

The Médecins Sans Frontières Intervention in the Marburg Hemorrhagic Fever Epidemic, Uige, Angola, 2005. I. Lessons Learned in the Hospital

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When the epidemic of Marburg hemorrhagic fever occurred in Uige, Angola, during 2005, the international response included systems of case detection and isolation, community education, the burial of the dead, and disinfection. However, despite large investments of staff and money by the organizations involved, only a fraction of the reported number of cases were isolated, and many cases were detected only after death. This article describes the response of Médecins Sans Frontières Spain within the provincial hospital in Uige, as well as the lessons they learned during the epidemic. Diagnosis, management of patients, and infection control activities in the hospital are discussed. To improve the acceptability of the response to the host community, psychological and cultural factors need to be considered at all stages of planning and implementation in the isolation ward. More interventional medical care may not only improve survival but also improve acceptability.

Lake Victoria marburgvirus (MARV), a member of the filovirus family, can cause epidemics of hemorrhagic fever in humans. Severe febrile illness, often accompanied by vomiting, diarrhea, shock, and disseminated intravascular coagulation, follows an incubation period of 3–21 days (mean, 7–8 days). Hemorrhagic signs (including petechiae) were found to occur in 42% of hospitalized patients in Uige, Angola (P.R., unpublished data), and in 69% of all patients in Durba and Watsa, Democratic Republic of the Congo [1].

The epidemic in Uige in 2005 was the largest Marburg hemorrhagic fever (MHF) outbreak ever recorded, with 374 putative cases (158 laboratory confirmed) and 329 deaths [2], although some cases may have been

missed and others wrongly diagnosed. The epidemic centered on the town of Uige, the capital of Uige province, with an estimated population of 180,000 served by a large provincial hospital.

The initial stages of the Uige epidemic were poorly characterized, with no clear index case. The virus isolates were genetically almost identical [3], suggesting a single or few entry points into the human population. Concerns about an unusual severe illness were raised by doctors in the pediatric unit in Uige Provincial Hospital for the first time in October 2004, and low numbers of these cases were reported during the subsequent months, with no recorded transmission to hospital staff. These may not have been MHF cases. In early 2005, the number of cases increased, and, on 9 March, the first death occurred among Uige Provincial Hospital staff (figure 1). On 23 March, MHF was confirmed by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. The hospital in Uige and some smaller health centers were principal sources of MARV infection early in the epidemic. During the epidemic, 18 staff members of Uige Provincial Hospital died of MHF, along with many patients and contacts.

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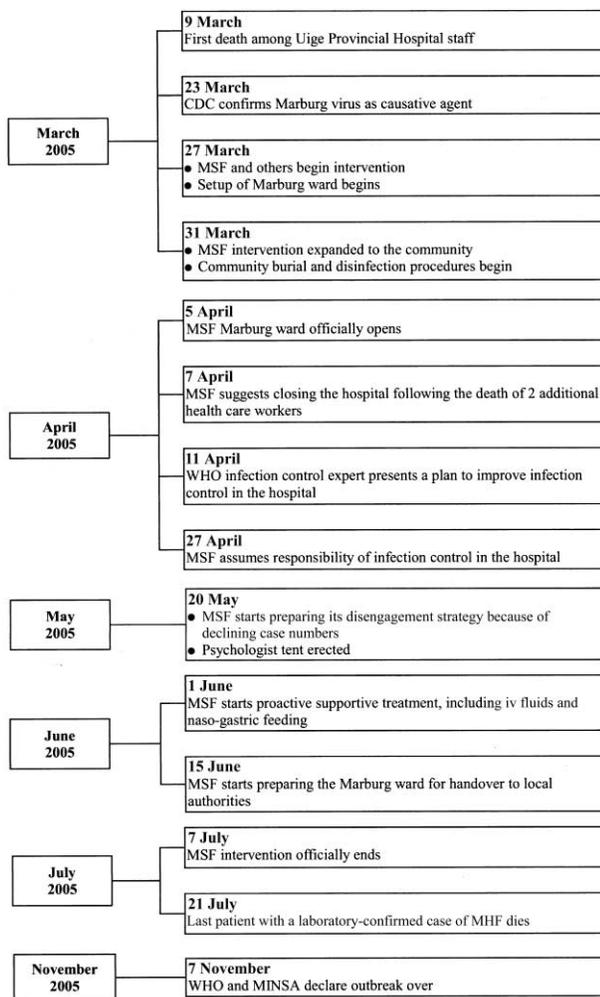


Figure 1. Time line of selected events during the Marburg hemorrhagic fever (MHF) epidemic, Uige, Angola, 2005. CDC, Centers for Disease Control and Prevention; iv, intravenous; MINSa, Angolan Ministry of Health; MSF, Médecins Sans Frontières; WHO, World Health Organization.

On 27 March, an international response was started, which was coordinated by the Angolan Ministry of Health (MINSa) and the World Health Organization (WHO), who also managed health education and epidemiological surveillance activities. The Médecins Sans Frontières (MSF) intervention in Uige included case management and isolation, as well as infection control activities in Uige Provincial Hospital (described here). MSF contributed to health education and epidemiological surveillance activities and conducted safe burials (described in another article in this supplement [4]). MHF diagnostics were provided by the National Microbiology Laboratory of the Public Health Agency of Canada (PHAC) in Uige, as well as by the CDC in Luanda, supported by the Institute of Virology of the Philipps-University, Marburg, Germany.

The number of cases remained high throughout April and then started to decrease. MSF Spain started the handover of

its operations and facilities in early June 2005, after no new patients with confirmed cases had been admitted to its facilities for 2 weeks, and MSF terminated its intervention on 7 July. The last patient with a confirmed case died on 21 July 2005 [2], and the epidemic was declared to be over on 7 November 2005 [5].

The present article reflects on the lessons learned by MSF Spain when responding to the MHF outbreak in the hospital.

DESIGN OF THE MARBURG WARD

Methods. When MSF teams started setting up the Marburg ward, there were 5 patients with MHF in a makeshift isolation room in the hospital, together with corpses that the hospital staff had been too afraid to remove. The patients were receiving no care. This makeshift ward was incorporated into the final Marburg ward. When completed, the Marburg ward incorporated 4 separate structures at the edge of Uige Provincial Hospital: 2 permanent buildings for patients with suspected or probable cases and 1 permanent building for patients with confirmed cases (figures 2 and 3), in addition to a large temporary ward that was kept as a reserve. The size of the structures allowed adequate spacing between patients with unconfirmed cases, reducing the risk of cross-contamination. Fences around the compound were made of thick plastic sheeting. Infection control, barrier nursing, and disinfection procedures followed MSF guidelines [6].

Results. The infection control procedures appeared to be effective, and there is no evidence for transmission of MARV within the Marburg ward. There was one entry and exit point for staff and another for patients and relatives. The distance between the 2 points, as well as the fact that the “clean” nurses’ area of the Marburg ward was at the back of the complex and inaccessible, made communication between patients and staff difficult.

Lessons learned. In the future, it would be sensible to place the nurses’ station where family members can easily communicate with them. Materials used for construction should be optimized to reduce stress and provide a friendly environment. Mesh fences that allow people to see through them may, to some extent, demystify what happens in the isolation area, reduce fear, and prevent rumors [7, 8]. However, more-solid, opaque fencing may improve security and reassure those working in the area or living in the neighborhood that the biohazard is contained. In the future, a combination of fencing material may be used.

CASE DIAGNOSIS

Methods. MSF was in charge of clinical diagnosis of MHF and management of patients with MHF within the isolation ward. Laboratory confirmation by reverse-transcription polymerase chain reaction (PCR) for a number of possible specimen

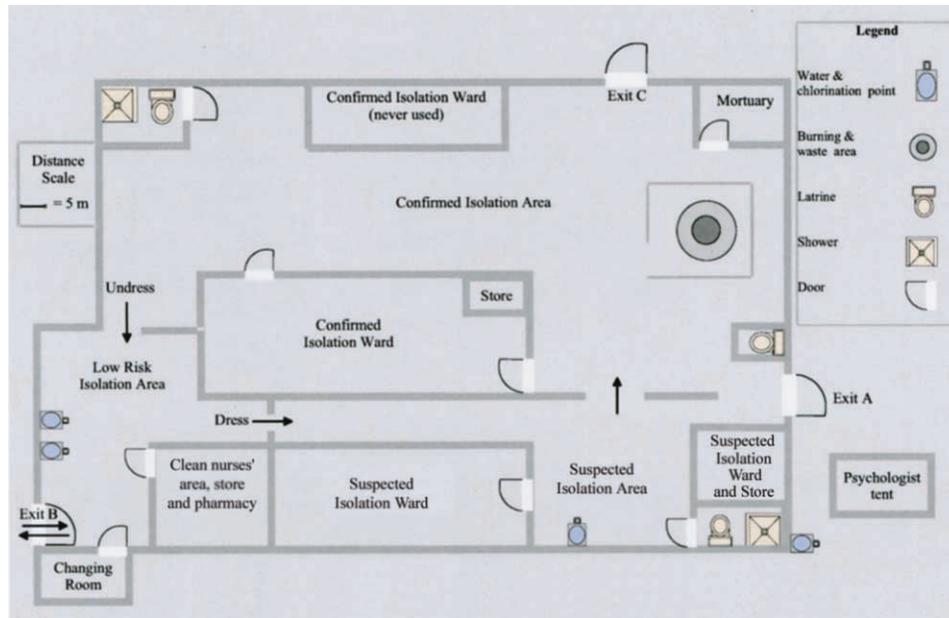


Figure 2. Layout of the Marburg ward and isolation area near the end of the Marburg hemorrhagic fever epidemic, Uige, Angola, 2005. The layout underwent a process of constant evolution, and this diagram reflects the layout toward the end of the epidemic. Arrows indicate the direction of staff flow. Exit A was used for the entry and exit of patients and their families, exit B was used for staff members, and exit C was used for the movement of corpses. The rooms marked as wards are solid buildings; the outer perimeter fence is made of thick plastic sheeting.

types (principally blood and gingival swabs) was usually available from the PHAC laboratory in Uige Provincial Hospital within 4–6 h. All results were confirmed within 1–2 days by the laboratory in Luanda, with 97% agreement overall and 99% agreement on MHF-positive results.

Patients were transferred to the “suspected” area of the Marburg ward for testing. Any positive PCR result, whether from blood or gingival swabs, was considered to be reliable, and the patient was then admitted to the “confirmed” section of the Marburg ward. Negative PCR results from blood were considered to be reliable if the blood had been sampled after the first 3 days of symptoms. Such patients were transferred from the Marburg ward to the main hospital. Negative PCR results from blood collected within the first 3 days of symptoms were considered unreliable, because there may have been too little MARV present to be detected by PCR. Such patients were retested after a further 48 h, during which they were held in the suspected area of the Marburg ward. However, many recovered fully during this period and were discharged without further testing. Negative PCR results from gingival swabs were considered to be unreliable because of their unknown sensitivity. The use of gingival swabs was confined to sampling in the community and for testing of corpses, whereas blood samples were used in the Marburg ward.

Results. A total of 107 patients were assessed in the isolation facilities, of whom 43 were confirmed to have MHF.

CASE DETECTION

Case Detection in the Community

Case detection in the community was principally performed by MINSA and the WHO. They organized a system by which community leaders alerted a WHO team about suspected cases, as well as contact tracing, with teams following all contacts of cases for 21 days and referring those who became ill. Patients fulfilling the suspected or probable case definition (Appendix) were admitted to the Marburg ward for testing.

Case Detection in the Hospital

Methods. Despite an informal system of screening for case detection among hospital admissions during the first week of the MSF intervention, MHF cases continued to be detected in the wards, and more hospital workers died. MSF suggested closing the hospital until infection control could be implemented. This was rejected because of the lack of alternatives to satisfy the population’s hospital care needs. However, non-essential services were suspended or reduced, and fears of contamination decreased overall hospital attendance.

WHO experts introduced protocols to improve infection control in the hospital, including screening for MHF at 3 separate locations—in the pediatrics, adult medicine, and maternity wards. Safety rooms were established. These were normal hospital wards in the main ward blocks where patients with



Figure 3. *Left*, Nurse being sprayed with chlorine while leaving the ward. This illustrates the protective clothing worn by nursing staff. *Right*, View showing a section of the isolation ward. The confirmed ward is on the left. The solid plastic sheeting used for the outer wall is shown in the distance.

fever with a low suspicion for MHF could be isolated outside of the Marburg ward while being assessed. They were less well set up than the Marburg ward. They did not, for example, have separate latrines. Nevertheless, they continued to be used throughout the epidemic.

On 27 April, MSF assumed responsibility for infection control in the entire hospital. MSF's intervention in the hospital consisted of screening all patients on admission, as well as active case detection in the general wards, screening of corpses, and improvements in general infection control.

MSF, by request from MINSA, continued to use 3 screening points. Patients were screened using a special admission form, and those fulfilling the suspected or probable case definition (Appendix) were referred to an MSF physician for assessment. Unless the physician made another diagnosis, these patients were admitted to a safety room or the Marburg ward for testing. Because of the difficulties of wearing a full protective suit for long periods, staff performing the screening wore only gloves, gowns, and masks for normal assessments, and the only examination performed during screening was the taking of the patient's temperature. Stricter safety measures were used for patients who were admitted to the Marburg ward or a safety room. The presence or absence of fever at the time of assessment was not found to be useful in deciding whom to isolate.

MSF regularly visited all wards to detect patients with MHF who had been missed by the screening system. All patients were screened for fever by the ward nurses, and febrile or severely ill patients were reviewed by MSF. To strengthen this ward surveillance system and ensure that all patients had their temperature measured twice per day, the WHO provided additional physicians and nurses.

Results. The initial case-detection systems failed to prevent patients with MHF from being admitted to the wards. The

system set up by MSF appeared to be more effective. This may have been because of increased levels of supervision by experienced MSF and WHO staff.

The assessment of pregnant women was difficult. Because bleeding is common in pregnancy, many febrile pregnant women in the hospital fulfilled the suspected case definition. It was often difficult to rule out MHF without testing, but, because many women required constant obstetric assistance, it would have been difficult to admit them all to the formal Marburg ward for assessment. Therefore, a well-equipped isolation area was set up in the maternity ward, including a delivery area and a ward area. Maternity staff were trained in infection control, and separate teams were assigned to the isolation area and the normal maternity ward. Any patient testing positive for MHF was admitted to the Marburg ward.

Occasionally, there were patients whom the MSF doctors felt clearly did not have MHF but for whom the hospital nursing staff were too frightened to provide care, because of their fear of MHF. Sometimes, hospital staff could not be persuaded to provide essential lifesaving treatment without prior exclusion of MHF by laboratory testing. The benefits of treatment had to be balanced against the risk of contamination with MARV, and a few such patients were admitted to the Marburg ward for essential treatment while laboratory results were pending. None of them became infected during isolation.

Lessons learned. The best way to organize screening at admission remained unresolved. MSF favored a single entry point to the hospital, where all patients could be assessed, because it required fewer staff for supervision. MINSA favored the use of 3 triage points, arguing that this allowed patients to go directly to the required service, as they were accustomed to doing. MINSA feared that major changes in the patient flow could further deter people from seeking care in the hospital.

The “safety rooms” were considered by MSF staff to be unhelpful. Although patients were admitted only if suspected to have MHF, infection control measures were less stringent in the safety rooms than in the Marburg ward. MINSA’s hospital nurses were poorly trained in the provision of care in these rooms and generally refused to do so. Thus, MSF was forced to provide care in them, despite an insufficient number of nurses to cover these rooms and the Marburg ward. Because laboratory diagnostics did not reliably rule out MHF during the first 3 days of symptoms, some patients needed to stay in these rooms for several days. The hypothetical advantage of safety rooms was that they allowed isolation of patients who refused admission to the Marburg ward. However, it was often difficult to persuade patients to enter the safety rooms, and it might have been possible to convince them to accept the Marburg ward if an alternative had not been offered. Furthermore, having these rooms next to normal hospital wards appeared to increase the fear in other patients.

MEDICAL MANAGEMENT OF PATIENTS WITH MHF

Methods. During the period in which the Marburg ward was being constructed, MSF medical staff were instructed not to enter the isolation area, because of safety concerns. When the ward was considered to be fully operational on 5 April, diagnostic and treatment protocols were implemented.

It was impossible to test for and exclude conditions such as malaria, because the hospital laboratory was unable to safely handle samples with possible MARV contamination. Therefore, all patients were offered oral artemisinin combination therapy for malaria and antibiotic cover with cotrimoxazole. Other treatments were given if indicated. All patients received oral rehydration. Nausea and discomfort were fairly universal in patients with MHF, so all received promethazine as an antiemetic and paracetamol. Stronger analgesics like morphine were available. Cimetidine was given for dyspepsia. In the first 2 months of MSF’s intervention, only oral treatments were provided, because medical staff felt that the risks to staff of providing injections or intravenous (iv) therapy outweighed possible benefits for patients. Fluids administered iv were offered from the third month, reflecting increased confidence of those working in the Marburg ward.

Several surviving patients had a prolonged recovery with pronounced weakness. After the severe acute illness, with frequent nausea and dysphagia, malnutrition was common. Nasogastric feeding was required for 1 severely malnourished child. Discharge decisions were often difficult with regard to these generally afebrile but symptomatic patients. These decisions were made by the MSF team on clinical grounds but were backed up by 2 negative blood PCR results on consecutive days, which was considered to demonstrate a low risk of transmitting

MARV. Patients were discharged to the main hospital for easier nursing, usually provided by MSF because hospital staff were reluctant to attend to these patients.

Results. The failure to provide nursing care until the isolation ward was completed had a negative impact. News about the initial lack of care spread in the community, which is likely to have reduced MSF’s standing and may have contributed to the reluctance of patients to be isolated.

The documentation of clinical data on the Marburg ward was generally poor, because this was not considered to be a priority. Safety concerns about transferring records from inside the Marburg ward to outside contributed to this. This makes comments on the effectiveness of treatments difficult. Care to relieve symptoms in patients with MHF was considered to be effective. The MSF team had the impression that the introduction of iv fluids provided a considerable benefit for some patients: 1 woman survived 5 days unconscious despite a very hot climate, and a girl 5 years of age recovered from severe shock; both had confirmed MHF and received iv rehydration.

The policy of discharging symptomatic patients no longer thought to have active MHF after a negative PCR test result was obtained did not result in transmission of MARV in the hospital wards, although it did place a considerable burden on MSF medical staff caring for them.

Lessons learned. The failure of the MSF team to provide care while the ward was being set up demonstrated a poor understanding of the principles of biosafety, which is based more on rigorously following appropriate protocols than on the availability of physical structures. With adequate protective clothing and safe undressing procedures, it should be possible to provide basic medical care before an isolation ward is constructed. This failure had a very negative impact on the intervention. In the tense atmosphere of a MHF outbreak, it is essential to make a good impression from the beginning, before rumors start to propagate.

Although no strong evidence is available on benefits of iv fluids for patients with MHF, and although the risks to staff cannot be denied, iv fluids were considered to be very helpful. Not only did they appear to improve survival, but they also appeared to greatly improve the patients’ and their families’ perceptions of the Marburg ward, which enhanced MSF’s standing in the community. Patients expect injections and iv treatment in this area of Angola, and the number of individuals presenting to the Marburg ward for assessment increased after these treatment measures were introduced. Therapy administered iv may be used to treat patients with MHF only if conditions allow this to happen safely. In future outbreaks, caregivers should strive to create these conditions, with good staff training and supervision, safe venipuncture material, and proper lighting. Furthermore, more effort should be made to collect good-quality clinical data, to contribute to the evidence

base for Marburg and Ebola case management. This has been given a low priority in this and previous filovirus infection outbreaks.

THE PSYCHOLOGICAL CARE OF PATIENTS WITH MHF

Methods. The psychological care of patients and their families intensified during the epidemic. After month 2 of the MSF intervention, a tent was erected at the patients' entrance to the Marburg ward, staffed by an MSF psychologist and trained local staff. The psychological team generally did not enter the Marburg ward, because counseling in a full protective suit would have been impractical. There was debate as to whether psychological staff should enter the Marburg ward with the reduced protective clothing worn by relatives (see below), but this was not allowed. Instead, counseling was offered to patients across the fence in a shaded area of the Marburg ward. Patients could also use this area to communicate with family members too frightened to enter the ward. Counseling was also offered to patients' families. MSF's psychological support network in the community is reported in more detail in another article in this supplement [4].

Results and lessons learned. It was difficult to collect data on the effectiveness of these interventions. However, the negative psychological impact of the epidemic was obvious, and the psychological care system appeared to reduce this negative impact and greatly improve relationships between MSF staff and the community.

NURSING CARE OF PATIENTS WITH MHF

Methods. MSF was able to recruit extremely competent local nursing staff to work in the Marburg ward, and all nursing care in the ward was provided by MSF staff. Family members were encouraged to provide supplementary foods appreciated by the patients and to enter the Marburg ward to support their relatives psychologically and to reduce their own anxiety about what was happening inside. Family members were given a mask, one pair of gloves, a gown, and boots. They were advised to avoid contact with the patients and were supervised while in the ward. Parents of small children were allowed to stay with their children.

Results and lessons learned. Reasonable nursing care could be provided to patients, although the limited amount of time that nursing staff could wear protective clothing in the tropical heat made this difficult. Allowing visitors to enter was considered to have improved the psychological care of patients and to have helped MSF's relationships with their families and the community.

There was considerable debate about what degree of protective clothing should be provided to visitors to the isolation unit. MSF provided visitors with a mask, gown, gloves, and

boots, and the nursing staff had an additional apron, hood, goggles, and a second pair of gloves. This was done for a number of reasons. The full suit worn by nurses was difficult to put on and take off and was extremely uncomfortable. Because visitors were asked not to have any physical contact with relatives, they should not have been at risk. It was felt that giving visitors the full suit might encourage them to take more risks, which would be dangerous, because they had not been taught to undress safely. However, some relatives questioned why our staff had a full suit and they did not. This issue was not clearly resolved.

Protecting the parents of isolated children was challenging. Parents provide essential psychological support to their children that cannot easily be provided by nursing staff. It would be difficult for parents not to touch their children, so the limited protective clothing offered to other visitors may be considered inadequate. However, it would also be impossible to wear full protective clothing in the tropical heat for more than a few hours at a time. Of the 4 parents with infected children whom we admitted, 3 were already infected with MARV or recovering from MHF, but 1 father who was not infected cared for his baby with limited protective clothing and did not develop MHF. One baby was looked after by ward staff without a parent. No clear answers as to how to care for small children were found, and decisions were made on a case-by-case basis.

INFECTION CONTROL IN UIGE PROVINCIAL HOSPITAL

Methods. The mainstay of the infection control system in the hospital was the detection and isolation of cases, but MSF also improved generic infection control. Before MSF became involved, protective equipment was not universally available and was often poorly used. Staff seemed to put more emphasis on protecting themselves than on preventing transmission between patients. Soiled gloves were often worn all day and used on multiple patients. MSF provided a store of protective equipment for hospital wards and provided training on its proper use.

The hospital water supply was inadequate, so tanks were installed to improve water storage. Containers were supplied to provide all wards with water. Because there was no safe system for the disposal of sharps and contaminated waste, sharps boxes were distributed, and temporary disposal pits were dug. Training for the correct handling and disposal of waste, supervision, and logistic support were provided. Protocols for oral treatment of conditions like uncomplicated malaria were also introduced in an attempt to reduce the number of unnecessary injections.

Results and lessons learned. Attempts to discourage Uige hospital staff from giving unnecessary injections were unsuccessful and appeared to be counterproductive. It was felt that

more time would have been needed to allow retraining of the staff to use alternative oral therapies and to change their habits, especially because training was also required in many other aspects of infection control. The local population had become accustomed to injections, perceived to be more effective than tablets, and put pressure on hospital staff to provide them. Not only was MSF unable to prevent injections for conditions like uncomplicated malaria, but trying to do so appeared to cause resentment among the staff, who were happy with their existing protocols.

CONCLUSIONS

An international response to terminate a filovirus infection outbreak is based on the early detection and subsequent isolation of patients. In Uige, only 44 of the patients with known cases were isolated. In the absence of obviously effective therapies, it is difficult to persuade people to accept isolation for the altruistic reason of preventing transmission within their families and communities, particularly when traditional healers often promise a cure. Proactive supportive treatment, including iv fluids and nasogastric feeding, may help to persuade people to accept isolation, because patients often value the perceived effort. Psychological support should be intensified and psychological factors be taken into account when planning physical structures and response activities.

MSF Spain hopes to offer an enhanced approach to isolation at the next occasion. We believe this may not only improve outcomes and well-being for patients and their families but also may improve the communities' perception of the isolation ward. This may encourage the population to accept isolation.

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APPENDIX

CASE DEFINITIONS FOR MARBURG HEMORRHAGIC FEVER, UIGE, ANGOLA, 7 MAY 2005

Suspected case

- Unexplained hemorrhage
- Fever plus 3 of the following symptoms: headache, anorexia, fatigue, myalgia, arthralgia, dyspnea, nausea, vomiting, diarrhea, dysphagia, and hiccup

Probable case

- Fever plus hemorrhage
- Death plus epidemiological link (see below)
- Two of the above symptoms plus epidemiological link (see below)

Any of the above were sufficient to define a probable case, even if the results of a polymerase chain reaction (PCR) from a gingival swab sample were negative.

Epidemiological link

- Contact with a probable or confirmed case
- Contact with a sick or dead animal
- Treatment (transfusions, injections, scarification, etc.) at health centers or from traditional healers

Confirmed case

- Any positive laboratory test result: PCR (gingival swab or blood), serological test, or virus isolation

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