



## International Cooperation Cracks a Mysterious Epidemic in Uganda

*A surprise outbreak of yellow fever in Uganda in 2010-11 sickened at least 263 people and killed 74 others. Nearly 40 years had passed since the previous recorded transmission of yellow fever in Uganda—long enough that it took an international team of human, animal and insect scientists nearly 42 days of collaborative work to identify the cause of the outbreak and then another month to receive and administer approximately 2.5 million doses of the vaccine.*

In November 2010, strikingly similar reports of a “strange disease” began pouring into the Ministry of Health; first from the western district of Bundibugyo, and then from the northern districts of Abim and Agago. Reported symptoms were consistent with a viral hemorrhagic fever: headache, fever, unexplained bleeding, and a high rate of mortality.

The only common denominator seemed to be that most cases occurred in men with a history of consuming locally brewed alcohol called ‘waragi’, explains Mac Farnham, DVM, assistant professor of Veterinary Population Medicine at the University of Minnesota in Minneapolis and member of the international team of investigators collaborating at the beginning of the outbreak to support the Ugandan Ministry of Health. “We wondered ‘Is this Ebola or could this be a cluster of cases of alcohol poisoning?’”

### **Mosquitoes, monkeys and a dangerous virus**

Yellow fever was not on the radar because the last reported case in Uganda had occurred nearly 40 years ago. The natural immunity level in endemic areas reaches about 50% by adulthood, and a person who has recovered from the disease or received vaccination typically develops lifelong immunity to re-infection. Travelers and health workers routinely receive vaccination for yellow fever, but most of Uganda’s rural population does not. The government of Uganda vaccinates portions of its population for “background” diseases, such as typhoid and yellow fever, only when prompted by emergency outbreaks.

A combination of natural immunity and vaccinated immunity leftover from French vaccination schemes in its former African colonies in the 1950s and 60s kept the number of cases of yellow fever low until the 1990s. What changed in Uganda is demographics: a younger, unvaccinated population that has not developed natural immunity has replaced a largely immune population, according to a 1998 WHO report on yellow fever.<sup>1</sup>

The virus that causes yellow fever typically infects humans through mosquito bites; but even when mosquito counts are low during the dry season, a reservoir of the virus remains in forest monkeys, who come to ground level to feed. When people hunt in the forest or log trees, bites

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<sup>1</sup> <http://www.who.int/vaccines-documents/DocsPDF/www9842.pdf>



from infected monkeys can transmit the pathogen—an increasingly likely scenario because of pressure from a growing, less affluent, rural population. The majority of cases of yellow fever resembles severe flu and resolve within a few weeks with supportive care, such as maintaining hydration and bed rest. However, about 15% of cases become more severe marked by jaundice, bleeding or liver failure. Severe cases of yellow fever resemble other diseases where people bleed to death, such as Ebola or Marburg.

The bleeding diseases are the most feared by local people, according to Farnham. When local media and word-of-mouth communication inflate fears, as happened in the early phase of the 2010-11 outbreak, people avoid clinics and hospitals. People may not seek treatment or bring food to their relatives receiving treatment. Clinicians and investigators struggle to gather adequate information, such as laboratory blood tests, which reveal the exact cause and nature of disease. This is one of the reasons it took 42 days to pinpoint yellow fever as the cause of the outbreak.

Logistics and finances also rank as major impediments. The government of Uganda has been decentralized for nearly a decade. “The major challenges the government faces [during outbreaks] are financial, logistical and technical. Uganda needs support with expertise we lack, for example in zoonoses, from international partners [such as RESPOND<sup>2</sup> and AFENET<sup>3</sup>],” writes by email Issa Makumbi, MD, head of the Epidemiology and Surveillance Unit for the Ugandan Ministry of Health and who also serves as the WHO International Health Regulations focal point for the country.

The surprise outbreak of yellow fever in Uganda in 2010-2011 sickened at least 263 people and killed as many as 74 others in the northern region.

### **Ready when you are**

The 2010-11 outbreak of yellow fever was not the first time Farnham and Makumbi worked together. They collaborated in 2010 on an outbreak of anthrax in Queen Elizabeth National Park that killed 90 hippopotamus and buffalo, threatening local people and domestic livestock who might contract the disease. They have also trained other health professionals in One Health techniques, like risk and crisis communication. “Issa Makumbi is a colleague and a good friend,” explains Farnham.

When Makumbi received the first case reports in November 2010, he turned to Farnham for help coordinating activities of support partners on a national level through the National Disease Task Force, which typically convenes during major outbreaks. At the time, Farnham was living in Kampala working for USAID’s Emerging Pandemic Threats RESPOND project. He helped the Task Force mobilize an international team of health professionals, including: various Ugandan

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<sup>2</sup> RESPOND is part of the United States Agency for International Development (USAID) Emerging Pandemic Threats program, located online at: [http://www1.usaid.gov/press/releases/2009/pr091021\\_1.html](http://www1.usaid.gov/press/releases/2009/pr091021_1.html)

<sup>3</sup> The African Field Epidemiology Network. <http://www.afenet.net>



ministries, WHO, U.S. CDC<sup>4</sup>, AFENET, USAID, UNICEF<sup>5</sup>, Doctors Without Borders, the Uganda Virus Research Institute and others. Within a few days the interdisciplinary teams were dispatched to western and northern Uganda to investigate and assist local health authorities in mounting a response.

The Task Force convenes every day or every other day as needed at both district and national levels in the early stage of an outbreak. What happens during the meetings is a flurry of information gathering and sharing: sub-committees form that are responsible for managing cases, laboratory diagnostics, disease surveillance, health education and vaccination; and then partners are expected to co-ordinate with officials and each other, report what they see and communicate needs. During an outbreak, district health professionals can quickly become overwhelmed with cases, making it critical that support relationships are already in place.

“We have set up our partnerships so that when a district reports a disease to the Ugandan Ministry of Health, it triggers us at the national level to send an investigative team. Typically, we send an epidemiologist and a physician, but because the yellow fever outbreak was so strange, I wanted to also send a veterinarian and an entomologist—to use the One Health approach,” explains Makumbi.

### **Easing fears**

Eventually, investigators collected enough blood and tissues samples from patients and sent the vials to the U.S. for tests performed by at highly specialized laboratories. The CDC Special Pathogens and Enterics laboratories in Atlanta, Georgia, identified yellow fever virus as the culprit. Then the CDC laboratory in Ft. Collins, Colorado, confirmed the finding. At the end of December 2010, the labs provided the One Health team with the break-through they needed to stop the epidemic.

The Ugandan Ministry of Health applied for two million doses of yellow fever vaccine through the Global Alliance for Vaccines and Immunization (GAVI). The vaccines arrived ten days later, and a massive two-week-long vaccination campaign ensued in five districts in January 2011.

“One thing which surprised me during this outbreak was many members of communities or extended families were willing and interested to help with surveillance and investigation for new cases. Typically, with so many unknown factors in what looks like an outbreak of viral hemorrhagic disease, there is a lot of fear and rumor circulating in the community. One potential difference in this case may have been that people saw friends and family members recover when they received treatment or vaccination, and that eased their fears,” suggests Farnham.

Another outcome of the yellow fever outbreak is that the government of Uganda must conduct a nationwide risk assessment to figure out why, exactly, the outbreak happened. The challenge

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<sup>4</sup> U.S. Centers for Disease Control. [www.cdc.gov](http://www.cdc.gov)

<sup>5</sup> The United Nations Children's Fund. [www.unicef.org](http://www.unicef.org)



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with outbreaks such as this, where disease mosquitoes transmit disease, is that researchers have to wait until the next rainy season to conduct environmental surveys. Even then, answers are not guaranteed because the short life span of mosquitoes means that the carriers could die off before investigators arrive. Further, nationwide surveys prove logistically challenging in a country that struggles with inadequate physical infrastructure and financial resources.

For this outbreak of a “strange disease”, Farnham and Makumbi credit the unique strength of collaboration across health disciplines, governments and institutions for correctly diagnosing the disease and then providing protection for millions of people.

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