An Investigation of a Major Outbreak of Rift Valley Fever in Kenya: 2006–2007

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Abstract. An outbreak of Rift Valley fever (RVF) occurred in Kenya during November 2006 through March 2007. We characterized the magnitude of the outbreak through disease surveillance and serosurveys, and investigated contributing factors to enhance strategies for forecasting to prevent or minimize the impact of future outbreaks. Of 700 suspected cases, 392 met probable or confirmed case definitions; demographic data were available for 340 (87%), including 90 (26.4%) deaths. Male cases were more likely to die than females, Case Fatality Rate Ratio 1.8 (95% Confidence Interval [CI] 1.3–3.8). Serosurveys suggested an attack rate up to 13% of residents in heavily affected areas. Genetic sequencing showed high homology among viruses from this and earlier RVF outbreaks. Case areas were more likely than non-case areas to have soil types that retain surface moisture. The outbreak had a devastatingly high case-fatality rate for hospitalized patients. However, there were up to 180,000 infected mildly ill or asymptomatic people within highly affected areas. Soil type data may add specificity to climate-based forecasting models for RVF.

INTRODUCTION

On December 14, 2006, during a period of unusually heavy rainfall and flooding, a livestock herdsman in Northeastern Province, Kenya was hospitalized at Garissa Provincial Hospital with a 2-day history of fever, hematemesis, and hematechezia. He died 2 days later. By December 20, 12 patients had been admitted to the same hospital with fever and bleeding manifestations and without evidence of malaria; 11 died. Rift Valley Fever (RVF) virus RNA or immunoglobulin M (IgM) antibodies against RVF virus were detected in blood or serum specimens from 10 of the patients during laboratory testing at the Centers for Disease Control and Prevention-Kenya Medical Research Institute (CDC-KEMRI). Testing was negative for a variety of other potential etiologies of severe febrile illness. Subsequently, the cause of the outbreak was confirmed by isolation of RVF virus from blood specimens.

In humans, RVF is an acute, febrile zoonotic disease caused by a phlebovirus belonging to the family *Bunyaviridae*.¹ Humans acquire RVF through exposure to the blood, body fluids, or tissues of infected animals, or through bites from infected mosquitoes or, potentially, other biting insects.^{2,3} Direct exposure to infected animals can occur during handling and slaughter or through veterinary and obstetric procedures.^{4–6}

The RVF virus was first described in Kenya in 1931.⁷ Major epidemics have been reported in Egypt (1977), Kenya (1997–1998), Saudi Arabia (2000–2001), and Yemen (2000–2001).^{8–11} Most infections result in no symptoms or in mild illness.¹² It is generally felt that 1–3% of patients with RVF develop severe disease including generalized hemorrhagic syndromes, encephalitis, and death, although attack rates for severe disease of up to 8% have been reported^{13,14}; in addition, 1–20% of patients develop ocular complications, including retinitis, leading to scotomata and other visual disturbances.^{10,12,15,16}

During the 4 months after the initial detection of the outbreak, several hundred additional cases were confirmed in Northeastern Province and additional clusters of cases occurred in 18 districts within 6 of 8 provinces in Kenya.¹⁷ Livestock deaths and abortions were noted within the same provinces. This report describes the magnitude and geographic scope of the outbreak and characterizes epidemiologic, ecologic, and virologic features of the epidemic in Kenya.

METHODS

The Kenya Ministry of Health (MoH) established nationwide surveillance for RVF, initially with intensified efforts in Northeastern Province. The Kenya Ministry of Health operates a national surveillance system for epidemic prone diseases and vaccine preventable diseases, known as Integrated Disease Surveillance and Response (IDSR). During the outbreak, IDSR surveillance officers in all districts of Kenya were informed about RVF and encouraged to report suspect or probable cases. The MoH teams were dispatched to areas where RVF cases were occurring. Because of the high degree of flooding in this normally arid area (Figure 1), many areas were inaccessible by ground transport and a helicopter provided by the World Food Program was used to move epidemic response teams and supplies.

Case definition and case detection. The MoH defined a suspect case of RVF as any person presenting since November 2006 with an acute febrile illness ($> 37.5^{\circ}\text{C}$ for > 48 hours), not responding to antimicrobial drugs or anti-malarial therapy in a district where human or livestock RVF was confirmed. A probable case was defined as a patient with fever and bleeding manifestations. Patients meeting the probable or suspect case definition were defined as confirmed cases if IgM antibodies to RVF were detected by enzyme immunoassay (EIA) and/or RVF RNA was detected by reverse transcriptase-polymerase chain reaction (RT-PCR). For the purposes of this report, we excluded all suspect patients (not confirmed by laboratory diagnostics), and probable cases from whom specimens were negative upon laboratory testing for RVF. We included in our

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FIGURE 1. Aerial photograph of a flooded village in the north eastern province, December 2006. Conical appearing structures are rooftops of huts.

analysis, probable cases without available specimens who died before specimens could be obtained or who did not access health care during their acute illness (usually because of the intense flooding).

A total of 700 cases (158 deaths) of RVF were initially reported with dates of onset of illness from November 30, 2006 through March 25, 2007. These cases were reported in 18 districts (among > 100 districts in Kenya) in 6 of the 8 provinces through the national IDSR system (see above). Of these 700 reported cases, 203 suspect and probable cases tested negative by enzyme-linked immunosorbent assay (ELISA) and/or PCR; these were classified as non-cases, removed from the total RVF case tally, and excluded from this study. There were 105 suspect cases from whom specimens were not available for laboratory confirmation and these patients were also excluded from the study. Of the remaining 392 patients: 272 were confirmed cases and 120 were probable cases (from whom specimens were not available either because 1) they died before specimens could be obtained, 2) they did not have access to health care during their acute illness, or 3) they were at clinics or hospitals where staff were not in place to collect specimens and information. Demographic information was not available for 52 of these patients—many of these were confirmed cases diagnosed early in the outbreak before the formal investigation began and were inaccessible to follow-up; thus, the focus of this report is on the 340 confirmed (225, 66%) and probable (115, 34%) cases for whom demographic information was available. We calculated incidence rates for the most heavily affected districts based on 2006 population estimates from the Kenya National Bureau of Statistics indicating populations of 445,850 for Garissa District, 90,287 for Ijara District, 309 361 for Baringo District, and 653,144 for Kilifi District.

Clinical and epidemiologic studies. Clinical and epidemiologic data were systematically collected from patients from multiple locations in Kenya, meeting suspect, probable, and confirmed case definitions. Proxies (usually spouses or adult siblings) were interviewed using a standardized data collection instrument to collect information from patients who had died before an interview could be carried out. Interviews were conducted by MoH staff and residents of the Kenya Field Epidemiology and Laboratory Training Program (FELTP).¹⁸

A serosurvey was conducted to define the scope and magnitude of transmission, and to carry out a risk factor study (results of risk factor study will be presented separately). Residents were systematically selected from three districts (Garissa, Kilifi, and Baringo) where most of the cases occurred during the outbreak. Methods for selection of participants in the serosurvey varied slightly in each of the three districts. Line lists of reported probable and confirmed cases were used to identify geographical units (usually villages) where clustering of cases occurred in these three districts. In total there were 161 affected villages in the three districts (Garissa 62, Baringo 52, and Kilifi 47); of these, 129 villages had > 1 case. Of these 129 affected villages with > 1 case, 55 (Garissa 18, Ijara 1, Baringo 11, Kilifi 25) villages with the highest numbers of cases were enrolled in the study to estimate the upper limit of anti-RVSV IgM antibody seroprevalence. In Garissa and Baringo districts, the village chief or elder (of villages with clustering of cases) compiled a list of all the households in their village. We used a random number generator to select 20–30 households per village. In Kilifi, a Global Positioning System (GPS) map of all households (generated by Wellcome Trust-KEMRI, Kilifi) within one square mile for each case was used to randomly select a household as a starting point; then, every other household along the road from that household was solicited for participation. Households were sought until up to 25 participants were enrolled for each case. All adults and one randomly selected child between 5 and 18 years of age were solicited from each selected household in all locations. Selected participants in each household were enrolled after obtaining informed consent. Each enrolled participant underwent phlebotomy and a standardized interview. Among 1,308 selected residents, 970 (Baringo 177, Garissa 322, and Kilifi 471) residents consented to participate and provided blood, which was separated into serum aliquots and sent to the CDC-KEMRI laboratory for antibody testing. The acceptance rate for Baringo was 90%, 75% for Kilifi, and 67% for Garissa. The Kenya Ministry of Health regarded this survey to be part of the emergency public health response, and that it did not represent research, and, as such requested that the work be expedited, determining that it did not require review by an Ethical Review Committee.

After confirmation of the outbreak on December 21, 2008, the rapid response team that was dispatched by the Ministry of Health systematically collected information on the initial 100 suspected RVF cases in Garissa District. The team used a case investigation form to elicit basic demographic, clinical, and risk factor information to characterize the outbreak at the initial stages. Clinical data from these 100 patients were tabulated to characterize the clinical presentation.

Laboratory case-confirmation and molecular studies. Sera from patients meeting suspect or probable case definitions were tested for the presence of RVF virus (RVFV) IgM antibodies or viral RNA to confirm acute infection. The RVF virus IgM antibodies were detected using the sandwich ELISA method, as described previously.^{19,20} Briefly, sera were added to ELISA plates coated with goat antiserum against human μ -chain of IgM, followed by addition of RVFV antigens. Immunoreactivity was detected using the 2,2'-azino di-ethyl-benzothiazoline-sulfonic acid as peroxidase substrate and optical density (OD) read at 405 nm. Mean OD readings were converted into a percentage of high-positive control serum (PP) value using the equation: (mean net OD of test sample/mean net OD of high-positive control) $\times$ 100. Viral RNA was detected using one-step real-time RT-PCR, as described.^{20,21} Briefly, primers from the G2 gene of the virus were used to amplify a 94 nucleotide fragment using a Taqman assay.

Garissa, the main town in Northeastern Province, is about 370 km north east of Nairobi. To expedite processing of laboratory specimens, we set up a field laboratory at the Provincial General Hospital in Garissa to process ELISAs for IgM antibodies and RT-PCR reactions for viral RNA. Thus, specimens were tested in either the Garissa field laboratory or at the existing CDC-KEMRI laboratory in Nairobi.

Virus isolation was performed in a biosafety level-3 laboratory at the KEMRI-CDC compound in Nairobi. A volume of 100 μ L of human sera from acute RVF cases was diluted 1:3 in Dulbecco's modified Eagle's medium (DMEM) and inoculated into confluent VERO cells in 25-cm² flasks. Infected cells were harvested when cytopathic effects (CPE), characterized by cell lysis were evident in greater than 90% of the cells. For genetic analysis of viruses involved in the outbreak, 6 isolates from Garissa District (KEN/Gar 001/06, KEN/Gar 002/06, KEN/Gar 004/06, KEN/Gar 008/06, KEN/Gar 117/06, and KEN/Gar 118/06), two from Baringo District (KEN/Bar 032/07, KEN/Bar 035/07), one from Kilifi District (KEN/Kil 006/07), and one from Malindi District (KEN/Mal 032/07) were recovered.

Viral nucleic acid extraction and nucleotide sequencing were performed as described by LaRue and others.²² Primers for sequencing were developed from previously sequenced RVFV strains.²³ Following reverse transcription, PCR was performed and the resultant products gel purified (Qiagen, Valencia, CA) and directly sequenced. Each segment was sequenced three times and the consensus sequence at each position taken. A total of 3,160 nucleotides from the M fragments of the RVF virus genome from each of the isolates were sequenced and compared. Nucleotide sequence editing and prediction of amino acid sequences were performed using DNASTar (Madison, WI) software. Alignments were performed using the CLUSTALW method²⁴ using the Kenya 9800523 strains isolated from the 1998 outbreak in Kenya (Genbank accession nos. DQ375400, DQ380196, DQ380169) and Saudi 2000-10911 isolates from the 2000-01 outbreak in Saudi Arabia (Genbank accession

nos. DQ375401, DQ380197, DQ380170). To determine relationships among the RVF strains, phylogenetic analysis of the predicted amino acids sequences for the translated region was performed by Phylogenetic Analysis Using Parsimony²⁵ software using both parsimony and neighbor-joining analyses. Both analyses resulted in duplicate phylogenetic relationships and were evaluated by 2,000 bootstrap replicates.

Geographic analyses. Maps showing soil types and land use patterns were obtained from the publicly available GIS site of the International Livestock Research Institute (<http://www.ilri.org/gis>). Data on soil type were obtained from the Kenya Soil Survey, Report E1, 1982. Soils were classified by physical and chemical properties using the FAO scheme.²⁶ The land use data were obtained from LANDSAT images obtained in 1987 by JICA (Japan International Cooperation Agency) for the Kenya National Water Master Plan. Daily rainfall data for sites in Kenya were obtained from the National Oceanic and Atmospheric Administration's Surface Data Global Summary of the Day file (<http://www.cdo.ncdc.noaa.gov/cdo/dataproduct>). Sites used were Garissa (for Northeast Province cases), Eldoret (for Baringo cases), and Mombasa (for Kilifi cases).

For geocoding, the country was subdivided into a grid containing 46,200 cells of 3.5 km on each side. Case locations were geocoded (assigned to specific cells) based on the location of the village or the centroid of each sublocation, which is the smallest administrative unit in Kenya ($N = 6,625$ in the 1999 census); 215 case locations were available and assigned GPS locations (55% of confirmed and probable cases). Reasons for cases not being geocoded were that either the village name could not be found in databases of village names or the case did not have either a village or a sublocation reported. The remainder of cells (for which a case was not assigned) was considered to be "non-case cells." Distributions of soil types and land use for case ($N = 215$) and non-case cells ($N = 45,995$) were compared using the χ^2 test.

RESULTS

Among the 340 cases included in this report, 192 (56%) were males. Median age for males was 28 years (range, 6-84 years) and for females median age was 31 years (2-85 years) (Figure 2). Among 225 laboratory-confirmed cases of RVF, 58% had IgM antibodies, 65% had RNA detected by real time RT-PCR, and 23% had both.

Illness resulted in death in 90 (26.4%) of cases. The case-fatality ratio (CFR) for probable cases was 48% (55/115), and was 16% (35/225) among confirmed cases; many probable cases died before appropriate specimens could be collected (likely biasing this classification to a higher case-fatality rate). The CFR was 42% among cases within the 21-30 year old age group, which was significantly higher than in other age groups (and may have been subject to the same bias as mentioned previously, given that many herders who died before testing could be done were in this age category) (Table 1). Males had a statistically significantly higher CFR (33%) when compared with females (18%); Case Fatality Rate Ratio 1.8 (95% Confidence Interval [CI] 1.3-3.8) (P value 0.002).

Over 85% of the 340 confirmed and probable cases were reported from the four districts of Garissa (107, 31%), Baringo (83, 24%), Ijara (75, 22%), and Kilifi (33, 10%) (Figure 3); Garissa and Ijara are located within the sparsely populated Northeastern Province. In addition, 17 other cases came from

FIGURE 2. Numbers of confirmed and probable Rift Valley fever cases by age group and gender, Kenya 2006/7.

Wajir, another district in Northeastern Province; thus, nearly 60% of cases came from this frontier province. Baringo is located within Rift Valley Province and Kilifi within Coast Province. The respective attack rates for Garissa, Ijara, Baringo, and Kilifi were 24, 83, 26, and 5 (per 100,000 population), respectively.

There were two epidemic peak periods (Figure 4), one occurring between mid-December 2006 and mid-January 2007 and the second between the end of January and mid-February 2007. In Northeastern Province, the index case (identified during the course of investigation) reported onset of symptoms on November 30, 2006. The first case in Kilifi District was retrospectively reported on December 1, 2006 and cases continued through the second week of February 2007. The first case in Baringo District reported onset of symptoms on January 25, 2007 and cases peaked acutely during the first week of February 2007 (Figure 1A). Cases in southern Kenya (Taita Taveta) near the Tanzania border were detected on 18 January and within a few weeks; the RVF epidemic was first reported in Tanzania.²⁷ The CFR was higher during the early part of the outbreak when cases were occurring in Northeastern Province and in Kilifi (Figure 4). Few deaths occurred among cases in Baringo (Figure 3).

Of 72 cases (42, 58% male) with occupation history available, 25 (35%) were herdsmen, 20 (28%) were housewives, 12 (17%) were farmers, and 12 (17%) were students. There was a history of consumption or handling of products from sick ani-

mals in 39 (57%) of these cases with 23 (32%) reporting the activity to be collecting milk, 16 (22%) reporting cooking, and 13 (18%) reporting slaughtering (13 of these patients reported > 1 of these activities).

Of the 970 residents tested during the serosurvey, 122 (13%) had RVF-IgM antibodies detected (including 66 [54%] residents who also had detectable immunoglobulin G [IgG]); 251 (26%) participants had RVF-IgG antibodies detected, including 66 (26%) with detectable IgM antibodies. The IgM (with or without corresponding IgG infection) sero-positivity rate (representing likely acute infection) was highest for Baringo District ($P < 0.001$) (Table 2). The rate of IgG sero-positivity without corresponding IgM antibody detection (tending to represent remote infection with the exception of those tested several months after infection) was highest for Garissa District,

FIGURE 3. Numbers of probable and confirmed cases in each of the districts. Numbers within parentheses indicate the number of deaths among the probable and confirmed cases.

TABLE 1

Case-fatality ratios for Rift Valley fever stratified by gender and age group*

Age group	Females		Males		Total	
	N	Deaths (CFR%)	N	Deaths (CFR%)	N	Deaths (CFR%)
Below 10 years	4	0	4	0	8	0
11-20 years	25	4 (16)	49	11 (22)	74	15 (20)
21-30 years	44	9 (20)	61	35 (57)	105	44 (42)
31-40 years	38	10 (26)	33	9 (27)	71	19 (27)
41-50 years	23	3 (13)	20	2 (10)	43	5 (12)
51-60 years	6	0	11	1 (9)	17	1 (6)
61-70 years	5	0	10	5 (50)	15	5 (33)
71-80 years	1	0	3	1 (33)	4	1 (25)
Over 80 years	2	0	1	0	3	0
	148	26 (18)	192	64 (33)	340	90 (26)

* CFR = case-fatality ratio.

FIGURE 4. Left Y axis refers to number of Rift Valley fever cases (represented by bars) and right Y axis refers to total biweekly rainfall in inches (represented by lines for each of the three districts) deviating from (above or below) average over the previous 5 years for the same biweekly period.

the epicenter for another RVF outbreak in Kenya during 1997–1998 (Table 3). Among the 122 participants who had IgM antibodies, 65 (54%) were males. Serosurvey data within the affected areas, extrapolated to the local (district) populations, would suggest that up to 185,000 people may have been infected within the epicenters of the outbreak. Many participants with RVF IgM antibodies experienced symptoms during the previous month—headache, fever, and myalgias were the most commonly reported symptoms (Table 3).

Eight RVF virus isolates from several locations around Kenya were analyzed for genetic sequencing diversity. The isolates were collected over a period of 2 months from the start of the outbreak in December 2006. Four isolates, KEN/Gar 001/06, KEN/Gar 002/06, KEN/Gar 004/06, and KEN/Gar 008/06, were from the earliest cases collected between mid-December 2006 from Garissa in Northeastern Province, and two isolates, KEN/Kil 006/07 and KEN/Mal 032/07, were collected from Coast Province in January. The KEN/Bar 032/07, KEN/Bar 035/07 isolates were collected from Baringo District in mid-February 2007. The eight isolates had between 96.6% and 99.6% nucleotide sequence identity with each other across the 3165 nt length of M segment of the genome (Table 4). The gene segment analyzed for these viruses also had a similarly high homology with the RVF strains involved in the 1996–1997 RVF outbreak in Kenya (Kenya 9800523 strain) and 2000 outbreak in Saudi Arabia (Saudi 2000-10911). Work is ongoing to perform complete genome analysis for strains from various geographic locations to more fully characterize the molecular epidemiology of this outbreak.

TABLE 2

Findings from systematic random serosurvey for Rift Valley fever antibodies among 970 participants from three heavily affected districts

Number	District	N	IgM antibodies detected (with or without presence of IgG antibodies n (%)) (likely recent infection)	IgG antibodies without IgM antibodies (likely past infection)
1	Baringo	177	35 (20)	29 (16%)
2	Garissa	322	41 (13)	104 (32%)
3	Kilifi	471	46 (10)	51 (11%)
Total		970	122 (13%)	184 (19%)

Heavy rains and moisture preceded outbreak peaks in the main affected districts by at least 1 month (Figure 4). In Baringo, heavy rains were noted during the end of December, more than 1 month before the onset of RVF in that area, resulting in the second major peak of RVF illness observed in Kenya (Figure 3); in fact, by the time the outbreak was peaking in Baringo, rainfall and moisture indices were not especially marked. However, rainfall was predominant in southern Kenya at that time, about 1 month before cases were detected in that part of the country and south of the Kenya border in Tanzania. Likewise, rainfall was heavy in Garissa about 1 month before the outbreak began; however, heavy rainfall in Kilifi District appeared to coincide with the onset of cases (Figure 4).

When comparing soil type in locations in Kenya where confirmed and probable cases were identified ($N = 215$) with all other locations within Kenya, as defined by a grid of 46,200 “cells” (Figure 5), case-cells within the grid were much more likely to have soil types referred to as solonetz, solonchaks, and planosols (FAO classifications: SNh, SCn, and PLc; $\chi^2 = 382$, degrees-of-freedom [df] = 4, $P < 0.0001$) (Table 5).

DISCUSSION

This outbreak of RVF resulted in nearly 400 cases of significant illnesses with many deaths. However, the outbreak

TABLE 3

Symptoms experienced during the previous one month by participants with evidence of recent infection

Number	Symptom	Participants with IgM antibodies (with or without IgG antibodies $N = 121$) N (%)
1	Headache	111 (92)
2	Fever	109 (90)
3	Muscle/joint pain	102 (84)
4	Vomiting/diarrhea	53 (44)
5	Blurred/double vision	37 (31)
6	Jaundice	21 (18)
7	Hemetemesis	18 (15)
8	Epistaxis	17 (14)
9	Melena	14 (12)
10	Gingival bleeding	13 (11)

TABLE 4
Percent nucleotide sequence similarity (upper triangle) and divergence (lower triangle) of RVF strains

	KEN/Gar 001/06	KEN/Gar 002/06	KEN/Gar 004/06	KEN/Gar 008/06	KEN/Kil 006/07	KEN/Mal 032/07	KEN/Bar 032/07	KEN/Bar 035/07	Kenya 98	Saudi 2000
KEN/Gar001/06	—	99.6	97.7	98	97.7	97.9	96.6	97.5	98.6	98.3
KEN/Gar 002/06	0.4	—	97.6	98	98	98	96.9	97.8	98.5	98.3
KEN/Gar 004/06	2.3	2.5	—	98.6	98.1	98.4	97.2	98	97.8	97.5
KEN/Gar 008/06	2	2	1.4	—	98.7	98.9	97.7	98.6	98.4	98.2
KEN/Kil 006/07	2.4	2.1	1.9	1.3	—	99.6	99.4	99.6	98.2	97.9
KEN/Mal 032/07	2.2	2	1.6	1.1	0.4	—	98.7	99.4	98.4	98.1
KEN/Bar 032/07	3.4	3.2	2.8	2.4	0.6	1.3	—	99.1	97.1	96.9
KEN/Bar 035/07	2.5	2.2	2	1.4	0.4	0.6	0.9	—	98	97.8
Kenya 98	1.4	1.5	2.3	1.6	1.9	1.7	2.9	2	—	99.6
Saudi 2000	1.7	1.8	2.5	1.9	2.1	1.9	3.2	2.2	0.4	—

potentially infected more than 180,000 people, based on the proportion of participants in the serosurvey who had IgM antibodies to RVF virus. We recognize that this extrapolation relies on the exposure rate to be fairly evenly distributed across the entirety of each of the districts and in a similar intensity as in the case villages, and therefore it may be an overestimation. Case detection guided the locations selected for the serosurvey. However, because case detection was presumably far less than 100% sensitive, it is likely that there were many other similarly affected villages that were not surveyed within these districts. We are not able to estimate the number of people infected in other areas in Kenya. This gross estimation of RVF virus infections in the three most-affected districts in Kenya remains useful because it indicates the large burden of this disease to Kenya during epidemic periods. The high mortality rate during this outbreak, was likely heavily influenced by the low proportion of patients infected with RVF (many with mild illness or who were asymptomatic) who sought medical care, and is unlikely to represent emergence of a lethal strain of RVF virus.

In addition to the toll on health, the outbreak likely had substantial economic impact. Bans on slaughtering were imposed in each of the affected areas and aggressive attempts were made to stop movement of livestock from affected areas to unaffected areas. In areas like Northeastern Province where the principal source of food is livestock and where a substantial number of people work in the livestock industry, the quarantines and slaughter bans were in effect for more than 2 months. While likely effective at minimizing the severity of the outbreak, these interventions had devastating impact on livelihoods.

This large outbreak of RVF followed heavy rains and flooding within the affected areas by 1 month or more. Although sporadic cases of RVF may occur during interepidemic periods, outbreaks are thought to occur when topographical depressions called dambos suddenly flood causing the eggs of dormant RVFV-infected floodwater *Aedes* spp. mosquitoes to hatch.²⁸ Northeastern Province is normally dry (mean annual rainfall = 40 cm or less for most of the province). However, during September through December 2006,

FIGURE 5. Location of Rift Valley fever (RVF) cases relative to soil types in Kenya. The dots represent the geographic locations of geocoded cases. Locations where cases occurred were more likely to be solonetz, solonchak, and planosol soil types than non-case locations. The solonchak soil types of the Baringo area are obscured because of the small geographic scale of that location.

TABLE 5
Soil type: FAO classification system by classification of area*

Soil type	Case-area (%)	Non-case-area (%)
Solonetz	36	12
Planosol	26	6
Chernozem	5	10
Solonchak	10	2
Other	24	70

*N for case areas = 255; N for non-case areas = 46,200; Chisq = 382; df = 4; $P < .0001$. See Figure 5 for geographic distribution.

39.4 cms of rainfall was recorded in Garissa with the subsequent formation of many dambos and large temporary lakes in low-lying areas. This flooding displaced entire villages and became breeding grounds for vector species. Infected *Aedes* transmit RVF to a variety of livestock and wildlife, which may develop high and sustained viremia,²⁹ and directly to humans; when virus levels in bloodstream are high, RVF may then be transmitted to other animals or to humans by other mosquitoes, and theoretically by any biting or blood-sucking insect. It appears that heavy rains and flooding preceded advent of outbreaks by at least 1 month in each of the affected areas.

The previous RVF outbreak in Kenya in 1997–1998, had a somewhat similar geographic distribution and pattern of spread,⁹ although the previous outbreak was not known to have significantly affected the Baringo area, a major geographic focus for illnesses during the recent outbreak. Despite flooding throughout Kenya around the time of both outbreaks and widespread availability of livestock, both outbreaks started within Northeastern Province and spared most of the western half of the country. While there are theories that certain areas are receptive for RVF transmission, there are no data that would provide explanation.³⁰

The predilection of specific soil types in RVF affected areas, and not in other areas, would be consistent with the notion that soil type may influence flooding, drainage and potentially the ability for infected *Aedes* egg stages (which remain in the soil) to remain infectious in the ground until heavy flooding at which time maturation of egg stages and mass breeding occurs resulting in epizootics and ultimately epidemics. Solonetz soils have a sodium-rich subsource, are low in organic matter, and often contain strata rich in mineral deposits.³¹ Solonetz is typified by a subsurface richer in clay than the topmost layer and are usually found in areas where annual precipitation is usually low, which is the case in most of the affected areas. Planosols are similar to solonetz and in that they are permeable on the surface, but have a much slower draining substrata—they are coarse textured soils often over a finer textured subsoil, usually clay. Both types of soils tend to retain water near the surface well during rainy seasons.³¹ During dry seasons, they often support grasslands—in the Northeastern province area, these are semi-sparse grasslands. Solonchaks, found in the Baringo area, are found in marshy, high saline areas and can form solonetz soils upon drying and leaching of surface sodium.³² The solonetz-solonchak transition provides a linkage between the soil types in the Lake Baringo and those of Northeast Province. It is not clear whether these factors contribute to “RVF geographic receptiveness” and, if they do, whether receptiveness occurs by promoting survival and maturation of potentially infected *Aedes* egg stages or through more rapid occurrence of flooding given excessive rainfall

(or both). Research, combining geologic, entomologic, and virologic components would be useful to examine this possibility and better characterize factors that promote regional RVF outbreaks.

During the peak of the outbreak in Northeastern Province, animals that could not be sold or slaughtered were transported from Northeastern Province to Kilifi, where the outbreak had not yet appeared. RVF viruses may have been transported to Kilifi District by infected animals and spread by competent vectors and transmission-facilitating animal practices rather than through flooding and breeding of infected floodwater *Aedes*, such as likely occurred within other high incidence areas. This would be consistent with differences in soil and rainfall patterns within Kilifi. If correct, this hypothesis would have important considerations for control of future RVF outbreaks, especially relating to tighter enforcement of restrictions of movement of livestock from affected areas, often strongly driven by hardship resulting from local quarantines and livestock bans. As with avian influenza control, a strategy for compensation of livestock owners for hardships brought on by public health restrictions might be needed to minimize potential for spread of RVF viruses to new areas.

As a zoonosis with a hypothesized mosquito-egg reservoir,²⁸ prevention and control strategies are complicated and expensive. Aggressive application of larvicides into flooded areas known to be receptive for RVF transmission (perhaps where RVF-specific *Aedes* are prevalent), livestock immunization, and community education focused on reducing risk exposures (like slaughtering or handling sick animals and drinking raw milk) would all be best applied before an outbreak occurs, based on accurate predictions of RVF outbreaks. Work is ongoing using extensive geographic information from human, veterinary, and entomologic surveillance during the outbreak, along with meteorological compilations and satellite images to develop refined RVF forecasting models. Such models, if highly specific, would be used to trigger large-scale pre-outbreak disease prevention measures. The models will need to be highly specific and sensitive to generate the will to use precious, limited funds in the resource poor areas where RVF is known to occur.

Evidence for transovarial transmission in floodwater *Aedes* mosquitoes, the basis for the mosquito-egg reservoir hypothesis, has only been demonstrated once in a study in Kenya in the 1980s. Thus far, we have not found substantially different genetic sequences from viruses isolated from humans in different geographic areas. Existence of such differences would have supported the concept that separate outbreaks of RVF occurred in each area, resulting from separate occurrences of maturation of infected *Aedes* egg stages. Genotypic findings included in this report are consistent with recent work showing low diversity of 5% at the nucleotide and 2% at amino acid levels when the full genomes of 33 RVF isolates collected over multiple years from divergent geographic regions were analyzed.²³ Given that most regions within the RVF genome are highly conserved, sequencing may not be a useful molecular epidemiologic technique for this virus; however, sequencing the entire genome should be pursued to rule out geographic-specific genetic differences. Thus, we cannot yet determine whether RVF was physically moved from area to area (i.e., by movement of infected animals or mosquitoes) or sprang up separately from maturation of infected *Aedes* eggs within recently flooded areas. The 2006–07 Kenya isolates displayed amino

acid differences that may be significant with further analyses to localize the viral epitopes affected by mutations. For example, across the 1,055 amino acid span of the M segment analyzed, the Kenya 2006 isolates had amino acid differences at 10 positions when compared with Saudi 2000-10911 and Kenya 9800523 strains (strains from earlier outbreaks had identical amino acids at those positions).

Although transmission of RVF virus to humans can occur by direct exposure to infected animal secretions, and also by infected mosquitoes, it is unclear whether the route of transmission is associated with disease severity. Direct exposure to infected animals may be more likely to result in symptomatic or severe RVF disease, because the inoculum from viremic animals is much greater than that transmitted by mosquitoes. Our finding that CFR was highest in young males supports this hypothesis, because livestock herding and slaughtering is practiced by young males. In contrast, the 128 participants in the serosurvey with evidence of recent mild or asymptomatic infection had a male:female ratio closer to one. In addition, the greatest number of cases of RVF illness during the outbreak was in Northeastern Province, where herding and slaughtering were very common practices; however, the highest seroprevalence was in Baringo, where animal handling is not a predominant occupation, and where mosquito densities during the outbreak were very high.³³

This outbreak resulted in substantial loss of human life and suffering. Ongoing studies will attempt to quantitate the short- and long-term economic impact, which are likely severe. Previous outbreaks of RVF have resulted in bans of importation of livestock from outbreak areas, lasting for many years after the outbreaks have concluded. Because outbreaks are intermittent, effective strategies for predicting and preventing them are needed. Recently published models focusing on climatologic and ocean temperature, have indicated a potential for reasonably specific and sensitive forecasting.³⁴

In addition to the direct health impact, this sudden outbreak, as with avian influenza outbreaks in other countries in Africa,³⁵ diverted already stretched public resources from addressing the major endemic public health problems in the region, like acquired immunodeficiency syndrome (AIDS), tuberculosis (TB), malaria, and childhood illnesses including respiratory and diarrheal diseases, all with far greater long term public health burden.³⁶ Very limited veterinary resources were also strained, making it unlikely that long term priorities or other epizootics could be addressed. Strategies for greater diagnostic, epidemiologic, and health systems capacity are needed in sub-Saharan Africa to make it possible to sustain focus on the critical health problems while addressing emerging disease threats when they occur. Furthermore, this outbreak highlights a critical need for new paradigms for how veterinary and human health organizations and ministries, so often functioning entirely independently, must develop combined and synergistic approaches to prepare, detect, and respond to outbreaks of zoonoses,³⁷ especially those with potential to have grave ramifications for human health and livelihoods.

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