

Lessons from the 2006–2007 Rift Valley fever outbreak in East Africa: implications for prevention of emerging infectious diseases



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*“Where there is much desire to
learn, there of necessity will be much arguing,
much writing, many opinions; for opinions in good
men is but knowledge in the making.”*
– John Milton (1608–1674)

In mid-December 2006, the Centers for Disease Control-Kenya Medical Research Institute (CDC-KEMRI) laboratory, Nairobi, received specimens from two patients from a remote area in northeastern Kenya who were severely ill with hemorrhagic symptoms. Immunological and molecular testing for etiologies of hemorrhagic fever viruses detected Rift Valley fever (RVF) in both patients. Over the ensuing 5 months, RVF was diagnosed in over 1000 patients in multiple locations in Kenya, Somalia and Tanzania [1,2] and over 300 patients died.

Working under the direction of the Kenya Ministry of Health, The International Emerging Infections Program (IEIP) at CDC-KEMRI set up a field laboratory for molecular and immuno-diagnostics at Garissa Provincial Hospital, within the epicenter of the outbreak in Northeastern Province of Kenya, to facilitate rapid diagnosis; over 1000 specimens were tested. Heavier than usual rains (Figure 1) had resulted in massive flooding in the region and helicopters were needed to transport medical and public health personnel to hard-hit areas. In an attempt to contain RVF, bans on slaughtering and transporting livestock from the affected areas were implemented. Although judged necessary, these restrictions created substantial hardship for the already impoverished local population, which depend primarily on livestock for their livelihoods.

Teams composed of local and international public health and veterinary officials and scientists were dispatched to various locations in Kenya and Tanzania to investigate the outbreak, identify risk factors, define principle mosquito vectors, provide clinical care and infection control, study the clinical syndrome and its sequelae, establish surveillance in livestock and wildlife, and assess economic impact. Health communication teams developed messages and disseminated them locally and nationally.

The 2006–7 RVF outbreak resulted in considerable suffering and death, and massive economic hardship across East Africa; the multifaceted direct and indirect costs – responding to the outbreak, managing patients, public health control interventions – and household losses in Kenya had substantial economic impact. Although it was undoubtedly justified to prioritize this outbreak and to commit intensive efforts and resources towards control, the efforts distracted the Kenya Ministry of Health and its partners from other priority programs focused on the major infectious disease burdens impacting people in the region, as has been observed with avian influenza outbreaks [3]. But could the outbreak have been better anticipated and either prevented or its impacts minimized? We suggest the answer is a qualified yes.

A Rift Valley fever model

RVF is principally a pathogen affecting livestock, although it may also affect wildlife. Epizootics have occurred periodically in East Africa since the pathogen was first recognized in Kenya in 1930 [4]. Outbreaks in humans occur more rarely; sporadically occurring cases and local epidemics are probably neither recognized nor reported. Transmission from animal to animal is believed to occur primarily via mosquitoes or other blood-feeding insects, which mechanically transfer infected blood to susceptible hosts; animal-to-human transmission results mainly from exposure to infected secretions, fluids or tissues.

Aedes mosquitoes appear to have a role in maintaining the virus between epizootics. Infected larvae can remain buried in suitable soils for long periods of time. When floods occur following unusually heavy rainfall, these emerge and develop into adult mosquitoes capable of spreading RVF viruses to sheep, goats, cattle and camels. When rains are particularly heavy, resulting in massive flooding, larvae blooming may occur synchronously over a wide geographic area resulting in extensive exposure of animal populations to the virus [5]. As the number of infected livestock grows with subsequent viral amplification, the potential for a human outbreak increases.

In RVF epizootics, infected mosquitoes are the critical factor for both the transmission and dissemination of the disease. The entomologic basis for the recurrence of disease outbreaks depends on transovarial transmission in *Aedes* mosquitoes [5]. This phenomenon appears to have been responsible for the recent outbreaks in Kenya and Tanzania where unusually heavy rains and flooding occurred just prior to local outbreaks. The previous RVF outbreak in East Africa during 1996–1997 also followed flooding [6].

Lessons learned

In recent decades, the majority of emerging infectious diseases have originated from animals [7,8]. With this knowledge, we have analyzed the 2006–2007 RVF outbreak to consider what innovations and changes need to be implemented to anticipate outbreaks or detect them earlier, thus preventing emergence and/or spread of zoonotic pathogens and their potentially devastating regional or global impact. Inherent in this analysis are the concept of infectious disease ecology and the convergence of human and animal health, which demand that we consider zoonoses as an animal health–public health continuum rather than separate occurrences.

When considered ecologically, the RVF virus maintenance and transmission cycles [5,9] have important characteristics broadly relevant to preventing emerging zoonotic diseases. RVF infects a variety of hosts, including at a minimum humans and livestock, with arthropod vectors playing a critical role in moving viruses among diverse hosts. In addition, requisite ecologic factors such as heavy rainfall and flooding [10], and possibly soil type, are integral to triggering outbreaks.

Today, we have more sophisticated technologies to better understand the natural history of RVF and enhance our ability for predictive analysis: satellite maps, the Global Positioning System (GPS) and knowledge of past ecological disease niches are all helpful in predicting outbreaks. Forecasting permissive weather patterns and mapping flooding and/or vegetation changes, and integrating these with data on densities of arthropods, are key predictive analytical components [11]. Yet we continue to be limited in our ability to provide adequate specificity to enable efficient, timely and cost-effective public health actions to be mounted.

In the future, data collected from high-risk RVF sites during interepidemic periods could improve the specificity of prediction models

Figure 1. Normally dry, flooded area in Northeastern Province, Kenya, January 2006.



Table 1. Factors predisposing to outbreaks of emerging and re-emerging zoonoses and capacity required to deal with these.

Factors	Skill sets and tools needed
Environmental/ecologic conditions	Meteorology Mapping Satellite imagery
Presence and movement of susceptible animals	Veterinary surveillance Conventional and sophisticated diagnostic capacity Local production and marketing systems
Presence and mobility of vectors	Entomologic surveillance
Human behavioral risk factors	Ethnographic capacity Epidemiology
Human and animal host (immunologic) predisposing factors	Epidemiologic surveillance Nutritional surveillance Immunologic testing
Population factors (density, hygiene/sanitation, mobility and prevalence of host risk factors, such as immunodeficiencies)	Population sciences (enumerating and characterizing populations)

and pinpoint imminent outbreaks. Such data are likely to include incidence of sporadically occurring RVF (clinical and subclinical infections in livestock, wildlife and humans), along with infection indices in arthropods [12]. For RVE, accurate and early forecasting of an imminent outbreak would allow measures to be put in place that could prevent its occurrence, or at least significantly attenuate its severity. These measures might include early vaccination of livestock, intensified vector control and public education on risk-reduction behaviors in known permissive environments. There are also potentially efficacious human vaccines under development that may become available in the future.

For the 2006–2007 East African RVF outbreak to have occurred in humans, we postulate that a number of factors needed to coexist:

- A sufficient number of susceptible or RVF-infected animals;
- A sufficient number of competent mosquitoes;
- The local presence of the virus, maintained within circulating *Aedes* mosquito populations that had been exposed to past RVF epizootics;
- Climate patterns resulting in widespread flooding;
- A related group of optimal ecologic conditions, including soil types favorable for moisture retention and both the introduction and survival of *Aedes* larvae.

Although some characteristics of RVF are unique, many are cross-cutting and should be considered when building capacity to addressing other emerging or re-emerging zoonoses (Table 1).

For understanding and discovering diseases that originate from animals, it would be useful to conduct systematic studies that explore the profile of colonizing and potentially zoonotic micro-organisms. New, sophisticated tools for pathogen discovery and detection, such as microarrays, can be used to identify emerging pathogens in specimens from normally sterile sites or respiratory secretions [13,14]. Systematic entomological studies to detect changes in vector density and species distribution, as well as circulating pathogens within vectors, may also enhance awareness and preparedness for emerging diseases. For example, microarray methods can be applied to specimens collected from animals and vectors during routine surveillance, making it possible to detect potential human pathogens circulating in animal and vector populations or in the environment before they cause an outbreak in humans, or even before an epizootic. If such surveillance and laboratory capacity had been present in Kenya, it is likely that the recent RVF outbreak would have been anticipated, allowing upstream prevention strategies to be put into place.

To recognize and prevent emerging zoonotic diseases, including viral hemorrhagic fevers and avian influenza, the collaboration between animal and human health agencies, organizations and experts must be significantly improved. Most resources for surveillance, outbreak detection and response are currently allocated to human health. To enable earlier outbreak detection, and more effective prevention and control interventions, more resources will be needed for animal disease surveillance, and for active

investigation of ecological, environmental, economic and potential vector factors responsible for disease emergence, maintenance and transmission (Figure 2).

Since 1998, the WHO has promoted a strategy of Integrated Disease Surveillance and Response (IDSR) to detect and respond to human outbreaks. While IDSR is critical, although lamentably under-funded and inadequately prioritized in most African countries, we suggest there is a parallel and pressing need to invest in animal health infrastructure, surveillance and diagnostics. For RVF and other zoonoses, good animal health strategies will often also be effective human health strategies. A strong bias currently exists toward clinical medicine and individual healthcare. There is little attention or investment for ‘up-stream’ strategies: reducing pathogen loads, distribution and transmission prior to human infection must be given a higher priority. Today’s complex and interconnected world, which brings together people and animals in a rapidly changing environment, requires a different mindset and paradigm to both consider and promote health across all domains.

We propose that capacity building in both the human and animal health sectors will improve our preparedness and prevention strategies for human illness associated with impending zoonotic outbreaks. Such additional capacity would, we suggest, have been helpful preceding the recent outbreak of RVF in potentially preventing it or minimizing its impact (Table 2).

Currently, such capacities are inadequate in most parts of the developing world but are, we consider, essential to combat emerging global threats. A recent assessment of emerging infectious diseases suggested that most such diseases are detected in the developed world where wealth enables investments in sophisticated surveillance and detection systems [7]. And yet a host of factors – high population density, poor hygiene and sanitation, malnutrition, HIV, poor infrastructure, increasing trade and commerce, poor mosquito control, greater opportunities for the convergence and interactions among animals, animal products and humans – make the developing tropical world the most likely place for new and potentially dangerous pathogens to emerge. Everyone in the world is now connected; everyone can be exposed to emerging threats.

Figure 2. Factors responsible for disease emergence, maintainance and transmission.

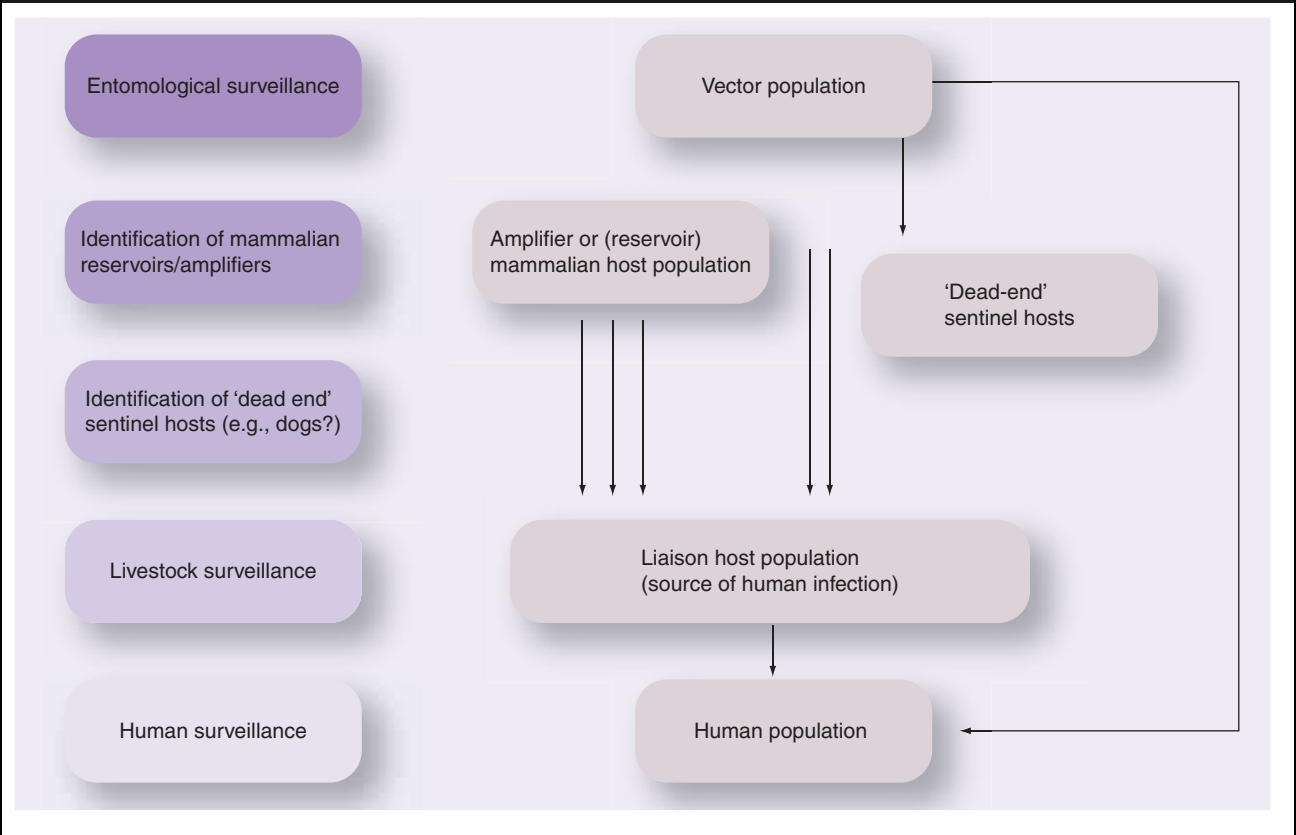


Table 2. Capacities needed to address emerging zoonoses in the 21st century.

Characteristic	Investments
Timely identification, characterization and response to emerging outbreaks in animals	Building veterinary centers of excellence and improving infrastructure
Identification of potential human pathogens (known and unknown) or potential human pathogens circulating in animals, especially animals that interact with humans	Initially can be managed with existing laboratories; further development of new assays may be required
Information on factors that increase the likelihood of transboundary transmission of pathogens, especially those resulting in severe disease and death	Investments in human and veterinary surveillance and knowledge of animal and wildlife populations and systems
Characterization of distribution and abundance of species-specific vectors of disease	Sustained support
Application of methods to screen large numbers of mosquitoes for known or potential human pathogens	Investments in entomologic surveillance efforts and expertise, as well as training of local entomologists and ecologists
Climatic and ecologic modeling, with short- and long-term forecasting of weather patterns (flooding and temperature extremes), soil-types, and human and animal population densities	Sustained and expanded support; develop and test new technologies and analytic tools
Rapid and effective health messaging system for behavior/practice modification to people at risk, including in remote areas	Mobile phone text messaging (SMS) needs to be developed as a resource for disseminating health messages; need local behavioral research teams working with health communications experts
Improved communication systems for rapid reporting of usual or unusual disease in animals or humans	Investments in establishing and sustaining SMS reporting systems; education to encourage public to report unusual events in animals or humans
Trained epidemiologists (medical and veterinary) and laboratory managers at country level able to recognize, diagnose and respond to reports of unusual disease occurrences	Expand training programs (such as Field Epidemiology and Laboratory Training Programs) to more countries within Africa and sustain the programs at both local and national levels; short courses: laboratory and rapid response training

Since emerging diseases are a global concern, we suggest that investments in these capacities should be a global responsibility.

Clearly, an integrated human, animal and environmental health system is needed to address these preparedness requirements: instead of entirely separate health systems, there should be intentional and functional collaborations. New efforts focused on human, veterinary and ecologic dynamics deserve urgent consideration. In concert with this need, CDC's IEIP in Kenya has been working to bring together relevant national or regional-level experts and country- and community-level officials to help implement balanced systems that place emphasis on both veterinary (for disease in livestock, pets and wildlife) and human surveillance. 'One Health', by definition and intent, is a construct and basis for designing such interdisciplinary strategies [15]. To make the concept of One Health functional at the local and country level in the developing world, a variety of tools will be needed to improve detection, diagnosis, prevention and response.

Detecting unusual clusters of disease in humans or in animals is difficult, especially in remote or sparsely populated areas. However, there are a growing number of individuals with mobile phones. Today, there are estimated to be over 3.3 billion mobile phone subscriptions worldwide, and availability and coverage is rapidly increasing, even in the developing world (the largest of two service providers in Kenya now has more than 10.5 million subscribers) [16]. Automated systems could be developed using existing, inexpensive technology to allow the public to report unusual events (e.g., animal die-offs or clusters of animals with severe, acute symptoms) by text messaging (SMS) using toll-free numbers. Local health and veterinary officers could then make judgments based on the type and number of reports to determine their validity and the need to investigate further. Mass text messaging could also be targeted to mobile phone users in at-risk areas to spread urgent health messages, although incentives and disincentives within agricultural and public health communities must also be considered and addressed.

Ultimately, trained human health and veterinary epidemiologists, laboratory managers and public health support staff are needed at the country level who are able to recognize, diagnose and respond to reports of unusual disease occurrences, outbreaks and other public health emergencies. The CDC Field Epidemiology and Laboratory Training Program, now operating in several countries in Africa [17], needs to be further expanded to cover more regions, and to include veterinarians as well as doctors, nurses and laboratory workers.

Veterinary laboratories throughout Africa are in need of substantial upgrading in terms of training, equipment and supplies to enable them to process specimens so as to determine the causes of epizootics and detect new pathogens. Diagnostic reagents for diseases with high morbidity and mortality should be made widely available, either through commercialization or international agencies. Field staff should be trained in specimen collection, biological safety, labeling and transport, and mechanisms need to be put in place to transport specimens to the veterinary laboratories. Capacity for rapid deployment of mobile field laboratories to efficiently diagnose diseases during an emerging outbreak may also be helpful. During the RVF outbreak in Kenya, the CDC-Atlanta Special Pathogens Branch (which has expertise in diagnostics for exotic diseases) trained Ministry of Livestock and Fisheries Development staff on conventional and real-time PCR testing, and also provided a real-time PCR machine and reagents for testing for RVF virus. With similar upgrades and training, these staff are now capable of testing for other important pathogens, such as avian influenza. Having such capacity will greatly increase the speed and accuracy of diagnoses, allowing timely and effective targeting of information about zoonotic diseases, especially when the potential risk to human health is severe and imminent.

‘Everyone in the world is now connected; everyone can be exposed to emerging threats. Since emerging diseases are a global concern, we suggest that investments in these capacities should be a global responsibility.’

Integrated approaches should be extended to applied research, focused particularly on factors associated with transmission of pathogens from

animals and vectors to humans, and on methods to interrupt or limit transmission. With this strategy in mind, CDC-KEMRI, in partnership with the University of Edinburgh, is establishing surveillance for a set of pathogens in domestic animals in western Kenya, in an area where we already conduct intensive population-based surveillance (in humans) for etiologies of key syndromes, including pneumonia, diarrheal disease and febrile illness. Organisms found in animals and humans will undergo genetic and other molecular epidemiologic testing, and epidemiologic studies will be carried out to assess factors associated with transmission and risk.

‘...good animal health strategies will often also be effective human health strategies.’

Conclusion

Paraphrasing a realistic twist to an old adage – “for every complex problem there is a simple solution, however it is inevitably wrong.” While this twist has some very important exceptions, experience with the recent RVF outbreak in eastern Africa, coupled with growing knowledge of epidemiology of other (re-)emerging zoonotic diseases, suggests that it currently holds true in a complex world where human and animal diseases increasingly converge. Lessons learned from RVF strongly support the notion that human diseases originating from animals and/or their products need to be viewed through a new set of lenses, and new strategies need to be implemented. These diseases need to be dealt with in a holistic and systemic way that includes animal, vector and environmental factors, and incorporates new interventions upstream from traditional clinical treatments in people after infection.

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