

Ebola Outbreak in Kikwit, Democratic Republic of the Congo: Discovery and Control Measures

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The Ebola epidemic in Kikwit, Democratic Republic of the Congo, was recognized because of a nosocomial outbreak in Kikwit General Hospital. Initially, a diagnosis of shigella infection was suspected because many patients presented with bloody diarrhea. On 4 May 1995, blood samples from 14 acutely ill patients were sent to the Centers for Disease Control and Prevention (Atlanta), and on 9 May, a diagnosis of Ebola hemorrhagic fever was confirmed. The major disease control measures that were undertaken were the isolation of patients in a quarantine ward at Kikwit General Hospital, the distribution of protective equipment to health care workers and family members caring for Ebola patients, the use of barrier nursing techniques, the distribution of health education material, active and passive case finding, and the burying of the deceased in plastic bags by a trained team of Red Cross volunteers who wore gloves and protective clothing.

Between January and June 1995, the town of Kikwit, Democratic Republic of Congo (DRC), and its surroundings were the epicenter of a severe outbreak of Ebola (EBO) hemorrhagic fever (EHF) that affected 317 people and killed 245 [1–3]. The epidemic occurred during a lengthy political transition in DRC that was characterized by the interruption of international cooperation, inadequate disease surveillance and reporting, and a breakdown of the general health care infrastructure, due in part to a lack of motivation among poorly paid health personnel. Herein, we describe how the outbreak was detected and what initial control measures were undertaken.

Identification of the First Case and Initial Laboratory Investigations

On 27 April 1995, the director of Kikwit General Hospital sent an alarming message to one of the authors (JJM-T) about an outbreak of bloody diarrhea that had already caused several deaths. On 28 April, in response to the alert, a laboratory technician from Kinshasa, DRC, was sent to Kikwit with laboratory supplies and reagents (table 1). On 29 April, the Diocese of Kikwit also sent an emergency message regarding the outbreak. Bacteriologic investigations were done from 29 April to 6 May at the laboratory of JJM-T in Kinshasa to determine the etiology of the bloody diarrhea and fever.

MacConkey's agar (Difco, Detroit), Salmonella-Shigella agar (Difco), and selenite buffer were used to isolate enteropathogenic bacteria from patients' stools. Inoculated culture

media were incubated at room temperature ($>30^{\circ}\text{C}$) because there was not an appropriate bacteriology incubator. Blood (10 mL) from febrile patients was inoculated into two 120-mL bottles containing either 50 mL of brain-heart infusion broth (bioMérieux, Lyon, France) for aerobic bacteria or 50 mL of Wilkins-Chalgren anaerobe broth (Oxoid, London) for anaerobic bacteria. A total of 97 blood samples were processed for *Shigella* species, the most frequent cause of bloody diarrhea. Most of the specimens were semisolid (44) or liquid (26); only 23 specimens were bloody on macroscopic investigation, of which only 4 were positive for *Shigella* species. No *Entamoeba histolytica* was detected in the stool smear after direct examination. All 9 blood culture results were negative for *Salmonella typhi*, the usual agent of protracted fever in DRC. Moreover, the distribution of diarrhea cases by age and sex of patients showed that 20- to 30-year-old adults of both sexes were affected by the disease and children were not. These preliminary laboratory findings ruled out *Shigella* species as the cause of the bloody diarrhea.

Clinical Investigations

On 2 May 1995, a case-report meeting was organized with physicians from Kikwit General Hospital, the epicenter of the outbreak; Kikwit II Maternity Unit, where the first cases were observed in early April; Mosango General Hospital, 110 km from Kikwit; and Bonga-Yassa General Hospital, 150 km from Kikwit, where a patient had been transferred. The disease as described by these physicians was characterized as acute with persisting fever that did not respond to antimalarial and antibiotic treatment, headache, intense fatigue, severe abdominal pain, vomiting, diarrhea, and bleeding signs, such as gingival and conjunctival injection.

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Table 1. Chronology of events during Ebola virus outbreak in Kikwit, Democratic Republic of the Congo.

Date (1995)	Events
13 January	Death of charcoal maker who worked in forest near Kikwit.
10–11 April	Laboratory technician from Kikwit II Maternity Unit underwent surgery in Kikwit General Hospital for suspected perforated bowel.
13 April	Two nurses (1 was an Italian nun) who worked in operating theater or cared for laboratory technician patient became ill.
18 April	Mayor ordered epidemiologic investigation on cause of numerous deaths in Kikwit.
25 April	Nurse (Italian nun) died.
27 April	Urban medical inspector instructed medical director of Kikwit General Hospital, who was on special mission to Kinshasa, to alert health authorities to outbreak of bloody diarrhea.
28 April	Laboratory technician was sent from Kinshasa to Kikwit with laboratory supplies and reagents.
29 April	Emergency message about outbreak was sent to health authorities by Diocese of Kikwit.
1 May	Local control commission against bloody diarrhea was set up, and preliminary laboratory findings were discussed.
2–3 May	Clinical diagnosis of viral hemorrhagic fever was established.
4–5 May	In Kikwit, blood samples from 14 acutely ill persons were collected and sent to CDC through Institute of Tropical Medicine (Antwerp, Belgium). First antiepidemic measures were taken: Isolation pavilion was opened; hospitals, health care centers, and schools were closed; and no. of personnel in contact with patients was reduced. In Kinshasa, government decided to send special mission to explore site of epidemic.

Epidemiologic Investigations

The EBO epidemic was recognized because of a nosocomial outbreak at Kikwit General Hospital. To find out how the disease was introduced into the hospital, the epidemiologic history of the disease was analyzed to identify the source of infection and its mode of transmission. The index case of the nosocomial outbreak was a 36-year-old male laboratory technician from Kikwit II Maternity Unit. He underwent laparotomy at Kikwit General Hospital for a suspected perforated bowel after protracted fever. Postoperative abdominal distention increased, and an abdominal puncture revealed bloody peritoneal fluid. The patient underwent a new laparotomy, which showed massive intraabdominal hemorrhage. Three days later, on 14 April 1995, the patient died.

Medical personnel who cared for the technician in the operating theater or hospital wards became ill with fever, headache, myalgia, asthenia, and, in some cases, hemorrhagic manifestations. The first cases among medical personnel at Kikwit General Hospital occurred on 14 April, 4 days after the first laparotomy. The mode of transmission through contact with body fluids suggested that the disease was a viral hemorrhagic fever (EBO or Marburg virus) and that bloody diarrhea was merely an advanced symptom of the disease. This clinical diagnosis was confirmed when blood from 14 acutely ill patients was sent to the Centers for Disease Control and Prevention (CDC, Atlanta) via the Institute of Tropical Medicine on 4 May 1995. CDC received the samples on 9 May and confirmed the diagnosis of EHF on 10 May, providing results by satellite telephone. Of the 14 samples tested, 1 had EBO antigen, 2 had EBO-specific IgM antibodies, and 12 had EBO virus RNA, as

detected by reverse transcriptase–polymerase chain reaction. Virus was isolated from specimens of 12 patients.

Control Measures

On 4 May 1995, the following control measures were taken to minimize the risk of virus spread: All hospitals, laboratories, and health centers were closed throughout Kikwit and its surroundings; patients were isolated in a quarantine pavilion at Kikwit General Hospital; a volunteer team of 1 physician and 3 nurses was isolated with the patients in the quarantine ward (although at that time they had barely any gloves or protective clothing); and a pamphlet that was prepared to alert the community of the outbreak was distributed throughout the city. These interventions had minimal impact because there was a lack of running water, electricity, and latrine facilities in the isolation ward, and food had to be provided by relatives of the patients. Most patients and 2 physicians fled the hospital.

On 8 May, the Zairian government officially declared the epidemic and requested the World Health Organization (WHO) to mobilize and coordinate international assistance. On 10 May, an international scientific and technical committee was formed in Kikwit to investigate and control the epidemic. It was composed of experts from DRC, WHO, CDC, Institute of Tropical Medicine, Médecins sans Frontières (Belgium), South African Medical Institute, Red Cross, Institut Pasteur (Paris), and Sweden. The objectives of the committee were to interrupt disease transmission and reestablish confidence in the health services [4].

Epidemiologic surveillance was the cornerstone of the control strategy and involved gathering information through city-

Table 2. Infections that may present with clinical manifestations similar to those of Ebola hemorrhagic fever (EHF).

	Clinical and epidemiologic differences from EHF	Laboratory diagnosis
Nonhemorrhagic infections		
Malaria	Bleeding infrequent, responds to antimalarial drugs	Thick smear
Typhoid fever	Only occasionally causes intestinal bleeding, responds to antibiotics	Blood culture
Shigellosis, Campylobacteriosis, <i>Escherichia coli</i> enteritis	Bloody diarrhea but no other hemorrhagic manifestations, responds to antibiotics	Stool culture
<i>Entamoeba histolytica</i> enteritis	Bloody diarrhea but no fever, responds to antiparasitic treatment	Direct stool examination
Meningococcal sepsis	Petechiae, neck stiffness can be present, responds to antibiotics	Gram's stain of material aspirated from petechiae and blood or cerebrospinal fluid culture
Other viral hemorrhagic fevers		
Yellow fever	Often icterus, no person-to-person or nosocomial transmission	Serology, culture, liver biopsy of fatal cases
Lassa fever	Endemic in West Africa, contact with excreta of rodents is risk factor, person-to-person or nosocomial transmission is rare	Serology, Culture
Crimean-Congo hemorrhagic fever	Transmission by tick bite, occasional nosocomial transmission, high risk groups include persons exposed to sheep and cattle or their tissues, or to mosquitoes	Serology, culture
Rift Valley fever	Transmission by tick bite, occasional nosocomial transmission, high risk groups include persons exposed to sheep and cattle or their tissues, or to mosquitoes	Serology, culture
Marburg hemorrhagic fever	Differential diagnosis with EHF impossible without virologic studies	Serology, culture

wide passive surveillance at reopened health centers; citywide active surveillance conducted by medical students from the University of Bandundu, who sought active cases and contacts throughout the city; establishment of a rumor registry of suspected cases and deaths within the community; and regional epidemiologic surveillance, using the local radio station of the Kikwit Diocese [5]. Protective equipment was distributed to health care workers so that they could safely provide care for EBO patients. Medical and relief personnel were trained on the proper use of protective clothing (gowns, masks, gloves), principles of patient isolation and management on the quarantine ward, cadaver management, and use of body bags. In Kikwit during the epidemic, all the bodies, regardless of the cause of death, were buried by a team of trained Red Cross volunteers who wore gloves and protective clothing. This was done to avoid the traditional burying rituals (cleaning of the dead body by family members, kissing and touching the body, transporting the body to the village of origin, keeping hair and nails as souvenirs). These burial rituals were an important cause of EHF transmission during the epidemic.

Discussion

The unusual increase of deaths from bloody diarrhea and fever among health care personnel triggered an alert of the Kikwit outbreak in late April 1995, but retrospective studies subsequently suggested that the index case was likely to have been a charcoal maker who became ill in early January 1995 and died on 13 January. The disease was introduced into the

Kikwit II Maternity Unit, causing a small outbreak that remained unrecognized.

As in previous epidemics in Yambuku [6] and Nzara [7], it was difficult to make a correct clinical diagnosis of EHF during the early phase of the epidemic because the signs and symptoms are not specific. The disease was confused with common diseases that frequently cause bloody diarrhea or fever, such as shigellosis and typhoid. Early recognition was further delayed by the lack of laboratory facilities. In addition, EBO disease is not well known to health care personnel, and an outbreak of EBO was unsuspected in the savanna area, which is distant and ecologically distinct from the forests around Yambuku.

In 1976, the epidemics in Yambuku and Nzara were first thought to be typhoid because the most frequent causes of fever in the tropics are malaria and typhoid. Under special conditions, malaria can cause epidemics; however, unlike the case with EBO, both adults and infants are usually infected. Mortality rates could be high due to antimalarial drug resistance in *Plasmodium falciparum*, but laboratory diagnosis is very easy if a microscope is available for examination of blood films. Typhoid is endemic in DRC and affects both infants and adults, and fortunately most strains remain susceptible to chloramphenicol and other standard antibiotics. Direct diagnosis is through blood culture.

In early 1995 during the first stages of the EBO outbreak in Kikwit, the symptom of bloody diarrhea was thought to be due to infection with *Shigella dysenteriae* type 1 [8], which had become increasingly common in DRC after emerging in the Great Lakes region of the eastern part of DRC and spreading to the western part of the country. More than 50% of the 306

health zones in DRC had experienced outbreaks, with high mortality rates among adults and children, and most strains isolated from patients were multidrug resistant. Intestinal amebiasis, which is also very common in DRC, is another cause of bloody diarrhea but is generally not associated with fever and usually does not cause epidemics with high mortality. Enterohemorrhagic *Escherichia coli* is not well documented in Africa, especially in DRC.

The etiologic diagnosis of EHF in a single patient with fever and hemorrhagic manifestations cannot be made by a physician in rural Africa without laboratory support (table 2). The differential diagnosis should also include other viral hemorrhagic fevers, such as Marburg virus, yellow fever, chikungunya, Rift Valley fever, Crimean-Congo hemorrhagic fever, and Lassa fever. Dengue hemorrhagic fever has not been reported from Africa [9]. EHF should be suspected when a cluster of cases with fever and bleeding manifestations occurs and certainly when health care workers are involved.

It was shown in postmortem skin biopsies obtained during the Kikwit epidemic that EBO virus antigen is present in large quantities in dermal endothelial cells and connective tissue [10]. On the basis of this finding, a skin-biopsy kit was proposed as a tool for EHF surveillance in Africa [10]. An advantage of this system is that the skin biopsies conserved in formol do not contain infectious virus. Therefore, specimens can easily be sent to a reference laboratory without special precautions.

As long as the hygienic conditions remain substandard in many African hospitals and health care workers are unable to adhere to universal precautions to prevent the transmission of bloodborne infections, there is a risk for new EBO outbreaks

in African cities. With the increased awareness of hemorrhagic fever among African health care workers and a stricter surveillance system, any new EBO outbreak hopefully will be diagnosed at a much earlier stage.

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