

Serologic Survey among Hospital and Health Center Workers during the Ebola Hemorrhagic Fever Outbreak in Kikwit, Democratic Republic of the Congo, 1995

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From May to July 1995, a serologic and interview survey was conducted to describe Ebola hemorrhagic fever (EHF) among personnel working in 5 hospitals and 26 health care centers in and around Kikwit, Democratic Republic of the Congo. Job-specific attack rates estimated for Kikwit General Hospital, the epicenter of the EHF epidemic, were 31% for physicians, 11% for technicians/room attendants, 10% for nurses, and 4% for other workers. Among 402 workers who did not meet the EHF case definition, 12 had borderline positive antibody test results; subsequent specimens from 4 of these tested negative. Although an old infection with persistent Ebola antibody production or a recent atypical or asymptomatic infection cannot be ruled out, if they occur at all, they appear to be rare. This survey demonstrated that opportunities for transmission of Ebola virus to personnel in health facilities existed in Kikwit because blood and body fluid precautions were not being universally followed.

Since first described in 1976, Ebola (EBO) hemorrhagic fever (EHF) has been characterized by its high case fatality and human-to-human transmission. The three early EHF outbreaks in Democratic Republic of the Congo (DRC) and Sudan in 1976 and 1979 [1–3] and the most recent in DRC in 1995 [4] have shown a pattern of amplification through nosocomial transmission. Nonspecific signs and symptoms in patients, high titers of virus in body fluids and secretions, and lack of compliance with precautions to prevent exposure to blood and body fluids placed health care workers and other patients at high risk of infection with EBO during these outbreaks. During the Kikwit epidemic in 1995, health care workers represented 80 (25%) of the 315 patients meeting the case definition for EHF [5]. To investigate the occurrence of asymptomatic or atypical forms of EHF among this highly exposed group and to increase the completeness of EHF surveillance, we conducted a serologic and interview survey among personnel working in hospitals and health care centers in Kikwit and surrounding towns.

Materials and Methods

Subjects and sample collection. From May to July 1995 (at the height of the EHF epidemic in Kikwit), we conducted a survey of health care workers and other personnel from Kikwit General Hospital, the epicenter of the EHF epidemic, four other hospitals (including one maternity hospital), and 26 health care centers in Kikwit and surrounding towns. Personnel working in the hospitals and health centers at the time of the survey were approached for participation; persons known to have met the EHF case definition were excluded. A list of personnel employed at Kikwit General Hospital aided identification of eligible workers there. A questionnaire was administered, and a blood specimen was obtained from each participant.

Information collected on the questionnaire included the subject's age, sex, work location (hospital, branch, or unit), type of work, recent health history (including disease with fever and hemorrhagic signs), possible contact with EHF patients or with body fluids or secretions from suspected EHF patients in health care or home settings, and nature of this contact. For a subset of workers from Kikwit General Hospital, more detailed information was obtained regarding occupational exposures and precautions taken to prevent spread of infection.

Blood specimens were obtained from the participants by venipuncture in vacutainer tubes. After coagulation at room temperature, specimens were centrifuged, and serum aliquots were initially stored at 4°C and then sent on dry ice for testing to the Special Pathogens Branch, Centers for Disease Control and Prevention.

Serologic tests: IgM and IgG ELISA. IgG ELISAs were performed by coating polyvinyl chloride microtiter plates overnight at 4°C with a basic buffer detergent extract of uninfected Vero E6

Informed consent was obtained from the participants in this research, which was performed according to guidelines of the US Department of Health and Human Services in conjunction with the Ministry of Health, Democratic Republic of the Congo.

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The Journal of Infectious Diseases 1999;179(Suppl 1):S98–101
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0022-1899/99/79S1-0017\$02.00

cells and Vero E6 cells infected with the Zaire subtype of EBO, which were further inactivated by irradiation with 20,000 Gy (2×10^6 rads). Sera were diluted 1:100 and then 4-fold through 1:6400 in 5% nonfat milk in PBS-Tween and allowed to react with the coating antigen. Bound IgG was detected with mouse anti-human IgG conjugated to horseradish peroxidase. Each serum specimen (diluted 1:100 and then 4-fold through 1:6400) was run in parallel with a control antigen of uninfected cells in suspension.

An ELISA IgM capture test was run on all positive IgG sera. IgM antibodies were detected by capturing IgM from serum with goat anti-human μ (Tago, Burlingame, CA) adsorbed to 96-well microtiter plates and then by allowing the captured IgM to react with viral antigen (crude suspension of medium and EBO [subtype Zaire]-infected Vero E6 cells, inactivated by irradiation with 50,000 Gy [5×10^6 rads], frozen and thawed twice, and sonicated) and measuring bound antigen with hyperimmune anti-EBO rabbit serum and anti-rabbit horseradish peroxidase conjugate. In the IgG assay, each serum specimen (diluted 1:100 and then 4-fold through 1:6400) was run in parallel with a control antigen of uninfected cells in suspension. The substrate used in both tests was ABTS (Kirkegaard & Perry, Gaithersburg, MD).

For both the IgG and IgM assays, optical densities at 410 nm (OD_{410}) were recorded, and the OD_{410} of the control antigen-coated well was subtracted from its corresponding test antigen well to yield the adjusted OD_{410} at each dilution. The result was considered positive when the sum of the adjusted optical densities for the 4 dilutions tested was >1.25 for IgG and >0.50 for IgM and the numeric titer or dilution was $\geq 1:400$. The development and performance of the serologic tests are described by Ksiazek et al. in this supplement [6].

Estimate of attack rate. Overall and job-specific attack rates for EBO infection among personnel working at Kikwit General Hospital were estimated by matching the most recent hospital personnel list (May 1995) with the EBO surveillance registry.

Results

At Kikwit General Hospital, 37 of the 429 workers on the personnel list met the case definition for EHF, for an overall attack rate of 9%. The attack rate was 31% (4/13) for physicians, 10% (22/212) for nurses, 11% (7/62) for technicians/room attendants, and 4% (4/111) for other workers. These Kikwit General Hospital employees and employees of other health care facilities who met the case definition were excluded from our survey.

Completed questionnaires and blood specimens were obtained from 402 persons, 168 women (42%) and 233 men (58%); the sex was not recorded for 1 person. One-third of the participants were working in a clinic or health center at the time of the interview, and 70% were working in a hospital. In table 1, participants are classified by job, according to their contact with patients and site of employment. Direct-contact jobs included those involving attending patients (nurses, physicians, medical and nursing students, and room attendants), removing and burying of cadavers (Red Cross workers and attendants), or collecting or processing clinical specimens

(phlebotomists and laboratory workers). Indirect-contact jobs included those involving the washing of bedding and other materials used on the wards or contact with clothing, food, or utensils used by patients (maintenance and support personnel). Jobs unlikely to involve patient contact included clerical, secretarial, and construction jobs. Of the 402 participants, 278 (69%) held direct-contact jobs, 9 (2%) held indirect-contact jobs, 99 (25%) held jobs unlikely to bring them into contact with patients, and 16 (4%) had job titles that were not specified, so their contact classification was unknown.

Participants reported on-the-job contact with an EHF patient or suspected EHF patient as follows: 204 (73%) with direct-contact jobs, 3 (33%) with indirect-contact jobs, 63 (64%) with jobs unlikely to involve patient contact, and 9 (56%) with unknown job classification (table 2). Of the 279 participants who reported on-the-job contact with at least 1 EHF or suspected EHF patient, 233 (84%) reported that they had been in the patient's room, 43 (15%) had performed examinations, 8 (3%) had performed surgery, 145 (52%) had given food to or conversed with the patient, 17 (6%) had handled body fluids in the laboratory, 37 (13%) had obtained patient blood, 10 (4%) had washed the patient, 7 (3%) had washed the patient's clothes, 20 (7%) had washed a cadaver, and 35 (13%) had "other" contact. Thirty participants who reported contact with an EHF or suspected EHF patient on the job also had contact with a patient at home; an additional 3 participants had contact at home but not on the job.

For a subset of 48 participants with direct-contact jobs at Kikwit General Hospital, detailed questions were asked regarding personal precautions against infection. These 48 workers reported a total of 151 on-the-job contacts (defined as in the above paragraph) with EHF or suspected EHF patients. The following information describes personal hygiene after contact with these patients (n indicates the denominator for the percentages, excluding those with missing information): For 74% of contacts ($n = 147$), the respondent reported washing his or her hands following contact, but the hand washing occurred immediately following contact for only 21% ($n = 132$), disinfectant was used for hand washing by 16%, disinfectant plus soap and water were used by 10%, and water and soap only were used by 74% ($n = 120$). For 76 of the 151 contacts, dates for the period during which contact occurred were available; all 76 contacts occurred prior to arrival of the international epidemic response team in Kikwit. Of the 75 contacts for whom information was available, 18 (24%) used complete protection (gloves, gown, mask, goggles) during the contact; 6 (8%) used only gloves; the remaining 24 (32%) used neither gloves nor complete protection.

None of the 402 persons interviewed had any signs or symptoms suggestive of EHF at the time of the interview; however, 129 recalled having been sick in the 3 months prior to the interview, and for 2 of them, the illness involved fever and hemorrhage. Both had negative EBO serologic test results. None of the other 400 specimens tested was strongly positive;

Table 1. Site of employment and job classification according to expected type of patient contact for 402 hospital and clinic employees.

Site	Expected patient contact			
	Direct	Indirect	Unlikely	Unknown
Kikwit General Hospital	110 (72)	6 (4)	22 (14)	14 (9)
Kikwit II Maternity Hospital	34 (83)	1 (2)	6 (15)	0 (0)
Mosango Hospital	20 (53)	1 (3)	17 (45)	0 (0)
Yassa-Bonga Hospital	15 (29)	0 (0)	36 (71)	0 (0)
Other	99 (83)	1 (1)	18 (15)	2 (2)
Total	278 (69)	9 (2)	99 (25)	16 (4)

NOTE. Data are no. (row %).

however, 12 specimens were borderline positive at an IgG titer of 1:400, and all had a sum of >1.25 for the adjusted optical densities for the 4 dilutions tested for IgG. Of these 12 workers, 1 was a cashier, 1 was an aide, 2 were room attendants, 4 were nurses, 1 was a secretary, 1 was a first aid worker, and 2 were security guards. The 12 participants with borderline positive test results were not significantly different from the others regarding patient contact job classification, reported on-the-job contact with EHF or suspected EHF patients, home contact, or any of the specific types of contact. A second specimen was later collected for 4 of the 12 borderline positive participants. All 4 second specimens were negative for IgG.

Discussion

In earlier EHF epidemics, infections among health care workers signaled an ongoing EHF epidemic or the potential for one, and in 1995, this pattern held in Kikwit, where one-fourth of all reported infections were among workers at health care facilities. The highest attack rate among health care workers in this epidemic was among physicians, with nearly one-third of those working at Kikwit General Hospital having been infected. This high attack rate among physicians is evidence of the disabling effect an EBO outbreak can have on the capacity to deliver health services.

Previous investigations have shown that EBO can easily be transmitted by percutaneous exposure through unsterilized needles, as in the Yambuku outbreak [1] and in laboratory accidents [7]. Person-to-person spread from a clinically ill patient is facilitated by direct physical contact or contact with blood, stool, or vomitus [8]. Our survey indicates that the opportunities for exposure of workers at the health facilities in Kikwit was high: 279 workers reported on-the-job contact with an EHF or suspected EHF patient (73% of workers with direct-contact jobs; 33% of those with indirect-contact jobs). It was somewhat surprising that as many as 64% of workers with jobs unlikely to involve patient contact reported on-the-job exposure to an EHF or suspected EHF patient. The fact that "exposure" was defined loosely (i.e., it included simply entering a patient's room) partly but not completely explained this finding. The only "contact" was entering the patient's room for 15 of 63 (24%) participants who reported contact but who held jobs unlikely to involve patient contact. It is also possible that response bias may partly explain this finding, or it may reflect that personnel not usually in contact with patients were pressed into service as the EHF case load increased (at Kikwit General Hospital alone, 184 persons meeting the EHF case definition were admitted during the epidemic) and as persons in direct-contact jobs themselves fell ill.

A main goal of our infection survey was to investigate the occurrence of atypical or asymptomatic EHF resulting in de-

Table 2. Job classification (according to expected contact with patients) and reported contact with Ebola hemorrhagic fever (EHF) or suspected EHF patients for 402 hospital or clinic employees.

Patient contact on job	Reported contact			Total
	Yes	No	Unknown	
Direct	204 (73)	66 (24)	8 (3)	278 (69)
Indirect	3 (33)	6 (67)	0 (0)	9 (2)
Unlikely	63 (64)	35 (35)	1 (1)	99 (25)
Unknown	9 (56)	7 (44)	0 (0)	16 (4)
Total	279 (69)	114 (28)	9 (2)	402 (100)

NOTE. Data are no. (%).

tectable antibody among health facility personnel not previously identified as having EHF. Twelve of those surveyed had blood specimens that tested borderline positive. However, second specimens from 4 of the 12 subsequently tested negative. It is possible that results for the first specimens were false positive or that these patients had atypical antibody responses [9]. Second specimens were not available for testing for the remaining 8 participants who tested borderline positive, so their serologic status is uncertain. None of these participants reported a recent illness meeting the case definition for EHF. Although an old infection with persistent EBO antibody production or a recent atypical or asymptomatic EBO infection cannot be ruled out, if these occur at all, they appear to be rare.

Our survey demonstrates that opportunities for transmission of EBO to personnel in health facilities existed in Kikwit because blood and body fluid precautions were not being universally followed. Given the high case fatality for EHF, the lack of an effective treatment or vaccine, health care workers' likelihood of exposure to the virus, and the possibility for amplification of an outbreak in health care facilities, prevention of EBO transmission in hospitals and health centers is critical [10]. Although exposure of health facility workers to infection during an EHF outbreak may be an unavoidable part of patient care, better understanding of transmission has led to recommendations for infection control [11]. Measures like those recommended have proven effective in breaking the chain of EBO transmission. As an example, no further transmission of EBO occurred after barrier-nursing techniques were instituted in a South African hospital where a nurse died after being infected by a patient (a physician from Gabon) [12].

An important feature of the Kikwit outbreak was that health care facility workers with jobs that in most settings do not usually involve patient contact appear to have had broader job descriptions, including patient contact. Whether this phenomenon predated the epidemic or whether it occurred in response to the epidemic is not clear; however, it does emphasize the need for prompt recognition and confirmation of EHF outbreaks and implementation of appropriate infection control measures by everyone in contact with patients. Finally, the opportunities for transmission of EBO in Kikwit point to a larger and more constant risk of transmission of other more common infections.

This further emphasizes the need to establish the routine practice of precautions to prevent exposure to blood and body fluids in health care facilities, including the provision of sufficient supplies of protective gear, the continuance of training, and locally adapted quality assessment and improvement programs.

Acknowledgments

We thank Scott Dowell for assistance with collecting blood specimens and John O'Connor for editorial review of the manuscript.

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