PERSPECTIVE

Marburg Hemorrhagic Fever in Angola — Fighting Fear and a Lethal Pathogen

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On March 21, 2005, the Centers for Disease Control and Prevention (CDC) in Atlanta confirmed the presence of Marburg virus in 9 of 12 patient samples of tissue and blood sent for analysis by health authorities in Angola. The samples came from a growing number of patients, almost all of them linked to a single pediatric ward in the main hospital in Uige Province, who were rapidly dying from an unknown disease with hemorrhagic manifestations. The identity of the causative agent came as a surprise: Marburg hemorrhagic fever is an exceedingly rare disease, and there had never been a case before in Angola. Diagnostic confirmation set in motion a large-scale international response that began the day after the CDC's finding. Both the features of Marburg hemorrhagic fever and the conditions in Angola have made this response an extreme test of the national and international capacity to hold a dangerous emerging disease at bay.

Like the closely related Ebola hemorrhagic fever, Marburg is a rare but severe and highly fatal disease caused by a virus in the Filoviridae family (see diagram). The viruses that cause these two diseases are among the most lethal pathogens known to infect humans. Both hide in some still-elusive place in nature, surfacing from time to time to cause a few sporadic cases and then disappearing again. Both diseases can flare into dramatic outbreaks, usually associated with unsafe practices that amplify transmission in a health care setting. The sudden onset, rapid deterioration of patients' condition, dramatic hemorrhagic symptoms, and high mortality rate invariably cause great anxiety in the affected populations. In the current Marburg outbreak in Angola, fear, albeit understandable, has been one of the greatest impediments to the control of the spread of disease.

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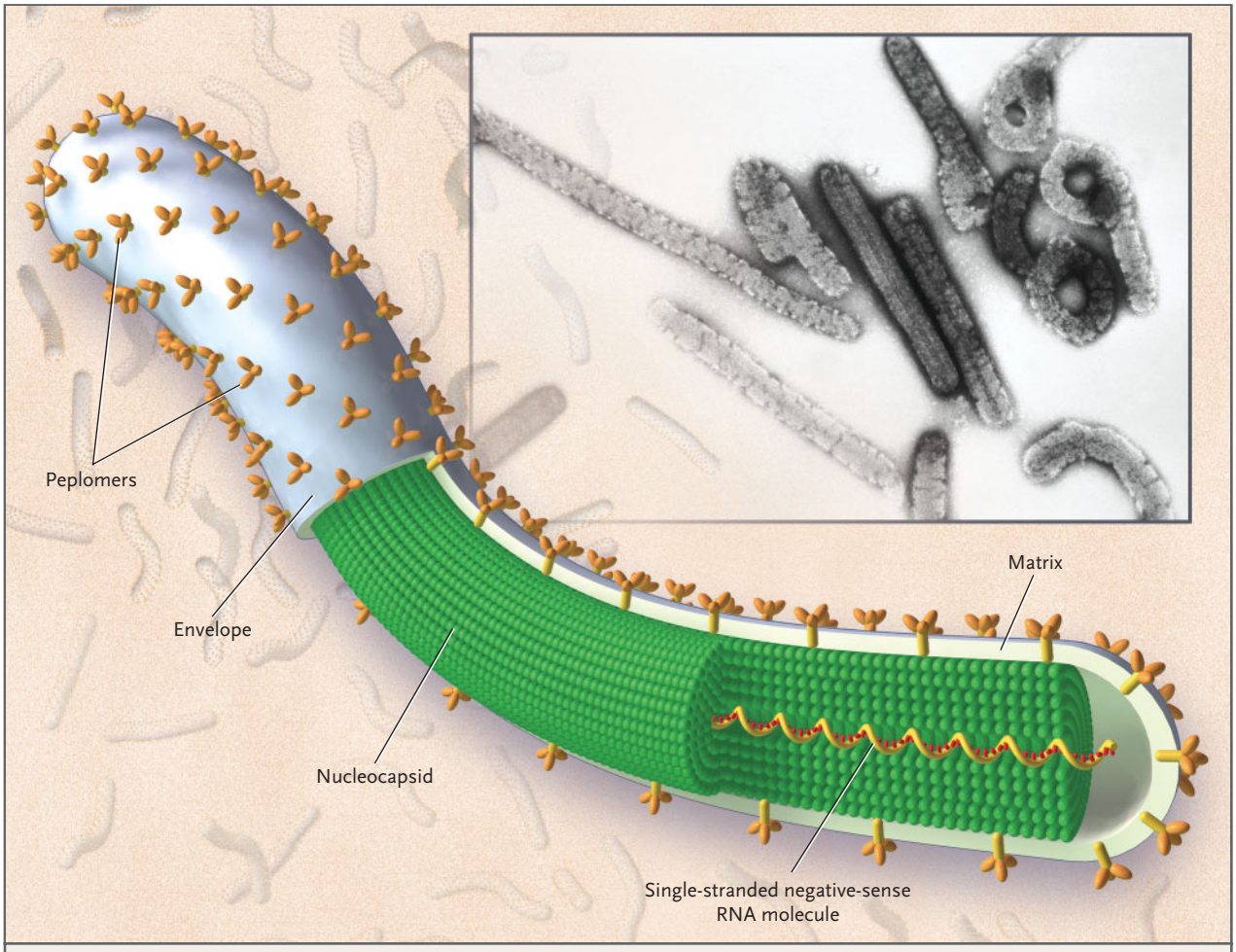
With more than 270 cases to date and almost as many deaths, this outbreak is the largest and deadliest of outbreaks of Marburg hemorrhagic fever on record. At present, the case fatality rate is 92 percent. It is also the first natural outbreak of the disease to take place in an urban setting. The only other large outbreak, which occurred in the Democratic Republic of Congo from 1998 to 2000, caused 154 cases and 128 deaths in two sparsely populated villages in a remote corner of the country.

In principle, the measures needed to contain the outbreak are few in number and straightforward in nature: rapid detection of cases and isolation of patients, tracing and care of contacts, infection control in hospitals, and avoidance of funeral and buri-

Obtaining Specimens from a Patient Who Has Died.

Courtesy of Dr. Pierre Formenty, WHO.



General Structure of a Filovirus.
The inset shows Marburg virus (courtesy of R. Regnery and E.L. Palmer, CDC).

al practices that allow close contact with bodies. The lack of public understanding of the disease, however, has impeded effective implementation of these measures. Since almost no one has survived this disease, communities associate the admission of patients to the isolation ward with certain death and have preferred to provide care at home, often hiding affected persons and then their dead bodies.

Apart from placing caregivers at great risk of infection, this resistance has also hampered efforts to identify and monitor contacts. Mobile surveillance and public-awareness teams were forced briefly to suspend operations on three occasions when they were stoned or threatened by hostile residents. The deaths of 16 doctors and nurses undermined the morale of hospital staff members who were working in already difficult conditions. When we arrived in Uige, the most immediate needs were to clean and disinfect hospital wards and the homes where patients had died, as well as to collect and bury corpses. We soon realized that building trust and securing community collaboration would play a critical role in bringing the outbreak under control.

Conditions in Angola have created additional challenges in the effort to contain the outbreak. Almost three decades of civil unrest have left the country with a population that is severely weakened by economic hardship, a hospital system in dire need of basic equipment and supplies, and inadequate communication and transportation infrastructure. Municipalities in the province have the crowding and poor sanitation common to urban settings, but the poor infrastructure is that usually seen in rural areas. Travel by road is often precarious, since many

roads are still heavily mined, necessitating air transport of staff and equipment and the use of helicopters to investigate alerts in remote areas.

Nonetheless, the success of the initial containment effort has surpassed our early expectations. Uige Province has remained the epicenter of the outbreak, currently accounting for 95 percent of all cases. No chains of transmission have been identified outside this province. Fears that the virus would establish a foothold in densely populated Luanda and its sprawling shantytowns have not been realized to date. Although the outbreak has not yet been contained, the numbers of new cases and deaths that occur daily have begun to decrease. The Uige municipality remains the hot spot of ongoing transmission.

The need to isolate patients has not been fully accepted by the population; on most days, the isolation ward has few, if any, patients. Home-based treatments involving the use of unsafe syringes have become an important route of transmission. Cases of Marburg disease have been confirmed in traditional healers. Procedures for infection control at the provincial hospital are not rigorously followed, and serious high-risk exposures on open wards have created worrisome opportunities for nosocomial amplification and a second wave of cases. During the last week of April 2005, an additional two doctors were directly exposed while trying to save the lives of patients who were later confirmed to be infected with the virus. Bodies are not always promptly collected, and beds are not always disinfected after deaths.

Every outbreak presents a unique set of problems that have to be solved innovatively and quickly, under emergency conditions. Each outbreak of international concern does, however, leave the World Health Organization (WHO) and its partners with accrued experience and more technical innovations to draw on when the next event inevitably occurs. Virtual networks and infrastructure, developed by the WHO during the past decade and seriously tested during the 2003 outbreak of severe acute respiratory syndrome (SARS), made it possible to quickly assemble the necessary expertise and laboratory support for the current outbreak. To date, more than 70 international staff members, drawn mainly from institutions within the Global Outbreak Alert and Response Network and rapid-response teams maintained by the WHO's regional office in Brazzaville, Democratic Republic of Congo, have participated in containment activities. Many of these professionals are experienced in the control of viral hemorrhagic fevers in African settings and understand the importance of working with communities as partners in controlling outbreaks.

Techniques for sensitizing local populations and gaining their trust and cooperation, developed during responses to outbreaks of Ebola hemorrhagic fever, have been applied with measurable success in Angola. Portable field laboratories were made available and operated in Uige by the Canadian National Microbiology Laboratory and in Luanda by the CDC. A virtual network of high-containment laboratories with personnel who are experienced in the diagnosis of viral hemorrhagic fevers has contributed essential support. The CDC sequenced the virus early in the outbreak, compared it with viruses from previous outbreaks, and put to rest questions about whether this outbreak was caused by an unusually lethal strain.

Daily teleconferences with the WHO offices in Uige and Luanda have made it possible to identify needs — whether for disinfectants and personal protective equipment or for vehicles, satellite telephones, and handheld radio sets — and meet them within a day or two. Surveillance has been greatly facilitated by basic and communications infrastructure that was put into place for the poliomyelitis-eradication initiative. The speed and intensity of the international response, including rapid funding of activities, underscore the heightened concern about emerging diseases and illustrate the resources this concern can generate in an emergency situation — even when the threat of international spread and economic disruption is far less than that posed by diseases such as SARS and pandemic influenza or the prospect of a bioterrorist attack.

But outside help can never fully compensate for inadequate national capacity, so another important goal is to transfer the skills and responsibilities for responding to an outbreak to local professionals, and training is under way with this result in mind. Past experience in many sub-Saharan African countries, where the viral hemorrhagic fevers sporadically resurface, suggests that the first cases in the next outbreak will almost certainly occur in hospitals. Health care facilities will therefore place doctors, nurses, and other patients at the greatest risk. As in Angola today, frontline workers will not only be at great personal risk but will also be facing patients for whom little, if anything, can be done — either to save their lives or to reassure and comfort their loved ones. This, too, is part of the human side of these devastating, yet fortunately rare, diseases.