly in the case of EBOV. The prevalence of high titre (≥128) EBOV antibody increased with age. Older females and males had higher EBOV antibody prevalences than younger people of the same sex (Table 3). Young females

Table 3. Sex and age distribution of individuals with high titres (≥1:128) in the indirect fluorescent antibody test against Ebola and Marburg viruses in the Central African Republic

Sex and age (years)	Survey population Total	No. positive (≥1:128)[a] EBOV	MBGV	Total
Female				
1–20	927	73 (7·9)	4 (0·4)	77 (8·3)
21–40	672	76 (11·3)	5 (0·7)	81 (12·1)
≥41	333	50 (15·0)	8 (2·4)	58 (17·4)
Male				
1–20	1186	43 (3·6)	7 (0·6)	50 (4·2)
21–40	560	55 (9·8)	3 (0·5)	58 (10·4)
≥41	400	38 (9·5)	1 (0·3)	39 (9·8)

[a]Numbers in parentheses are percentages. EBOV=Ebola virus, MBGV=Marburg virus.

had a higher prevalence than young males; the female and male prevalences become equivalent in the 21–40 years age group ($P=0·45$). Although EBOV reactive antibody prevalences were higher for females than for males in all ecological zones except the dry wooded grasslands, statistically significant differences ($P<0·01$) between the sexes were observed in the dry grasslands only ($P<0·01$) (Table 4). Antibody prevalence rates were consistently higher in older than younger populations (Table 5). Stat-

Table 4. Sex distribution of individuals with high titres (≥1:128) in the indirect fluorescent antibody test against Ebola and Marburg viruses in the different ecological zones of the Central African Republic

Ecological zone	Sex	Survey population Total no. surveyed	No. positive (≥1:128)[a] EBOV	MBGV	Total
Dry grassland	Female	1071	128 (12·0)	11 (1·0)	139 (12·6)
	Male	1099	85 (7·7)	7 (0·6)	92 (8·4)
Dry wooded grassland	Female	99	3 (3·0)	0 (–)	3 (3·0)
	Male	156	5 (3·2)	1 (0·6)	6 (3·8)
Moist wooded grassland	Female	226	17 (7·5)	3 (1·3)	20 (8·8)
	Male	295	13 (4·4)	3 (1·0)	16 (5·4)
Pre-forest grassland	Female	195	7 (3·5)	4 (2·0)	11 (5·6)
	Male	210	1 (0·5)	1 (0·5)	2 (1·0)
Moist forest	Female	381	41 (10·8)	1 (0·3)	42 (11·0)
	Male	418	32 (7·6)	0 (–)	32 (7·6)

[a]Numbers in parentheses are percentages. EBOV=Ebola virus, MBGV=Marburg virus.

Table 5. Age distribution of individuals with high titres (≥1:128) in the indirect fluorescent antibody test against Ebola and Marburg viruses in the different ecological zones of the Central African Republic

Ecological zone	Survey population Age (years)	Total surveyed	No. positive (≥1:128)[a] EBOV	MBGV	Total
Dry grassland	1–20	1286	67 (5·2)	7 (0·5)	74 (5·8)
	≥21	844	131 (15·5)	10 (1·2)	141 (16·7)
Dry wooded grassland	1–20	108	3 (2·8)	0 (0·0)	3 (2·8)
	≥21	137	5 (3·6)	1 (0·7)	6 (4·4)
Moist wooded grassland	1–20	152	7 (4·6)	2 (1·3)	9 (5·9)
	≥21	370	23 (6·2)	4 (1·1)	27 (7·3)
Pre-forest grassland	1–20	224	7 (3·1)	1 (0·4)	8 (3·6)
	≥21	196	9 (4·6)	1 (0·5)	10 (5·1)
Moist forest	1–20	360	25 (6·9)	0 (0·0)	25 (6·9)
	≥21	432	53 (12·2)	1 (0·2)	54 (12·5)

[a]Numbers in parentheses are percentages. EBOV=Ebola virus, MBGV=Marburg virus.

istically significant differences were observed also between younger and older inhabitants of the dry grassland ($P<0.01$) and moist forest ($P<0.05$). There was no statistically significant difference between young and old human populations in the MBGV specific seropositive populations.

Discussion

Our results demonstrated that filovirus infections were common among residents of the Central African Republic. Virus activity in diverse environments of equatorial Africa is influenced by sex and/or age related factors. The infections appear to occur without apparent overt disease, suggesting that the African filoviruses may be less pathogenic in their natural settings than commonly thought. Most human filovirus disease has been described in epidemic settings, which may involve atypical modes of exposure (SIEGERT, 1970; JOHNSON, 1978; SMITH, D. I. H., 1978).

Serological evidence of filovirus activity has been recorded consistently for high risk groups in diverse ecological zones of central Africa since 1984 (MEUNIER et al., 1987). The majority of the filovirus seropositives identified in our study expressed EBOV group specificity, reacting with both the Zaire and Sudan EBOV strains. These observations are the first field serosurvey results supporting earlier findings indicating that EBOV exposure leads to broad filovirus group specific serological responses in humans (JOHNSON et al., 1978; WEBB et al., 1978; RICHMAN et al., 1983).

The finding that only 27·4% of the seropositive specimens we examined exhibited EBOV strain specific re-

activity was unexpected (Table 1), though numerous EBOVZ strain specific responses have been reported by others (BLACKBURN et al., 1982; IVANOFF et al., 1982). The concept of mild immunizing EBOV infections has been difficult to accept in view of the high mortality and very low incidence of mild or subclinical infections observed during the Zaïre epidemic (JOHNSON, 1978).

The virus specific reactions in our study may reflect distinct EBOV strain activity. If these antibodies are the results of a single exposure to one of the African EBOV strains, the resulting antibody response is of low titre (Table 2; <1:64 in 85% of subjects). Furthermore, the high EBOV group reactive antibody prevalence, which was greater than would be expected from the fraction of monospecific or EBOV strain specific reactions in the population tested, suggests that the EBOVs do not circulate independently and that our study population shares common risk factors for exposure to the 2 viruses.

An alternative interpretation of our data could be that EBOV infections induce the formation of group reactive antibody of varying specificities depending upon the virus strain, nature of exposure, and host reactivity. Virus specific reactions would, therefore, reflect a past infection in which the heterologous strain responses have decayed unequally, and EBOV group reactives would represent a recent infection. The latter interpretation, which we favour, is supported by the observation that non-fatal EBOV infections during the Zaïre outbreak frequently caused the production of short-lived, relatively high-titre (JOHNSON et al., 1978) and cross-reactive antibody (WEBB et al., 1978; RICHMAN et al., 1983).

Finding filovirus antibody seropositives demonstrating

both EBOV and MBGV sero-reactivity was also unexpected. This may be a consequence of multiple filovirus exposures among a small group of Central African Republic inhabitants. The distribution of MBGV antibody titres may support the possibility of recurring filovirus infections. MBGV reactions accompanied EBOV antibodies in a higher proportion than expected from the number of EBOV or MBGV monospecific reactors in the study group. In contrast to the situation with EBOV group reactions, none of the filovirus family reactions had high titres of MBGV reactive antibody, while 33% (16/48) of the MBGV specific responses were greater than, or equal to, 128. This may reflect the lack of a detectable serological relationship between MBGV and EBOV (WEBB et al., 1978; RICHMAN et al., 1983).

The frequency of low filovirus antibody titres often observed in African HFV sero-surveys deserves comment; 0·3% (3/996) and 0·5% (1/200) of human samples collected in non-endemic areas, France and Panama (J. P. Gonzalez et al., paper in preparation; VAN DER GROEN et al., 1978), respectively, had low antibody titres to Ebola virus. These low prevalences and low titre (≤1:64) reactions in populations without an African exposure history suggest that some of the low titre filovirus sero-reactives observed in our survey were false positives. However, the distribution of EBOV IFAT titres (Table 2) is similar to that observed during sero-surveys in regions of Central and West Africa where HFV activity has been confirmed by virus isolation from clinical specimens (McCORMICK et al., 1987). Our conclusion, that filovirus activity has occurred in the Central African Republic, is unchanged by basing it on only high titre (≥128) IFAT reactions. At least 11·2% of the female and 6·8% of the male populations have been exposed (Table 3). Age specific prevalence rates for the 1–20 years old age group suggest that young females are exposed more frequently than are males of the same age group (P<0·01). The statistically significant differences between female and male EBOV reactive antibody prevalences observed in our study are not unique, similar observations having been made during sero-epidemiological studies in northern Zaïre (HEYMANN et al., 1980).

Filovirus activity in the Central African Republic was not limited to a specific habitat. Serological evidence of human infection was found in all ecological zones, though MBGV infections were rare in the dense forest. This contrasts with the previous report of EBOV antibodies being confined to forest populations (JOHNSON, 1978; SMITH, D. I. H., 1978; VAN DER GROEN et al., 1978). The observation that filovirus family specific seropositives occurred among grassland populations where EBOV and MBGV co-exist may indicate the presence of a unique human population expressing cultural or behavioural risk factors for both EBOV and MBGV infections or filovirus re-infections (Table 1). The variation in antibody prevalence between ecological zones may indicate the importance of host-related factors in regulating human filovirus exposures rather than differential circulation of filoviruses. Unfortunately, the putative risk factors were not identified due to the low frequency (2·4%) of filovirus family specific seropositives among diverse grassland populations.

Sex and/or age were clearly identified as important risk factors for filovirus infections in both dry grassland and moist forest communities (Tables 4 and 5). Communities in these ecological zones differ from those in the more centrally located wooded grasslands. Rural communities of the less populated far northern and southern zones are geographically isolated with little influence from outside factors, and people in these communities interact closely with their immediate natural environment without causing dramatic changes in the ecosystem. The high filovirus prevalence in females (Table 4) suggests that filovirus exposure may be a notable health risk for women living in the Central African Republic. Subsistence activities are a primary responsibility of rural women; men spend less time on them (HEWETT, 1991). Young and old women share a close association with the family compound and fields. Males (>6 years old) associate less with the family compound or crops (MURDOCK & PROVOST, 1973). The high filovirus prevalence among young women (Table 3) suggests that filovirus exposure may occur within the family compound. The prevalence of filovirus antibody in guinea-pigs maintained as a supplemental food source in kitchen huts in Zaïre (STANS-FIELD et al., 1982) may support this view.

The significance of similar antibody prevalences in the remote northern and southern regions of the Central African Republic must be interpreted carefully. The grassland and forest zones share many factors, but there are significant differences in agricultural practices and ethnic backgrounds, which may also affect risk (BAUREE & BERGMANN, 1983). The grassland survey population consisted of cultivators and/or pastoralists. The forest communities were comprised of agriculturalists and hunter-gatherers; subsistence farmers infrequently hunt and hunter-gatherers seldom cultivate vegetable foods.

Although our sero-epidemiological surveys clearly documented non-fatal filovirus infections, the results do not resolve the paradox of significant antibody prevalence for the highly virulent filoviruses without demonstrable disease in Central Africa. Continued surveillance and intense epidemiological investigations are needed to evaluate the true pathogenicity of the African filoviruses and the likelihood that unidentified, serologically cross-reacting and non-pathogenic members of the filovirus family are present in the region (MEUNIER et al., 1987). The recent isolation of a presumptive Asian filovirus from Philippine monkeys (Macaca fascicularis) emphasizes the possibility that additional filoviruses may be active also in sub-Saharan Africa (JAHRLING et al., 1990); these viruses could resemble the newly isolated strain in being serologically cross-reactive with, but distinguishable from, the Zaïre and Sudan EBOV strains and less pathogenic for man. Based upon our results, the search for Ebola annd Marburg viral infections in central Africa should be conducted in non-urban moist forest and dry grassland communities where serological evidence suggests frequent but non-fatal infections. The probability of successfully resolving the paradox may be increased by focusing upon defining the relationship between filovirus sero-reactivity and sex-specific subsistence strategies practised in equatorial Africa.

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