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Perspective

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Rift Valley Fever — The Need for an Integrated Response

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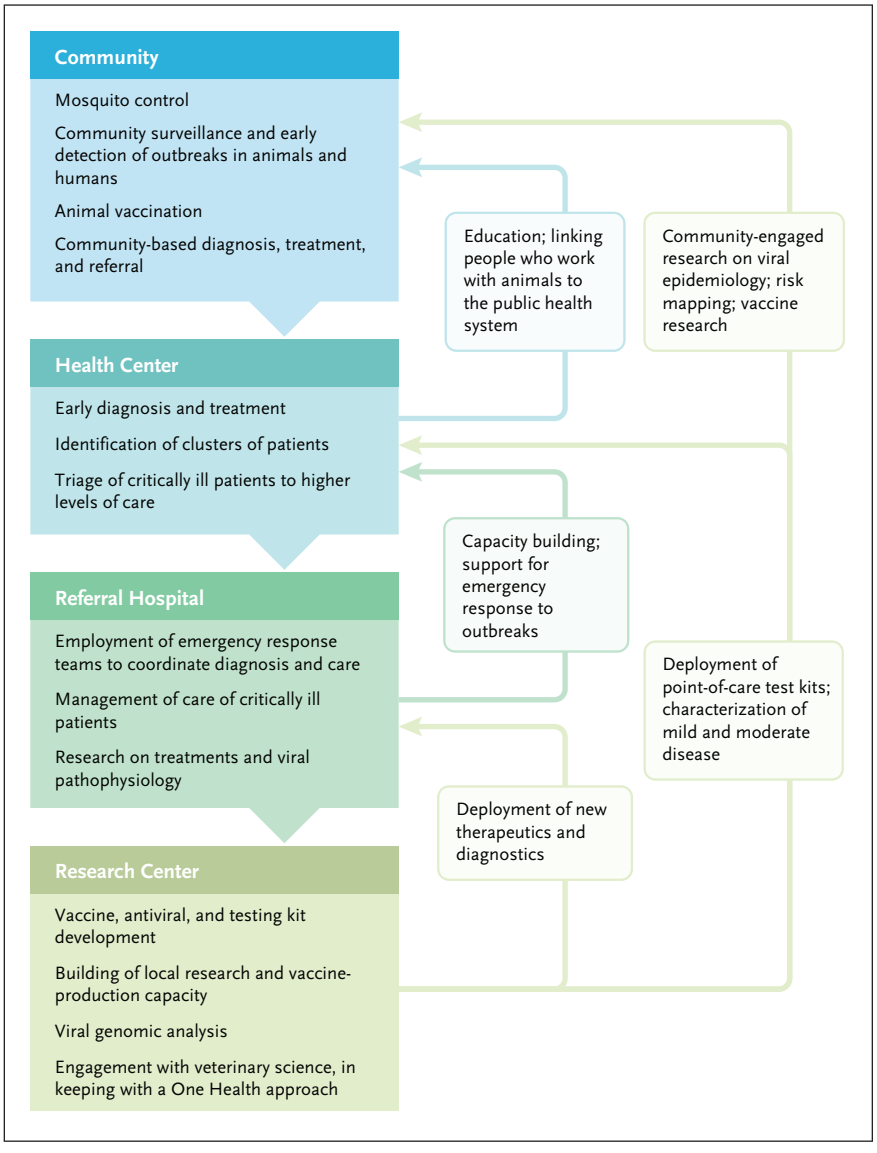
Uganda is currently experiencing an outbreak of Rift Valley fever virus (RVFV). Mbarara Regional Referral Hospital in southwest Uganda, where we work, treated 33 patients with RVF between February and September 2023, 8 of whom died. This outbreak is part of a growing problem; 39 countries in Africa and the Arabian Peninsula have reported RVFV outbreaks, involving about 1000 total confirmed deaths, since 1999.[1] The World Health Organization (WHO) has identified RVF as one of nine priority diseases because of its potential to cause outbreaks, and health care practitioners remain without vaccines licensed for use in humans, treatments that have been proven effective, or adequate diagnostic and surveillance tools.[2] Because of this lack of diagnostic and surveillance tools, the true prevalence of RVF is unknown. Addressing the growing threat associated with RVF and other emerging diseases using an integrated approach that spans health systems could improve care delivery in affected regions and protect against future outbreaks.

Initially identified in Kenya's Rift Valley in 1931, RVFV is a mosquito-borne phlebovirus that infects humans and ungulates, including cows, goats, and sheep. The virus causes a wide range of health effects in animals and humans, from mild illness to life-threatening hemorrhagic disease, encephalitis, hepatitis, kidney injury, and retinitis, with spontaneous abortions having been reported in animals.[2] Since RVFV sickens both humans and livestock, the virus's human health burden is compounded by the economic effects of loss of stock because of the deaths and slaughtering of sick animals. A 1997–1998 outbreak affecting the region of Somaliland led to a ban on livestock exports that caused an estimated $290 million in economic losses.[3] The current international response to RVFV relies predominantly on the One Health approach, which involves collaboration, coordination, and communication among communities, physicians, environmental health experts, and veterinarians to prevent and contain outbreaks.[4]

Mbarara Regional Referral Hospital serves a catchment area of 8 million people. Our patients with RVF are predominantly poor, rural farmers and butchers, who present in late stages of disease when they are often too sick to benefit from the services available at the hospital. In response to this outbreak and in collaboration with the Mbarara University of Science and Technology



An Integrated Response to Rift Valley Fever Virus.

and the Ugandan Ministry of Health, we developed a multidisciplinary response to RVFV in our region, which involves engaging affected communities, increasing training at local health centers, and expanding treatment at the referral hospital. This work has identified gaps in the current approaches to RVFV that prioritize prevention over treatment and highlights the need to move beyond reactive, siloed programs and toward a response that spans the health services delivery system (see figure). An integrated health systems approach to RVFV aligns with and complements the One Health strategy. Such an approach could advance care for people with RVF and research on the disease while helping health systems prepare for other emerging pathogens.

The first component of an integrated approach is community engagement. The response to RVFV should begin with working with affected communities, addressing local needs, providing disease education, and building trust. Community members, especially herders and butchers, are the first line when it comes to monitoring for RVFV because they can identify symptoms in livestock. Community engagement is a critical component of the One Health approach.[4] In Uganda, however, there is no pathway that includes incentives for community members to report potential animal cases of RVF to the public health system. In collaboration with veterinary health systems, global health organizations and local health officials could create clear, bidirectional communication pathways between animal workers and public health response teams, with incentives (including financial incentives) for herders to report cases and vaccinate animals. Community health workers are a clear choice for facilitating such communication. Community engagement, coupled with improved diagnostic tests to be used on farms or in animal herds, would also permit much-needed disease-surveillance programs and long-term relationship building, which could support emergency responses during outbreaks. Ultimately, early community engagement isn't specific to RVFV but will be critical to making health systems more responsive and equitable and is an important piece of the WHO goal of universal health coverage.

The second component of this approach involves empowering primary health centers. Government-run primary health centers are typically on the front lines and need resources to properly

identify, triage, and manage the care of patients with RVF. Although clinicians are routinely trained in identifying signs and symptoms of RVF, collecting samples, and reporting cases, many health centers have severe personnel shortages, inadequate personal protective equipment, and no reliable apparatus for transporting samples for testing. Testing in our region is done in central laboratories with a turnaround time of 48 to 96 hours, without commercially available rapid diagnostic tests for RVF. Providing diagnostic and treatment tools to primary health centers would allow patients to receive earlier treatment, and identifying more cases of RVF would add to knowledge of the spectrum of possible consequences of infection in humans. In addition, health centers could manage communication between affected communities and the public health system, in part by relying on community health workers, which would allow earlier identification of outbreaks.

Better-equipped hospitals will also be necessary. Severely ill patients with RVF receive care in referral hospitals where resources and expertise are concentrated. But most hospitals in Uganda are ill equipped to handle substantial numbers of patients with viral hemorrhagic fevers such as RVF because of inadequate isolation areas, a dearth of ventilators and dialysis machines, insufficient staff, and few protocols for care management. Building capacity at referral hospitals would provide opportunities for critical research into RVF pathophysiology and treatment. Although we assume that people with RVF require aggressive supportive care, outcome data on approaches to care are lacking, since many patients die before receiving a full evaluation or being enrolled in a clinical trial.

An audio interview with Nelson Wandera is available at NEJM.org

In regions prone to regular disease outbreaks, such as ours, there is a need for emergency response teams at referral hospitals that can coordinate the response to RVFV. Such teams could not only coordinate care during outbreaks but also facilitate training sessions and community outreach, oversee regional testing and referral systems, and communicate with appropriate government agencies to ensure that the resources provided for addressing RVFV match the need. Such teams have been proposed by the Africa Centres for Disease Control and Prevention and are standard (known as disaster medical assistance teams) in the United States, where two of us are based, but haven't been available in Africa.

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Finally, an integrated approach will require support for research centers. Too often, global health research priorities are set by Global North (e.g., U.S. and European) institutions and don't match the burden of disease in the Global South. This disparity in research priorities is changing, though there is a need for ongoing advocacy and funding in the area of neglected diseases, such as RVF. Researchers in affected countries and throughout the world should be supported and encouraged to work at all levels of the health system to effectively address RVF: they could engage with communities to support disease surveillance, including viral genomic surveillance, and vaccine trials; work with health centers to validate rapid diagnostic tests and describe pathogenesis; and collaborate with hospitals to develop and study therapeutics. Research and funding organizations in the Global North will also need to address the well-described institutional, national, and global structural barriers to localizing research.[5] Honoring Covid-19–related pledges to support vaccine-production capacity globally would facilitate efforts to address RVF and other emerging diseases.

RVFV is a growing viral threat with emerging potential for global spread that has been largely neglected by major public health entities.[2] We believe a coordinated international and interdisciplinary response will be critical for curbing the virus and its health effects. Such an approach would support the response to the ongoing outbreak, would provide flexibility to help health systems adapt to new pathogens, and could be integrated into the broader One Health framework, which would assist health systems serving vulnerable populations and

help build capacity to safeguard against future pandemics.

Disclosure forms provided by the authors are available at NEJM.org.

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Implanting a Recalled Device — Choices for Patients, Physicians, and Public Health

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Millions of patients worldwide depend on implantable cardioverter–defibrillators (ICDs) for protection against sudden cardiac arrest. ICDs are effective but require durable integration of complex implanted hardware and software systems intended to last for years. During more than three decades of clinical use, every major ICD manufacturer has issued safety advisories or recalls because of device problems identified by means of postmarketing surveillance.[1] When an ICD model is recalled because of a defective component or feature, the devices are usually no longer implanted, and patients living with these permanent implants undergo either prophylactic replacement or, more commonly, close follow-up to monitor for problems related to the device. However, today many patients are receiving ICDs that are subject to a Class I recall (the highest risk level), even though the underlying issue is not fully corrected. We believe this situation has important lessons for manufacturers, regulators, and clinicians invested in the safe use of these lifesaving devices.

In June 2022, physicians learned that certain models of ICDs previously and currently marketed by Medtronic might not deliver a full-energy shock when responding to a ventricular arrhythmia.[2] This problem occurs when the device erroneously detects the presence of a short circuit and then truncates the high-energy shock, delivering less than the programmed shock energy to the patient's heart. The outcome may be failure to terminate a ventricular arrhythmia, exacerbation of an arrhythmia, or misinterpretation of the short-circuit event as a failure of a defibrillator lead. As of April 2023, 95 devices, or 0.07% of those distributed, had been observed to deliver a reduced-energy shock. The Food and Drug Administration (FDA) categorized the manufacturer's recall of the devices as a Class I recall, which it uses when "there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death." In August 2022, a software update for already implanted devices became available; it ensures that a full-energy shock will be delivered when there is a low-level–current pathway in the high-voltage circuitry. The manufacturer estimated that the risk of death associated with this issue is 0.002% at 2 years, which is lower than the risk of death associated with prophylactic replacement of an ICD or cardiac resynchronization therapy defibrillator (0.032% to 0.043%).[2]

In May 2023, Medtronic issued another advisory for the same ICD models.[3] This advisory pertained to a defective "glassed feedthrough" that may result in a reduced-energy shock or no shock being delivered; the feedthrough links the electronic circuitry in the pulse generator to the lead connector. As of September 2023, 32 devices had been