The worldwide distribution of Crimean-Congo hemorrhagic fever (CCHF) virus has been demonstrated in association with epizootic transmission during May 1988 near the Senegal River border. IgG antibodies were detected at various slaughterhouses in Senegal during the late 1960s. The seroprevalence among sheep and humans in the Senegal River border area was highest. The abundance of Hyalomma sps., ticks predominated in those biotopes where antibody prevalence was highest. The abundance of Hyalomma ticks may be the proximal determinant of endemic transmission.

Factors that influence transmission of CCHF virus include the density of competent vector ticks, particularly of the genus Hyalomma, and the abundance of vertebrates that serve as hosts to these ticks and as possible reservoirs of the virus. At least 30 species of ticks have been shown to be infected. Sustained transmission is found only where Hyalomma ticks are present, and epizootic or epidemic transmission is believed to occur during periods of increased abundance of these ticks. However, the relationship between tick species diversity and the magnitude of CCHF virus transmission within a particular geographic region has not been studied systematically.
compared with various bioclimatic variables and the relative abundance of ixodid ticks.

MATERIALS AND METHODS

Animal serology

Blood samples from sheep throughout Senegal were obtained as part of a project initiated by l’Institut Senegalais de Recherches Agricoles (ISRA). The country was divided into 80 sample districts of approximately equal areas that corresponded to 1 or more governmental administrative districts. Of these sample districts, 26 were randomly chosen for study. The number of animals sampled in each district was predetermined at 1:3,000 of the estimated resident sheep density, which had been calculated previously from a government census undertaken by personnel of ISRA. Villages from the interior of each district were chosen and flocks were selected randomly. In large flocks, 10–20 sheep were bled; in small flocks, all sheep were bled until the predetermined sample size for that district was achieved. Between November 1986 and January 1987, sheep from 26 sample districts in 9 of Senegal’s 10 governmental regions were bled. The sex and age for each animal were recorded. Sheep were categorized into 4 groups based on age estimated by dental examination: <14 months, 14–28 months, 29–36 months, and >36 months. Blood samples were centrifuged and sera were stored at −20°C in the field and later tested at the Pasteur Institute in Dakar.

Sera were examined for evidence of IgG to CCHF virus using a direct ELISA modified slightly by adding a saturating solution of PBS with 0.05% Tween 20 and 1% non-fat bovine milk. Ninety-six well plates (Immulon II, Dynatech Laboratories Inc., Alexandria, VA) were coated with 100 μl of diluted CCHF virus hyperimmune mouse ascitic fluid produced against CCHF virus strain 1AB1020 from Sokoto, Nigeria. Sera were tested against 2 local CCHF virus strains: Dak H49199, isolated in 1988 from a human in the Ross, Mauritania; and Ar 43396, isolated in 1996 from a Hyalomma marginatum rupes collected in 1985 in Yonofere, Senegal. The identity of these strains was confirmed by complement fixation at the WHO Collaborating Center for Arbovirus Reference and Research at the Pasteur Institute in Dakar. CCHF virus in crude sucking mouse brain was heat inactivated (1 hr, 60°C); 100 μl CCHF virus suspension was added followed by 100 μl of test sera, diluted 1:400 in ELISA buffer. Then 100 μl of test-species-specific anti-gamma-chain immunoglobulin conjugated with horseradish peroxidase (Biodyne, Compiegne, France) was added to detect the IgG. Finally, 100 μl of chromogenic substrate (orthotolidine, Sigma, LaVerpilliere, France) was added for colorimetry. All plates included a control of crude sucking mouse brain without CCHF virus antigen. Differences in optical density (OD) between the test and control wells were measured at 450 nm using an automatic reader (Titertek, Multiscan MCC/340, Flow Laboratories, Irvine, Scotland) coupled to a microcomputer. By iteration of the distribution of OD values, we determined the mean of the population of negatives. Sera were considered positive if the OD was >3 SD above the mean of negatives.

The specificity of this test was examined by using Doghe, Bandia, and Bakel viruses as antigens, the 3 other major flaviviruses that have been frequently isolated in Senegal and identified at the WHO Collaborating Center for Arbovirus Reference and Research. These viruses were tested against sera from a sheep inoculated with CCHF virus, a large sample of wild sheep that had tested positive against CCHF virus, and 3 human infections from which CCHF virus had been isolated.29 Virtually no cross-reaction was observed and the few weak positives were eliminated by diluting sera to 1:400.

Human serology

Human blood samples were collected during 1986–1988 from 8 different sites in Senegal and southern Mauritania. In addition to 1 sample from Yonofere, Dakar, Bandia, and Kedougou, we tested sera collected as part of other studies from Dagana and Ziguinchor by Alain Jouan, from Tambacounda by Jean-François Saluzzo, and from Senegal by Elizabeth Mass. Details of the sampling methods varied among the sites; however, all blood was obtained by venipuncture from apparently healthy people who were asked to donate for medical research. Blood was held from 1–4 days at ambient temperatures and sera was frozen at −20°C and later tested as above.

Distribution of ticks

The relative abundance and distribution of ixodid ticks was determined from our systematic samples of domestic ungulates25 combined with similar data from Gueye and others25–27 that were reanalyzed for this purpose. Ticks were detached from sheep, goats, or cattle monthly for 1 year in order to avoid bias due to seasonal variation in tick activity. We sampled 3 sites in northern Senegal: Yonofere, Dahra, and Bandia. In Yonofere, 5 flocks of sheep were chosen monthly by chance encounter from May 1987 through May 1988 and 10 randomly selected individuals from each herd were sampled. All ticks were removed with forceps and stored for later identification. The same methods were used in Dahra from May 1987 through August 1989. In Bandia, 12 sentinel goats and 2 cows were examined similarly 3 times each month from April 1987 through March 1989.

Published data from other sites in Senegal23–27 were reanalyzed to make them consistent with our methods. We calculated the mean number of adult ticks per host from monthly samples of 40 cattle, sheep, or goats for 12 consecutive months during 1985–1989. Because these ticks differ somewhat in their propensity for feeding on the 3 hosts, we transformed the data from all 7 sites to qualitative values that represent the relative abundances of each tick species among the sites. Each tick was categorized as either very abundant (≥2 ticks/host), moderately abundant (0.1–2 ticks/host), rarely (rarely (0.1–2 ticks/host), extremely rare (a few encounters), or absent.

Data analysis

Serological results for sheep were analyzed using x2 test with continuity correction, linear correlation analysis, and curve fitting from the Microtest 4.1 statistical software.

RESULTS

Animal infection

A total of 10.4% of sheep were found positive for IgG to CCHF virus from the 942 sera tested. Prevalence varied in seropositive sera was similar for rams and ewes (Fig. 1) in each region where infection was observed. Furthermore, a comparison of village rates using multiple stepwise regression of mean age, sex ratio, and number sampled regress against IgG prevalence rates revealed a correlation solely with age (r2 = 0.10, P = 0.016). Furthermore, rams and ewes showed equal evidence of past infection among each of the 4 age categories and within each governmental region (all P values >0.10).

Antibody prevalence increased with age. Only 21.6% of the youngest animals (aged <14 months) tested positive, whereas 18.2% of the oldest sheep (≥3 years) were seropositive. This age-related increase in seropositivity was similar for rams and ewes. Antibody prevalence was lowest in younger sheep. Evidence of CCHF virus transmission varied among governmental regions and sample districts. Average antibody prevalence among the 22 sample districts appeared highest in northern Senegal and decreased to nil in the

<table>
<thead>
<tr>
<th>Region</th>
<th>No. villages sampled</th>
<th>No. sheep sampled</th>
<th>Ratio male/female</th>
<th>IgG prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Louis</td>
<td>2</td>
<td>37</td>
<td>1:3.3</td>
<td>75.7</td>
</tr>
<tr>
<td>Louga</td>
<td>7</td>
<td>78</td>
<td>1:10.1</td>
<td>10.3</td>
</tr>
<tr>
<td>Thiès</td>
<td>3</td>
<td>48</td>
<td>1:2.4</td>
<td>0</td>
</tr>
<tr>
<td>Fatick</td>
<td>3</td>
<td>41</td>
<td>1:7.2</td>
<td>9.1</td>
</tr>
<tr>
<td>Koalack</td>
<td>3</td>
<td>65</td>
<td>1:4.9</td>
<td>4.6</td>
</tr>
<tr>
<td>Tambacounda</td>
<td>2</td>
<td>20</td>
<td>1:4</td>
<td>0</td>
</tr>
<tr>
<td>Kolda</td>
<td>4</td>
<td>12</td>
<td>1:3.3</td>
<td>0.16</td>
</tr>
<tr>
<td>Ziguinchor</td>
<td>3</td>
<td>37</td>
<td>1:7.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Totals</td>
<td>66</td>
<td>942</td>
<td>1:4.7</td>
<td>10.4</td>
</tr>
</tbody>
</table>
between November 1986 and January 1987. Sheep from the 4 governmental regions where antibodies were found are included. Number of sheep in sample is shown at the base of each bar.

southern part of the country. Evidence of past infection was compared to vegetation and climatic characteristics by dividing the country into 5 bioclimatic zones. Sheep from the northernmost Sahelian zone averaged 75.7% seropositivity, a proportion that decreased to 0% in the southernmost Sudan-Guinean and sub-Guinean zones (Table 2). Similar analyses of 6 geological formations, 4 altitude ranges, 6 soil types, and 3 levels of sub-surface water revealed no relationships. The sole physical characteristic that correlated with our measure of CCHF virus seroprevalence was that which defined bioclimatic zones.

Because rainfall alone constitutes a principal determinant of the bioclimatic zones of West Africa, we compared antibody prevalences with precipitation. Sheep were grouped according to the mean annual rainfall (100 mm ranges) of the village from which they were bled. Antibody prevalence systematically increased as annual rainfall declined (Fig. 3). Within Senegal, increased precipitation correlated negatively with evidence of more active transmission of CCHF virus. The predominant ticks sampled throughout the north and lowest in the south, a pattern that corresponded to that found in the sheep.

Spatial distribution of potential vectors

The predominant ticks sampled throughout the country were *Hyalomma* species, particularly in the north (Table 3). Indeed, *H. truncatum* was abundant throughout the northern sites, as was *H. m. rufipes* in north-central Senegal. In addition, *Rhipicephalus guilhoni*, considered synonymous with *R. sanguineus* before 1962, was also abundant in the north. These ticks became progressively less abundant in the semi-arid Sudanian zone and the more humid habitats of the Guinean zone, being replaced by other *Rhipicephalus* species, *Boophilus species*, and *Ambytoma variegatum*. In general, each species of tick was relatively more abundant in only 1 or 2 bioclimatic zones.

**Human infection**

Human IgG prevalence varied by as much as an order of magnitude among the villages sampled (Table 2). In northern sites along the Senegal River, 11.3% of people from Rosso and 5.5% of people from Dagana were seropositive. In the northcentral Sahel plains, 4.7% and 21.1% of residents from Dahra and Yonefere exhibited IgG, respectively. In Bandia, further south along the coast, 3.2% of adults tested showed evidence of previous infection. Low IgG prevalence was found in southern sites, including 1.2% in Tambacounda, 0.9% in Kedougou, and 0.7% in Ziguinchor. The prevalence of IgG was highest in the north and lowest in the south, a pattern that corresponded to that found in the sheep.

**DISCUSSION**

The prevalence of IgG to CCHF virus in sheep varied among sites from high to none, indicating...
that transmission was either spatially focal or temporally sporadic. In some sites, IgG prevalence was such that half of all sheep could be infected during their lifetime. In other nearby villages, however, little evidence of recent virus infection was found despite apparent similarities in local ecology. We previously demonstrated a similar spatial heterogeneity in antibody prevalence among nearby villages may indicate that similar spatial heterogeneity in antibody prevalence may also occur elsewhere in Africa. 

Such variation in antibody prevalence of CCHF virus among domestic sheep, cattle, and goats is based on our observations in Dobra, Yanofere, and Bandia and on data previously published from studies by Chunikhin. 

**TABLE 3**

<table>
<thead>
<tr>
<th>Tick species*</th>
<th>Dobra</th>
<th>Yenouve</th>
<th>Louga</th>
<th>Niayes</th>
<th>Bandia</th>
<th>Tambacounda</th>
<th>Kolda</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. truncatum</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>H. impeltatum</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>H. m. rufipes</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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</tr>
<tr>
<td>H. impressum</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td>H. dromedarii</td>
<td>+++</td>
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<tr>
<td>R. antilopii</td>
<td>+++</td>
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<td>+++</td>
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<tr>
<td>R. e. evertsi</td>
<td>+++</td>
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<tr>
<td>R. sunegetensis</td>
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<tr>
<td>R. lundatus</td>
<td>+++</td>
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<tr>
<td>R. muhsamiae</td>
<td>+++</td>
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<td>+++</td>
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<tr>
<td>A. varigatum</td>
<td>+++</td>
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<tr>
<td>B. decoloratus</td>
<td>+++</td>
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<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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</tr>
<tr>
<td>B.olgii</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
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<td>+++</td>
<td>+++</td>
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</tr>
</tbody>
</table>

* Oron unc H. truncatum, H. impeltatum, H. m. rufipes, and H. impressum. 

Relative abundances of adult ixodid ticks on domestic sheep, cattle, and goats in selected sites and bioclimatic zones in Senegal. 

Human seroprevalence varied considerably. In northern Senegal, 2-3% of people showed evidence of previous CCHF virus infection. An antibody prevalence of 1% was found in Bandia, 0.1% in the Sahelian zone of Senegal, and 0.0% in the Guinean zone of Senegal. A similar bioclimatic relationship has been observed elsewhere in Africa, Eurasia, and the Middle East, where the prevalence of CCHF virus infection is generally lower than that of sheep, even though the average age for sheep was <2 years. However, the spatial pattern of human seroprevalence varied in a manner similar to that of sheep. Presumably, the spatial pattern of CCHF virus infection is influenced by local migration. 

Nomadic migration may have affected some of our results. Principally undertaken by certain young men in northern Senegal who herd their animals in search of food, such activity is irregular and occurs during only part of the year. Such movement by a small subpopulation of the population, however, would not be likely to have a major influence on the observed spatial variation. Indeed, such migration, when it occurs, also increases the risk of exposure to questing ticks, thereby elevating the prevalence of infection. 

**Relative prevalence for sheep, cattle, and goats in selected sites and bioclimatic zones in Senegal.** 

Because of their relatively low life-span as compared with that of humans, sheep may serve both as an index of recent transmission and as an index of recent infection in sheep. Presuming that human IgG remains detectable for many years, risk of infection among people who herd sheep appears to be greater than that for people. Because of their relatively low life-span as compared with that of humans, sheep may serve both as an index of recent transmission and of the spatial distribution of human risk. 

Human seroprevalence varies considerably. In northern Senegal, 2-3% of people showed evidence of previous infection. An antibody prevalence of 1% was found in Bandia, 0.1% in the Sahelian zone of Senegal, and 0.0% in the Guinean zone of Senegal. A similar bioclimatic relationship has been observed elsewhere in Africa, Eurasia, and the Middle East, where the prevalence of CCHF virus infection is generally lower than that of sheep, even though the average age for sheep was <2 years. However, the spatial pattern of human seroprevalence varied in a manner similar to that of sheep. Presumably, the spatial pattern of CCHF virus infection is influenced by local migration. 

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**Relative prevalence for sheep, cattle, and goats in selected sites and bioclimatic zones in Senegal.** 

Because of their relatively low life-span as compared with that of humans, sheep may serve both as an index of recent transmission and of the spatial distribution of human risk.
sheep in southern Senegal, low-level transmission was suggested by the presence of human antibodies, and by the previous results of Chuûikhit and others4 showing tick infestations in the southeastern Senegal. Indeed, cattle may represent a more sensitive indicator of low level CCHF virus circulation, as they can be infected more readily than sheep.5 Similarly, low-level transmission was reported from those areas with antibodies. Indeed, cattle are often considered to be the main reservoir of CCHF virus and to be the main source of infections among people there was only 1.5%.6 In conclusion, the presence of CCHF virus in remote villages may go unreported or may be reported without etiology. Thus, understanding the significance of these severe disease fatalities in the region is essential. Moreover, CCHF virus appears to be weakly- or non-pathogenic to domestic ungulates, and is rarely diagnosed in humans, only large-scale epidemiological studies will be able to expose the true intensity of virus circulation. More systematic, prospective serological studies and intensive tick surveillance to the etiological agent in hemorrhagic fever cases may reveal widespread transmission of CCHF virus and its true frequency as a cause of human morbidity and mortality.

Acknowledgments: We thank Jean-Pierre Digoutte and Arna Gueye for their cooperation in this study. Robert Sylla and Magaye Ndiaye provided expert technical assistance. Louise E. Ciopean and Elizabeth A. Dykstra offered useful suggestions regarding the manuscript.

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Reprint requests: Mark L. Wilson, Department of Tropical Public Health, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115.

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BOOKS REVIEWED


I hate to tell people that I am a parasitologist because I always get the same responses. Most often the person I'm talking to changes the subject, since he probably has no idea of the functions of a parasitologist. The second most common response is, "It must be really fascinating to study ESP." Sometimes, the person has had a stool examination at one time, and thinks that parasitologists spend all their time looking at feces. These people usually ask me what made me decide to choose such an "interesting" career. I used to have trouble answering this question. Well, not anymore. Now I simply tell them to read Ben Kean's book.

I count myself among the 5,000 or so Cornell Medical School students who have heard Kean lecture on parasitology. Some teachers of parasitology give dense, detailed lectures about life cycles, epidemiology, symptomatology, and control. Not Ben Kean. He tells stories. Out of a 50 minute lecture period, he may tell anecdotes for 40 minutes and then show a life cycle picture he painted of a strange and primitive, yet critically important, field. It was during one of his lectures that I decided to become a parasitologist.

This book contains Kean's best parasite stories. He recounts in detail, for example, his experiences with an elderly uranium baron and his entourage (including a voluptuous blond mistress named "Baby") as the boss is purged of a tapeworm. And how he was caught by a female physician while watching a movie starlet gyrate nude in an attempt to make her acquir dizzy.

There are also fascinating medical detective stories, such as how he discovered the cause of an epidemic of trichinosis among telephone company employees and the cause of an epidemic of toxoplasmata among medical students.

Kean's non-tropical adventures are equally amusing and interesting. There are wonderful sections about post-war Germany and about the Shah of Iran (his patient), which give a doctor's perspective on important historical events. He tells about his meeting with FDR to discuss whether sharks really ate drowned airmen and his debilitating attack of vertigo just prior to his meeting with the Pope. And his stories about his famous patients, such as Salvador Dali, Oscar Hammerstein, Martina Navratilova, and Frank Locolser, are funny and touching (this chapter could have been entitled "Feces of the Rich and Famous").

Kean was born in Indiana and grew up in Greenwich Village. After finishing his medical training, he spent the war years as a pathologist at the Gorgas Memorial Laboratory in Panama and several years after the war in the U.S. military as a health officer in Germany. He returned to New York and began a double life as a physician on Park Avenue and a professor in academia. In both worlds, Kean has had a knack for adventure, and he has collected some truly fascinating and funny anecdotes in this book.

STEPHEN R. MESHACK
DEPARTMENT OF MICROBIOLOGY
CITY COLLEGE OF NEW YORK
MEDICAL SCHOOL
NEW YORK, NEW YORK 10031

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