Caring for Critically Ill Patients with Ebola Virus Disease

Perspectives from West Africa

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Abstract

The largest ever Ebola virus disease outbreak is ravaging West Africa. The constellation of little public health infrastructure, low levels of health literacy, limited acute care and infection prevention and control resources, densely populated areas, and a highly transmissible and lethal viral infection have led to thousands of confirmed, probable, or suspected cases thus far. Ebola virus disease is characterized by a febrile severe illness with profound gastrointestinal manifestations and is complicated by intravascular volume depletion, shock, profound electrolyte abnormalities, and organ dysfunction. Despite no proven Ebola virus–specific medical therapies, the potential effect of supportive care is great for a condition with high baseline mortality and one usually occurring in resource-constrained settings. With more personnel, basic monitoring, and supportive treatment, many of the sickest patients with Ebola virus disease do not need to die. Ebola virus disease represents an illness ready for a paradigm shift in care delivery and outcomes, and the profession of critical care medicine can and should be instrumental in helping this happen.

Keywords: Ebola; Africa; critical care; outbreak; viral hemorrhagic fever

Origins of the 2014 West Africa Ebola Virus Disease Outbreak

On March 21, 2014, the World Health Organization was notified of a rapidly evolving outbreak of Ebola virus disease (EVD) in the forested regions of southeastern Guinea that subsequently spread to the capital city, Conakry, marking the world's first EVD outbreak in a major metropolitan area (1). Since March, Ebola virus (formerly labeled Zaire Ebola virus and typically associated with mortality rates of 50–90%) has ravaged West Africa, including Guinea, Sierra Leone, Liberia, Senegal, and Nigeria (Figure 1). With 5,335 confirmed, probable, or suspected cases and 2,622 deaths thus far, this is the largest and most devastating Ebola virus outbreak in history (2).

West Africa has never before experienced an Ebola virus outbreak. Despite experience with Lassa fever, the initial challenges of EVD experienced in Guinea are emblematic of those throughout the region. The Guinean population of approximately 11,451,000 persons has a life expectancy at birth of 58 years, a gross national income of 970 international dollars, and 67 international dollars expenditure

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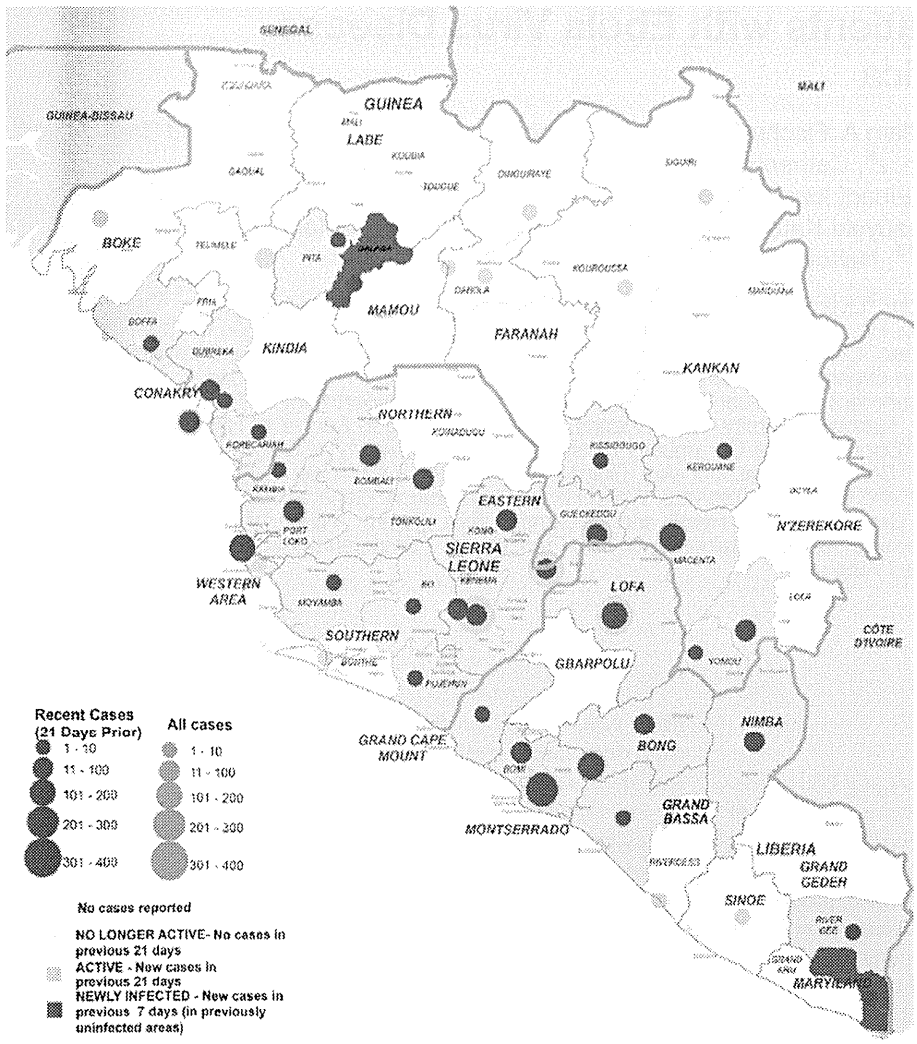

Figure 1. Locations of confirmed cases of Ebola virus disease in West Africa, August 7, 2014. Reproduced with permission from Reference 21.

on health *per capita* per year (3). In West Africa, the stark and undeniable reality is that baseline public health and acute care resources are severely limited (3, 4). Rural residents travel long distances for basic healthcare needs. In Guinea's largest public hospital, the intensive care units have no piped oxygen and no mechanical ventilators. Basic infection prevention and control is plagued by an unstable supply of running water and insufficient personal protective equipment, which facilitates spread of communicable diseases such as Ebola. The constellation of limited public health infrastructure, low levels of health literacy, few acute care and infection prevention and control resources, densely populated areas, a mobile population, and a highly transmissible and lethal viral infection have created a perfect storm underlying this outbreak. We offer the following insights from the perspective of clinicians who have assisted in the treatment of patients with EVD throughout West Africa during this outbreak.

Public Health Challenges in Responding to EVD

Ebola virus outbreaks occur at relatively frequent intervals (two dozen outbreaks over the past 30 yr). They occur most commonly in central Africa but are often confined to rural areas with limited external transmission (5). The natural reservoirs include bats, with primates and possible other mammalian species regarded as the susceptible end hosts. An Ebola virus outbreak amid an increasingly mobile population to densely populated areas with large numbers of inhabitants per household is an enormous public health challenge. In addition to family-based transmission, urban outbreaks provide access to hospitals and often paradoxically lead to nosocomial amplification of transmission chains. In China and the Hong Kong Special Administrative Region, Singapore, and Toronto, the critical care community learned firsthand about the ease of nosocomial spread of another virus—severe acute respiratory syndrome (SARS) (6). Possibly the most humbling lesson was the effectiveness of transmission when infectious patients are admitted to hospitals with inadequate infection prevention and control practices. We also learned the perils of letting down our guard too early in an outbreak (6); it only takes one new patient to set off a new chain of transmission. The 2014 West Africa Ebola outbreak has proven these to be generalizable outbreak lessons, with many healthcare worker infections and deaths and multiple epidemiological waves of transmission (2).

It is difficult to respond with perfect intensity and timing to outbreaks of new and evolving pathogens such as SARS, Middle Eastern respiratory syndrome, influenza, or Ebola because the "sweet spot" is very thin. Robust responses, as for the 2009 pandemic, are met with criticism of excess resource mobilization at best and pandering to pharmaceutical company interest at worst (7). However, under constant financial constraints, most health care systems evolve to a state of little or no excess capacity: any excess demand can either be just met, or the system is overwhelmed. In West Africa, a lack of baseline capacity, a lack of sentinel surveillance, and a lack of accessible and reliable diagnostics lead to late recognition and delayed responses. The local, national, and international health system response to this outbreak has been characterized by some as too slow and with too little mobilization of support on the ground.

Clinical and Pathophysiological Features of EVD

Ebola, like, Marburg, is an RNA filovirus that is usually transmitted through direct mucus membrane or percutaneous exposure to infected body fluids (typically

stool, vomit, or blood) (8, 9). Monocytes, macrophages, and dendritic cells help to disseminate the virus to lymph nodes, followed by hematogenous spread to the liver and spleen. Beginning as a febrile illness, often with fatigue and myalgias, the most prominent feature in this outbreak has been of progressive gastrointestinal symptoms: anorexia, nausea, and abdominal discomfort followed by vomiting and diarrhea that lead to intravascular volume depletion and complications including profound electrolyte disorders, hypoperfusion, and shock. The "hemorrhage" of viral hemorrhagic fever is a late manifestation, usually occurring as gastrointestinal bleeding, but occurs only in a minority of patients; hence the adoption of a more contemporary name, Ebola virus disease.

Point-of-care or other laboratory testing inside the treatment facility, once available, transforms the appreciation of illness pathophysiology. Hemoglobin levels were almost never profoundly low, and hypoxia by pulse oximetry was only impaired in the terminal phases of multisystem organ failure. Hypoperfusion is ubiquitous and frequently evidenced by metabolic lactic acidosis (ranging from 4 to 10 mmol/L among many patients with clinical suspicion), diarrhea-associated profound hypokalemia (sometimes <2 mmol/L), and very common renal insufficiency. Hepatocellular injury marked by aminotransaminase elevation was very common.

Although there may be pathophysiological similarities between Ebola infection and bacterial sepsis with a systemic inflammatory response, there is much less clinically recognizable capillary leak syndrome and little compromise of oxygenation or ventilation, which often accompanies bacterial sepsis–related critical illness. Although endothelial infection and injury have previously been postulated as part of the pathophysiology of Ebola infection, there is scant direct evidence of this, resonating with the observed clinical differences between bacterial and Ebola sepsis (8); however, there is much to learn.

Supportive and Specific Treatments of EVD

The early clinical response to EVD outbreaks is often limited. Patients usually present for care late in their illness course, and there are often precious few personnel, little equipment, and no specific therapy to offer. In Guinea, for many days, although we had an isolation facility (Figure 2) and the ability to diagnosis infection with international laboratory support of RT-PCR, there were no beds and no monitoring mechanism to check blood pressure, fluid balance, basic potentially life-threatening biochemical abnormalities, or oxygenation. Thankfully we had the most important aspects of supportive care—oral rehydration and intravenous fluids—when patients could not maintain oral intake. Beds and mosquito nets eventually arrived. Antibiotics for empiric treatment of ongoing fever and gastrointestinal symptoms, malaria rapid antigen assessment and antimalarials, potassium, and antiemetic agents were donated or scavenged along with automated blood pressure cuffs, thermometers, and oxymeters.

Despite no proven EVD-specific medical therapies, the potential effectiveness of supportive care is great for a condition with high baseline mortality and one usually occurring in resource-constrained settings. Many patients have concomitant malaria infection, which can be treated and may influence outcomes. The influence of secondary or complicating bacterial infections is uncertain; however, empiric treatment for enteric pathogens is part of most clinical treatment protocols (5, 10) for patients entering the severe gastrointestinal phase of illness, even though the importance of gastrointestinal bacterial translocation is uncertain.

The most important aspect of supportive care is aggressive prevention of intravascular volume depletion, correcting profound electrolyte abnormalities, and preventing the complications of shock. This is an underlying tenant of critical care medicine and one that can and should be applied in both resource-constrained and resource-rich settings (11). Optimal supportive care is sometimes not possible due to a lack of personnel and limitation on time spent at the bedside due to the challenges of personal protective equipment. In West Africa, this involves placing and replacing intravenous and occasional intraosseous catheters and delivering fluid boluses during the periods that you are on the ward. Patients are mostly unmonitored and frequently remove intravenous access, and there is little ability to safely or with sterility place and maintain central venous access. In resource-rich settings, maintaining intravenous access with peripherally or centrally inserted catheters and increased opportunity for nursing care will help deliver treatment. Aggressive correction of electrolyte depletion and acid–base derangements is critical to avoid life-threatening metabolic complications. In West African treatment centers, routine biochemistry is sometimes possible but is infrequently deployed as part of the international laboratory response; therefore, such abnormalities are often unappreciated and untreated. For patients who develop multisystem failure, oxygenation, ventilation, and hemodynamic support are generally unavailable. However, lending strong support to the argument of greater supportive care leading to better outcomes is the experience with Marburg hemorrhagic fever, with case fatality rates in Africa typically 70 to 85%, compared with the 1967 outbreak in Germany and the former Yugoslavia, which had mortality rates of 20 to 25% (8). With improved supportive care, we can improve outcomes for EVD.

Although critical care units in developed countries have become expert at "sterilizing" critical illness and death, this is often impossible in West African Ebola treatment centers. Whole families arrive at treatment facilities, but when parents die, Ebola orphans remain; some children or babies are transported to the facility without any knowledge of who the parents are or were. Diarrhea and vomiting are ever present, and keeping patients and the environment clean is often impossible. Patients who die in the night are usually discovered the following morning. Symptom control with narcotics and benzodiazepines is often our best end-of-life therapy. All of these challenges could be improved with more personnel and a greater ability to monitor and treat patients.

The Importance and Challenges of Personal Protective Equipment

Adherence to transmission- and evidence-informed infection prevention and control procedures is a critically important aspect of clinical care. Appropriate use of standard and contact precautions along with personal protective equipment, including gloves,

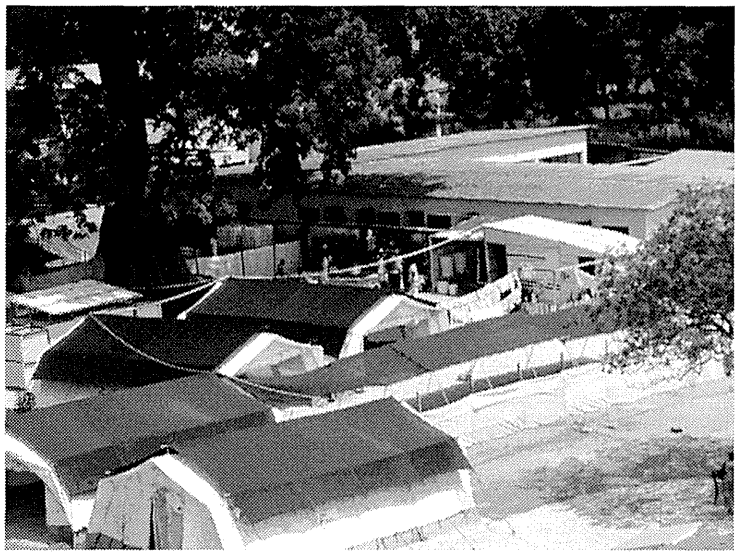

Figure 2. Conakry, Guinea Ebola virus treatment facility.

a disposable impermeable gown and apron, and facial protection with a face shield or goggles and a mask, are effective at protecting healthcare workers from coming into contact with infectious body fluids (12). Although there is a distinct lack of respiratory involvement, additional precautions may be warranted if droplet or aerosol-generating procedures are performed; however, procedures such as intubation and ventilation are not practical options in most West African outbreak locations.

Adoption of personal protective equipment that is not based on known modes of transmission poses challenges to patient care and possibly even risk to healthcare providers. In the treatment facilities, personal protective equipment unfortunately limits human interaction and hides facial expressions that normally convey empathy and build patient–clinician connections. Temperatures exceeding 45°C inside impervious equipment manufactured to guard against penetration of virus at higher than possibly attainable atmospheric pressures lead to rapid build-up of liters of sweat and conspire against the time needed to deliver fluids and medications, to insert intravascular catheters, and to talk with patients in the midst of the most stressful experience in their life (13). Determining the appropriate personal protective equipment on the basis of known mechanisms of transmission is necessary to ensure healthcare worker safety and to enable, as opposed to limit, care and care duration for infected patients.

Sociocultural Context of Clinical Care

There are many challenges in delivering best care that are well upstream of treatment centers. Social mobilization and public health education in the setting of high mortality and community mistrust is difficult but is vitally important to gaining acceptance of the illness and the necessity for care. A disproportionate influx of international personnel with an often unique geo-social-ethnic culture contributes to communication challenges. This is evidenced during outreach to community members with suspected EVD that is occasionally met with strong resistance from family and neighbors of symptomatic patients. When most patients historically do not leave the treatment facility alive, early resistance is easy to understand. Yet, with ongoing community-based work, this initial mistrust often gives way to acceptance and profound appreciation for international staff and foreign medical teams.

The Imperative to Improve Clinical Outcomes of EVD

The current weighted case fatality rate of nearly 70% for all Ebola virus outbreaks is an unacceptable outcome (5). In addition to improving local, national, and international response with personnel and supportive care, epidemiology, contact tracing, and social mobilization, we must also consider observational and experimental research as a core component of an EVD outbreak response. Although improving the care of infected patients takes precedence, we must concurrently improve our research response by implementing observational studies, biological sampling protocols, and interventional studies that have been developed, vetted, funded, and then approved in the jurisdictions likely to be affected (14). If we attempt to initiate clinical research only during the outbreak, it rarely occurs. Although the history of critical care therapeutic advances teaches us that the greatest benefit to patients is likely to emerge from consistent application of a system of critical care focused upon timely recognition, early resuscitation, supportive care, and prevention of complications, without the prior approval for research, promising interventions such as vaccination, convalescent plasma, or monoclonal antibodies will remain untested and unavailable (8, 15–17). A lack of history of research acceptance in many jurisdictions is another challenge; however, not engaging these challenges before the next outbreak represents an irresponsible approach to improving medical care. We need to fundamentally change the model of clinical research development and funding for outbreaks and pandemics from reaction to research-ready preparedness.

Despite often overwhelming challenges in an Ebola virus outbreak, there is hope. Teamwork emerges among the national healthcare workers, the Ministry of Health, Médicines Sans Frontières, the Red Cross, the World Health Organization, and many others. Nurses and doctors, initially shaken and frightened to see their colleagues falling ill, come back to work to try and help them recover. Deep mutual respect and professional friendships emerge between West African and international staff in treatment facilities and the community that will provide mechanisms to improve care well after this outbreak is over.

Although the primary goal during any outbreak is to stop it as quickly as possible, discharging increasing numbers of cured patients to their community provides affirmation that supportive and specific acute care should play an increasing role in delivering care to critically ill patients, irrespective of the presence of an intensive care unit. It is our belief that many of the sickest patients with EVD do not need to die. We need to demystify EVD as a near-certain killer from the middle of Africa and one for which little can be done and instead apply the basic principles of critical

care (*see* box, How Critical Care Medicine Can Improve the Outcomes of Ebola Virus Infection). We need to change the nomenclature of our care from "isolation centers" to "treatment centers." This can be done safely with adequate attention to infection prevention and control. Even without specific medical therapy, a combination of earlier presentation to care, personnel, and more aggressive volume and electrolyte repletion to prevent intravascular volume depletion and its complications and the addition of basic laboratory resources to track patients' metabolic response to therapy is very likely to improve survival as it has for virtually all other forms of critical illness (18–20). EVD represents an illness ready for a paradigm shift in care delivery and outcomes, and the profession of critical care medicine can and should be instrumental in making this happen.

How Critical Care Medicine Can Improve the Outcomes of Ebola Virus Infection

- Demystify Ebola virus disease by reconsidering it as one of the many examples of transmissible infection-related critical illnesses that benefit from goal-directed supportive and specific intensive care.
- Recognize that the predominant Ebola virus disease clinical syndrome is gastrointestinal—nausea, vomiting, and diarrhea—and can lead to profound intravascular volume depletion and metabolic abnormalities and require prevention and treatment.
- Appreciate the important role for basic biochemistry and laboratory markers to diagnose metabolic abnormalities and guide the response to therapy.
- Advocate that these therapies truly can and should be available to all patients in resource-constrained and resource-rich environments.
- Understand that the fundamental skills of critical care clinicians represent the fundamental needs of patients with Ebola virus disease.
- Anticipate that with better supportive care, the outcomes of infection will improve. ▩

Author disclosures are available with the text of this article at www.atsjournals.org.

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Perspective Piece

Being Ready to Treat Ebola Virus Disease Patients

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Abstract. As the outbreak of Ebola virus disease (EVD) in West Africa continues, clinical preparedness is needed in countries at risk for EVD (e.g., United States) and more fully equipped and supported clinical teams in those countries with epidemic spread of EVD in Africa. Clinical staff must approach the patient with a very deliberate focus on providing effective care while assuring personal safety. To do this, both individual health care providers and health systems must improve EVD care. Although formal guidance toward these goals exists from the World Health Organization, Medecin Sans Frontières, the Centers for Disease Control and Prevention, and other groups, some of the most critical lessons come from personal experience. In this narrative, clinicians deployed by the World Health Organization into a wide range of clinical settings in West Africa distill key, practical considerations for working safely and effectively with patients with EVD.

An unprecedented number of health care professionals from a variety of clinical settings, in a wide range of countries are thinking about, preparing for and caring for Ebola virus disease (EVD) patients. Guidance documents on infection prevention and control (IPC) practice and clinical care have been produced by organizations with EVD experience.[1–3] The World Health Organization (WHO) produces guidance for implementation across a wide range of resource settings. Medecin Sans Frontières produces guidance for medical team activities across the outbreak. The Centers for Disease Control and Prevention (CDC) focus on measures which can be taken by the United States health system and extrapolated by others involved in preparedness and response. There are no short cuts to clinical preparedness for EVD. These documents and their revisions should be reviewed carefully.

As important as guidance documents are, many lessons must be learned from specific hands-on experience. The WHO has mobilized clinical consultants in support of EVD response in each of the affected countries in West Africa. This short list of key points attempts to consolidate practical lessons learned that do not always percolate into technical documents. Having landed in unconstrained, resource-limited settings at the start of local EVD clinical operations in an outbreak, and more established EVD care centers, we hope that others might adopt some of these lessons and avoid some of the risks inherent to the steep learning curve associated with delivering EVD care. The points are geared toward the daily care of patients as opposed to the critical mechanics of establishing a care center and developing its procedures. They are focused on the outbreak setting and also have relevance to the referral hospital setting.

BE GUIDED BY THE SCIENCE

EVD patient care must be deliberate and vigilant. Anxiety around EVD reflected in media reports or shown by communities directly, and rapidly evolving events on the ground, sometimes blur facts. The science behind basic aspects of how clinicians can safely approach the patient in these settings should be respected. It is based on decades of laboratory research and field observation. Although much remains to be discovered, Ebola virus is spread only during the symptomatic phase of illness, especially in the setting of diarrhea, vomiting, or bleeding. Although the longest incubation period is 3 weeks, most cases present in < 2 weeks.[4] Safe and effective care is possible and has been achieved repeatedly, in resource fortunate and resource poor settings. To do so, steps must be taken to ensure appropriate training and safe working conditions.[5] These steps must be shaped by science and experience and not undermined by anxiety. Ebola virus, like all micro-organisms,

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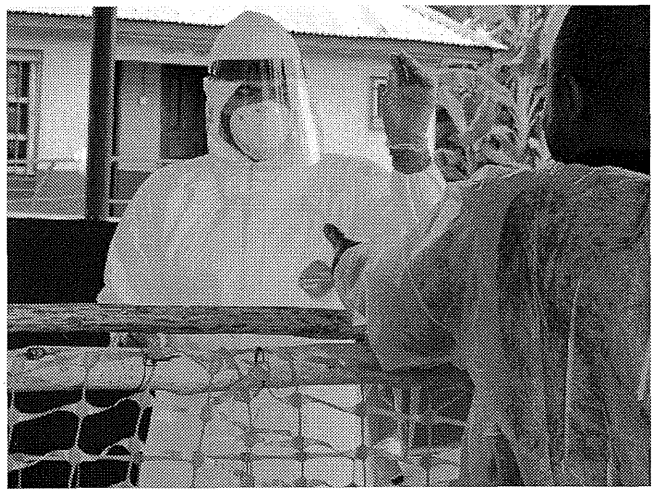

FIGURE 1. One of the authors delivers a suspect EVD case patient's diagnostic blood sample to a local healthcare colleague waiting in the low-risk area.

possesses and follows defined physical and biological principles. Understanding these principles helps to eliminate a sense of mystery, reduces stress, and keeps responders' focus on the work (Figure 1).

THINK AGGRESSIVELY; ACT SAFELY

Safe and effective care for EVD patients has been achieved in both resource-poor and well-resourced settings. A targeted strategy of aggressive volume repletion and electrolyte management, vigilance for patient safety in the isolation environment, attention to hypoperfusion-related complications and co-infection (particularly malaria among those from endemic areas), and general supportive management for hospitalized patients improves survival.[5] Both oral rehydration solution (ORS) and parenteral fluid and electrolyte resuscitation can be given aggressively and safely while following standard, contact and droplet infection prevention and control precautions. Peripheral and central venous access, dialysis, and mechanical ventilation have been performed safely in the right settings.

All procedures in the high-risk area, just as in patient care everywhere, must follow a careful risk-benefit assessment. "First do no harm" applies to the patient, the staff, and the community. Taking a few minutes before conducting any intervention to ensure the procedure will benefit the patient, and is adequately prepared with the necessary materials, support, and environment, may dramatically enhance staff safety. Team approaches enhance the preparation and execution of procedures. Procedures should be appropriate to the mix of need and resources at hand. They should be practiced. For each procedure, refine movements so that they are deliberate and carefully consider the placement of supporting staff.

ENSURE THAT THE WORKING ENVIRONMENT IS SAFE FOR BOTH YOU AND YOUR PATIENTS

EVD care must occur in a work environment that draws on non-clinician expertise. Clinicians typically do not manage environmental aspects of health facilities. In EVD care, they have a critical stake in it. For instance, the health unit where EVD patients will be treated requires a thoughtful layout taking into consideration staff and patient flow through low- and high-risk areas, sufficient numbers of staff (clinician and non-clinician), and robust water and sanitation, hygiene, and waste management support.

BE CONFIDENT BUT CAREFUL IN THE USE OF PERSONAL PROTECTIVE EQUIPMENT

Personal protective equipment (PPE) protection requires careful and comprehensive training, repeated practice, and competency assessment. This must be in the context of on-site IPC and clinical procedures that are safe, sensible, functional, and reproducible. Training and practice must occur before and during work with suspect or confirmed EVD patients. Mentoring by more experienced clinicians is critical. Systems should include a designated controller of the doffing and decontamination area, and constant co-supervision of each other using a buddy system to reduce errors and the risk of infections.

ANYONE CAN AND SHOULD CALL A SAFETY STOP

Everyone associated with running an EVD care center, in and out of high-risk areas, is responsible for contributing to safe and effective patient care. Regardless of job, rank, and culture, anyone can and should flag concerns for staff and patient safety. Sometimes having a single, universal word that anyone can say to freeze activity is helpful. Usually we use the word "stop." It is not commonly used for other reasons. When a concern is present, "stop" reminds people to cease all movement and activity until the concern is voiced and addressed through a risk-benefit assessment. This approach also prevents multiple people trying to provide instructions at once—a common occurrence, which can increase a person's risk in doffing areas where multiple people are observing the removal of PPE.

PROTECT AND CALL "STOP" ON YOURSELF

Proper IPC practice requires practice, patience, monitoring, assessment, and intervention. Donning and doffing of PPE, safe sharps use and disposal and patient movement procedures must be carefully rehearsed and not rushed. Almost inevitably, despite the best of preparations, a process occasionally will go wrong when in an isolation area. Visors, glasses, or goggles fog, face masks become saturated and collapse toward the nose or mouth, suits and gloves tear, light fades, power outages occur, a patient becomes agitated, fatigue or heat stress intrudes. When this happens to us, we stop, stand upright, place hands in a neutral position folded in front and take a few breaths. We then decide whether there really is a problem. If there is, we decide whether it inhibits completing the task at hand, whether we should finish that task or redesign it, or immediately exit the high risk area and safely doff PPE. Regularly ask yourself "is it safe for me to do this now?" When in doubt, exit expeditiously with your buddy system partner. Take fluids—many of us have been slow to take fluids aggressively enough—reassess the situation and either decide to get dressed again for short re-entry to complete a task or turn it over to someone else.

The PPE and its use is only part of good IPC practice. The PPE brings specific challenges. The removal of contaminated

PPE presents risk and requires a structured process and attention to detail including real-time guidance and monitoring. The process of doffing will take many minutes and must not be rushed. This must be factored into both planning and the exit decision.

Complications with PPE are not the only set of challenges that may require a clinician to take stock of the situation acutely. An agitated patient may interrupt a needle procedure. A pause can allow some tasks to be redesigned such as changing to alternate routes of medication administration. Sometimes, critical interventions such as peripheral intravenous (IV) placement must be deferred until a subsequent entry into the high-risk area.

Patients and staff are far better served with more frequent entries into the high-risk area over time than single long entries that increase fatigue and the possibility of risky behavior. Time scheduled in PPE may need adjustment to fit the individual, climatic conditions, and the tasks. Remember to alert teammates when exiting. There is no shame in an unexpected exit.

TIME IN PERSONAL PROTECTIVE EQUIPMENT SHOULD BE TIME WITH THE PATIENT

Patients require bedside clinician care. The most important aspect of clinical care is close interaction between the healthcare provider and the patient. In the field, this can be compromised by marked resource-need mismatches. Furthermore, even the most acclimatized professional with the best working conditions gets fatigued and potentially distracted in PPE while observing comprehensive IPC practice. Solid preparation and planning of activities in the high-risk area preserves time with the patient, increases general efficiency, and increases safety. For example, procedures requiring the use of sharps such as adding electrolytes to crystalloid solutions can be done before entering the high-risk area, preserving time with the patient and limiting use of sharps in a high-risk environment.

TREAT THE PATIENT, NOT THE IDEA OF THE PATIENT

Clinicians carry many preconceived notions about what a viral *hemorrhagic* fever patient looks like. In fact, hemorrhage is *not* a prominent sign or symptom in most patients presenting with EVD. Respect the clinical syndrome observed in the individual patient. Like any severely ill patient, an EVD patient requires objective and longitudinal evaluation and intervention. These patients can have waxing and waning clinical courses or precipitous deteriorations. All of us have been humbled by how quickly some EVD patients progress from being moderately stable to severely ill. Young patients can appear compensated longer before rapid declines. In part, this may be a result of barriers in achieving an optimal clinical examination in PPE and a lack of clinical laboratory testing in field settings. Nonetheless, patients in referral intensive care unit (ICU) settings with severe multiple organ dysfunction and requiring ventilator and dialysis support have recovered.

Although the dominant clinical challenge in most EVD patients is volume and electrolyte resuscitation, common non-infectious co-morbidities such as diabetes, hypertension, and heart disease may complicate disease course, particularly in older patients. In addition to malaria, other endemic health risks are present in West Africa including helminthic infections, amoebiasis, acute thiamine deficiency, and sickle cell disease. Patients and families remain the best sources of information. Many barriers exist to obtaining it. They include challenges of communicating through PPE, short amounts of time with individual patients, and language and cultural barriers. Like all care settings, each patient is unique. Among cases presenting for care, the signs, symptoms and in the field even the history of an EVD patient may be non-specific. Suspect case definitions are necessarily sensitive. Good individual and collateral history taking, and the use of systematic testing and empiric treatment protocols addressing common health risks and care challenges are important.

Symptom-control strategies should be adopted early and throughout illness—myalgias, arthralgias, sore throat, abdominal and atypical chest pain, nausea and vomiting, and anxiety are common features that can be addressed in the care of moderately and severely ill EVD patients.

ENGAGE PATIENTS FOR HELP WHEN APPROPRIATE

Even the best staffed EVD care centers may be challenged in delivering continual care to patients. Tasking patients to drink specific quantities of ORS and reviewing their performance frequently builds rapport, empowers patients, and improves intake volume. When resources become stretched, and sometimes in the best of circumstances, recovering patients may be invaluable as informal aides in the care of others. The EVD care center becomes a microcosm for community organization. Other patients often contribute to the care of pregnant women, young children, and the elderly—encourage this sense of community. It gives patients more control of a daunting care environment. Telephones in the isolation area for patient use can help care and morale. Recovering patients sometimes can be tasked to help monitor the sickest of patients, prepare and coach taking of ORS solution, potentially change IV bags, call health staff, and translate. In other resource-constrained settings, family members have alerted clinicians when IV fluid bags are empty during the resuscitation of a patient.[6] After recovery, survivors and their families can be invaluable in building community relationships outside treatment centers.

BEWARE OF THE CHALLENGES OF PATIENT CARE ON THE *SUSPECT* WARD

Patients present for triage and screening for EVD when they are sick. These patients might have EVD, another severe illness, or both. Admitting a patient into isolation, particularly one not yet confirmed with EVD, provokes a careful risk-benefit analysis for this reason. The suspect ward admits patients awaiting laboratory confirmation of their EVD, or exclusion of EVD as the cause of their illness. Patients may need to stay in the suspect ward for 3 or more days while waiting for reliable diagnostic test results. The objective is to provide sufficient benefit to both the patient and the community to outweigh the risk to the patient if negative. The level of care necessary here can be high. We have observed the manifestations of severe malaria, gastrointestinal bleeding in human immunodeficiency virus (HIV), viral hepatitis co-infected patients with cirrhosis, pulmonary hemorrhage in the setting of severe heart failure, epistaxis caused by malignant

hypertension, complicated pregnancy, and non-Ebola viral hemorrhagic fevers.

Use the same caution as in the high-risk area with confirmed EVD patients. However, some—if not many—of the patients admitted to the suspect ward will not be EVD infected and will be discharged rather than admitted to the confirmed ward. Regardless of their EVD infection status, they need a combination of individual patient and epidemiology-directed empiric therapy. Careful practices for patient toileting, patient placement, and triage for communicability and clinician hygiene in between assessing individual suspect patients are important to mitigate patient risk of acquiring EVD infection if not yet infected.[7]

Assessment and management of infants and children pose specific challenges in the field. Occasionally children without symptoms have entered facilities with their ill caregiver, such as the breastfeeding infant of an ill mother. These infants and children, who cannot communicate symptoms clearly yet sometimes move freely around the care center, may need to be monitored with particular attention throughout their time in the care center and for 21 days after release. They will have care, nutrition, and EVD screening needs in and out of isolation. Many of them will fall ill with EVD. When infants and children have been ill with EVD, sometimes a healthy adult has elected to enter to care for them. Healthy adults require considerations similar to those for healthy children.

DECREASE BARRIERS BETWEEN THE PATIENT AND THE COMMUNITY WHEN APPROPRIATE

Isolating a patient introduces a high burden of care and may create social barriers between the outbreak response and patients, families, and their communities. Healthcare providers are wrapped in PPE, giving patients very limited ability to make eye contact or read facial expressions. Patients, their families and communities frequently witness deaths, followed by decontamination of corpses and placement in body bags. These experiences are traumatic and promote not only alienation of the outbreak response from the community, but also increase patients' sense of isolation from caregivers and the outside world.

Ensure that patients have ways to safely communicate with healthcare workers, family, and friends. This can be done using open line of sight areas with low barriers where ambulatory patients can speak with visitors across a safe distance. In well-appointed hospitals, glass and electronic communication devices can be used. Seek mechanisms for patients to charge their cellular phones to allow continued communication with family and friends. Provide positive feedback to families and friends that come to the visitation area. When resources allow and when appropriate and acceptable to the patients, consider family entry into the high-risk area in PPE, escorted for a supervised visit after prior training and indoctrination. Some patients, though, want time before interacting with others. When discussing burial with families of deceased patients, allow for their viewing of the body and participation in a safe burial. This basic respect for patients and families helps to build and maintain positive relationships with communities, overcoming common misunderstandings and making activities in the EVD care center more transparent.

BALANCE STAFF AND PATIENT NEEDS; CARE FOR EACH OTHER

Physical and emotional fatigue may contribute to errors in clinical decision making and IPC practice. Staff must protect and monitor their health and the health of their colleagues. Be wary of physical symptoms of dehydration, fatigue, and psychological stresses caused by working in resource-constrained and high-risk environments. This is true at the care site, after hours and after the period providing care. For international staff, the post-deployment period may present additional but under-appreciated stressors. Returning to a higher resourced health care setting leads to an *inequity-tension* experienced by many people working both in low- and high-income countries. Colleagues, neighbors, and others at home may have considerable apprehension about interactions with returning healthcare workers, even though they may have little reason to suspect EVD or other illness. Recently announced quarantine of asymptomatic health care workers in some jurisdictions inevitably adds to this post-deployment stress. We have used our network of consultants not only as a technical sounding board but also for personal support in and away from the field.

Following both general and specific principles, we can provide effective and safe care regardless of geography. In an outbreak, clinicians must focus on the part they play in practicing the best EVD care possible. They also should appreciate that direct patient care is both inextricably linked with the overall outbreak response and only one part of what is necessary to control an outbreak. An effective public health response brings patients to care. Direct clinical care builds trust, which facilitates other elements of the response. Strong surveillance, contract tracing and monitoring, social mobilization, and risk communication are essential. A well-functioning EVD care center promotes the integration of all of these aspects while respecting the broad range of work being accomplished by others.

Clinicians and all staff participating in outbreak response should strive to leave a legacy in improved systems for local outbreak response. Ideally, these will enable effective local responses, obviating the need for deployment rotations for future outbreaks. Until then, *more* prepared, fully equipped, and supported clinical teams are needed to confront EVD in West Africa. Clinical *preparedness* is needed in at risk countries.

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エボラ出血熱の現状～臨床医の立場から～

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要　旨

2014年，西アフリカにおいて，エボラ出血熱(Ebola virus disease：EVD)の過去最大の流行が発生した．これまでの報告と同様に，患者に出血症状は少なく，消化器症状が目立つ．流行地では，限られた医療資源の中，支持療法の最適化が試みられている．医療従事者への感染リスク評価は一定せず，適切な個人防護具や先進国における医療体制について様々な考え方がある．我が国においても，未承認薬の使用などの課題を投げかけている．

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Key words　エボラ出血熱，新興感染症，職業感染，個人防護具，コンパッショネートユース制度

はじめに

エボラ出血熱(Ebola virus disease：EVD)は，1976年に現在の南スーダンとコンゴ民主共和国で，家族や医療従事者におけるアウトブレイクを契機に見出された急性発熱性疾患である．病原体の*ebolavirus*は野生動物を宿主とし，致死率が高いことなど，新興ウイルス感染症を代表する疾患でもある．2014年はこれまで想定されていなかった規模（2014年10月17日現在，患者報告数9,216例）で，西アフリカを中心にEVDが流行している[1)]．筆者は，5月から9月にかけて，流行国のリベリアとシエラレオネにおいて，世界保健機関（World Health Organization：WHO）の短期専門家（治療および感染防止）として，アウトブレイク対策に関わる機会を得た．臨床医の立場から見た今回の流行について述べる．

1．患者の臨床像・現地における診療

EVDの臨床像に関する報告は少ない[2)]．発生地では流行の封じ込めが優先され，個々の患者の治療や臨床像の記録はこれまで十分に検討されてこなかった．約7日間続く高熱に加えて，第1病週後半に出現する嘔吐，下痢，腹痛といった消化器症状が以前から注目されていたが，今回の流行でも同様の傾向が認められる[3)-4)]．出血症状の認められた患者は全体の約15％に留まって

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Progress in Diagnostic Technology and Management of Infectious Diseases. Special Columns：Ebola virus disease：From the viewpoint of clinicians.

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おり，致死率は約50%である．

患者の治療は，臨時に設営されたEbola treatment unit(ETU)で行われる．患者はconfirmed caseとの接触歴があるprobable case，あるいは，接触歴がない，または不明のsuspected caseとしてETUに入院する．特異的な症状や所見に乏しいことから，PCR検査用の採血が行われた後に，抗マラリア薬，抗菌薬の投与と輸液療法が行われるのが一般的である．資源の乏しい医療環境の中で，支持療法の最適化を図ろうと努力がなされている[5]．例として，敗血症ガイドラインに基づいた初期蘇生輸液の推奨が挙げられる．しかし，定員を超えて患者を収容しているETUでは，バイタルサインの測定もままならない．しばしばコレラに類似した大量の水様下痢が経験されるため，電解質測定などに基づいた輸液療法などにより，致死率の改善はある程度期待できると考えられる．

2. 医療従事者の感染・個人防護具

今回の流行では，約10%の患者が医療従事者であると報告されている[4]．一次医療機関において，適切な個人防護具(personal protective equipment：PPE)を着用しないで患者に接触したことによると思われる事例が多いが，曝露の詳細な報告は限られている．稀ではあるが，明らかな曝露を認識しない事例もある．嘔吐している患者からのエアロゾルによる感染やPPEを脱ぐ際に粘膜を汚染することも想定しておく必要がある．また，家族内感染した職員を通じて職場で伝播した事例もあった[6]．職業感染のリスクはゼロにはできないことを前提とした医療従事者の心理面を含めた健康管理は重要である．

筆者（加藤，古宮）が関わったリベリア・モンロビア市のJohn F. Kennedy Memorial Medical Centerに設置されたETU(35床)では，医師，医師助手，看護師だけでなく，清掃，消毒，給食，後方支援担当者など約100名が8時間交代で勤務していた．国境なき医師団の推奨するPPEは皮膚が露出しないことを重視したものである．ボディスーツの蒸し暑さ，ゴーグルの曇り，N95マスクの息苦しさがあり，連続勤務時間は2時間までに制限していた．開設から幸い2カ月間，ETU内での職業感染事例は報告されていない．一方，筆者（足立）が関わったシエラレオネのKenema Ebola Treatment Centerでは，WHOの推奨に従い，ゴーグルの代わりに曇りにくいフェイスシールドを採用していた．快適性と感染リスクのバランスの中で最適なPPEについて議論が続いているが，致死率が高い疾患であり，両者の整合性を取ろうとする努力は成功していない．

3. 先進国における医療体制・未承認薬使用

EVDなどのウイルス性出血熱に対する医療体制は，先進各国においても違いが認められる．欧州では，専用の高度隔離病室(high-level isolation unit)を国内に数カ所設置してきた国が多い．陸路や空路による患者搬送体制と併せて，適正な数と配置が検討されてきた[7]．これらの施設は現在，西アフリカで感染した支援者の診療に利用されている．一方，米国は，BSL（biosafety level)-4実験室の近隣に同様の病室を少数設置してきたものの，適切な感染防止策をとれば，特別な医療施設を必要としないという立場である[8]．我が国では感染症法の施行以来，全国に第一種感染症指定医療機関が設置され，都道府県単位で患者への医療を含めたアウトブレイク対策が行われることになっている[9]．

先進国では人工呼吸や血液浄化療法なども実施可能ではあるが，重症急性呼吸器症候群（severe acute respiratory syndrome：SARS）のアウトブレイク時に明らかとなったように，医療

行為により職業感染のリスクは高まる可能性がある[10]．また，先進国では，未承認のモノクローナル抗体や抗ウイルス薬がコンパッショネートユース制度を通じて使用された．我が国ではこの制度は未整備であり，今後の課題と考えられる．

おわりに

臨床医の関わる患者の治療はアウトブレイク対策の一部分に過ぎない．しかし，様々な制約の中で患者に最善の医療を提供することは，患者の早期受診にもつながり，社会への安心を与えるものである．臨床医の国際的なアウトブレイク対策への参加は，発生地ばかりでなく，我が国の新興感染症に対する医療体制の整備にも貢献すると信じる．今後も我が国から国外の感染症アウトブレイクの際に現地に赴く臨床医を増やすことについて，関係者の理解と支援を得られれば幸いである．

謝辞　筆者の西アフリカ派遣にあたり，多大なる支援をいただいたWHOジュネーブ本部の進藤奈邦子先生に感謝いたします．

著者のCOI (conflicts of interest) 開示：本論文発表内容に関連して特に申告なし

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総　説

エボラ出血熱：西アフリカにおける流行と対策

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Key words: Ebola virus disease, prevention, transmission

要　旨

西アフリカでエボラ出血熱の過去最大の流行が続いている．筆者らは世界保健機関（WHO）の短期専門家としてリベリアとシエラレオネに派遣され，最前線の治療センターで診療や感染対策に従事した．本稿では，西アフリカにおける流行の状況，現地での疾患対策，臨床的特徴，医療従事者に起こった感染について報告する．

現地では，WHO「ウイルス性出血熱患者の臨床管理」ガイドにもとづき，汚染区域と非汚染区域の明確な区別，症例定義に沿った患者のトリアージ，適切な個人防護具の着用，適切な消毒液の使用などの方法により，患者の受け入れと診療を継続した．

看護師など医療従事者の感染は深刻な問題であった．感染の直接的原因は特定されていないが，流行規模に比べて診療要員は決定的に不足しており，汚染区域での単独作業，個人防護具装着による作業のしづらさや視界不良，疾患対策の長期化による疲労の蓄積など，複合的要因が考えられた．

筆者らの観察した臨床的特徴と，これまでのアウトブレイク対策で既に報告されている知見をふまえて，エボラ出血熱患者の診療に際しての合理的な対策について提言する．我が国の対策の一助となれば幸いである．

〔感染症誌　89：223～229，2015〕

序　文

2014年の西アフリカにおけるエボラ出血熱の流行が，ギニア，リベリア，シエラレオネ3カ国を中心に続いている．2014年12月の本稿執筆時点で，3カ国における患者は19,000人以上，死者は7,000人以上に達している[1]．1976年に病原体であるエボラウイルスが発見されて以来，アフリカ大陸で400人規模までの流行はあったが，今回は過去を遥かにしのぐ規模の流行であり，未だに終息する兆しがない．

エボラ出血熱は，重篤な症状，高い致死率といった独特の疾患自然史に加え，厳しい感染対策，隔離を含む強制措置，特異的治療薬がないことなどから，一般市民の心理にも影響を与える．途上国の医療現場におけるデータ収集の困難さと相まって，未知の部分が多い疾患と考えられてきたが，これまでアウトブレイク対策にあたった専門家による優れた洞察を通して，既に分かっていた知見もある．

筆者（加藤，古宮，足立）は世界保健機関（World Health Organization：WHO）の短期専門家として，2014年5月から9月にかけて順次リベリアとシエラレオネに入り，流行地の最前線で疾患対策に関わった．エボラ出血熱の流行地への影響はきわめて深刻であり，疾患対策のテーマは広範囲にわたる反面，診療要員が決定的に足りない医療現場でデータ収集するのは容易ではない．本稿では，従来の研究論文の手法には必ずしもこだわらず，エボラ出血熱の流行に対して現地でどのような対策が立てられ，実行されたかを記述し，これまで知られている科学的根拠と合わせて，この疾患の本態について可能な限りの考察を試み，教訓を抽出することとしたい．

現地の状況と対策

1．西アフリカにおけるエボラ出血熱の流行

西アフリカにおけるエボラ出血熱の発生は，2013

別刷請求先：（〒173-0015）東京都板橋区栄町33―1
東京都保健医療公社豊島病院感染症内科
足立　拓也

平成27年3月20日

Table 1 Ebola virus disease case-classification criteria[1]

Classification	Criteria
Suspected	Any person, alive or dead, who has (or had) sudden onset of high fever and had contact with a suspected, probable or confirmed Ebola virus disease (EVD) case, or a dead or sick animal OR Any person with sudden onset of high fever and at least three of the following symptoms: headache, vomiting, anorexia/loss of appetite, diarrhoea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccup OR Any person with unexplained bleeding OR Any sudden, unexplained death.
Probable	Any suspected case evaluated by a clinician OR Any person who died from 'suspected' EVD and had an epidemiological link to a confirmed case but was not tested and did not have laboratory confirmation of the disease.
Confirmed	A probable or suspected case is classified as confirmed when a sample from that person tests positive for EVD in the laboratory.

年12月のギニアでの発端者に遡る．病原体は*Zaire ebolavirus*である[2]．2014年3月23日にWHOはギニアにおけるエボラ出血熱の流行発生を報告し，3月29日にリベリアで，5月25日にシエラレオネで最初の患者が確認された．8月8日にWHO事務総長は「国際的に懸念される公衆衛生上の緊急事態」を宣言した[3]．WHOの緊急要請を受け，加藤と古宮はリベリアに，足立はシエラレオネにそれぞれ派遣された．

流行国における症例定義をTable 1に示す[1]．診断の確かさの順にconfirmed，probable，suspectedの3分類である．原則としてsuspectedの該当者は全員採血を受け，逆転写ポリメラーゼ連鎖反応（RT-PCR）でエボラウイルスRNA陽性ならconfirmedに分類され，陰性ならnon-caseとして除外される．ただし，発病早期でウイルスRNAが検査閾値に達していない可能性があれば，48時間後に再検査を行う．また，発病後間もなく死亡したり，死体で発見されたりして，病原体診断ができなかった場合，発生状況からエボラ出血熱の可能性が高いと判断されればprobableとして集計される．

2014年12月24日のWHO situation reportによれば，3カ国から報告された患者数は19,463名，死者数は7,573名である[1]．リベリアではsuspectedが3,020名と非常に多く，患者の発生規模に対して検査が追いついていないことが示唆される．また，患者数と死者数から算出される致死率は，ギニア62%，リベリア43%に対して，シエラレオネは29%と大幅に低いが，後述するようにシエラレオネの死者数については明らかに過小報告である．Suspectedの血液検体は検査センターに搬送されるが，肝心の患者の相当数が追跡できなくなってしまう，現場の対策要員が足りない同国の事情が反映されている．

2．流行国における疾患対策

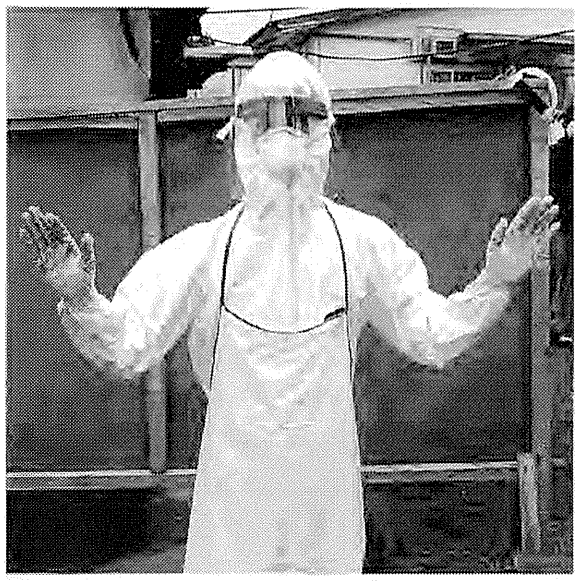
筆者（足立）が派遣されたシエラレオネでは，7月当時はギニアとリベリア国境に近いKenemaとKailahunの両県が二大流行地であった．WHOは首都Freetownの事務所を本拠とし，首都から東に300km離れたKenema国立病院を前線基地として，疾患対策を展開した．Kenema国立病院は，従来から米国Tulane大学の支援でラッサ熱治療センターと付設検査室があり，5月に同国初のエボラ出血熱患者が確認されて以来，エボラ治療センターとして患者収容を開始した．

7月当時は，疑い患者（suspected）病棟14床と，確定患者（confirmed）病棟19床があり，患者の急増に対応するため仮設病棟24床が増設された．多数の患者を収容するため，廊下にもベッドを並べ，ベッドも足りないときはマットレスを敷いて，患者が横になれる場所を作って対応した．毎日40名程度の確定患者と十数名の疑い患者が入院中であった．

Kenema国立病院のエボラ対策チームには，診療班，看護班，検査班，消毒班，遺体搬送班，感染対策班があった．診療班は，シエラレオネ人の治療センター責任医師のほかにWHOから派遣された国際支援医師2名，感染対策班はWHO専門家，検査班は米国人技術者と現地スタッフ，他の班は現地スタッフで構成されていた．治療センター外で活動するチームとしては，接触者追跡班，疫学分析班，病院の管理部門があった．筆者の滞在後半にWHOジュネーブ本部よりチーム調整役と物資調達担当者が到着してからは，それまで頻発していた個人防護具，医薬品，医療材料の在庫切れが解決しはじめ，活動はかなり効率よく行われるようになった．

治療センターでは，汚染区域（hot zone）と非汚染区域（cold zone）を厳密に区画し，hot zoneに入る

Fig. 1　Staff in personal protective equipment



スタッフは，軽装の上下とゴム長靴の上に，ボディスーツ型ガウン，厚手エプロン，二重手袋，N95マスク，フェイスシールドを装着した（Fig. 1）．エボラ出血熱の感染様式を考慮すれば，直接的な身体接触を避け，偶発的な体液飛散を防御できればよいことから，WHO指針はサージカルマスクも可としているが[5]，N95マスクの十分な供給量があったことからサージカルマスクに切り替えるには至らなかった．フェイスシールドに代えてゴーグルを試したことがあったが，高温多湿の環境では曇りやすく，静脈路確保の際に針先や血管が見えず，足元に落ちている異物が見えないなどかえって危険なため，結局ゴーグルではなくフェイスシールドを選択した．一方，筆者（加藤，古宮）が派遣されたリベリアの首都Monroviaの John F. Kennedy記念病院エボラ治療ユニットでは，皮膚が露出しないことを重視し，ゴーグルを使用した[5]．

Hot zoneでは毎日大量の消毒液が必要になるため，蛇口を取り付けた大型バケツの中に0.5%次亜塩素酸水を常に補充した．患者を一人診察するごとに，肉眼的汚染の有無にかかわらず，外手袋を次亜塩素酸水で洗い流してから外手袋のみ取り替えて，次の患者を診察した．Hot zoneから出るときには，消毒班の立ち合いのもと，個人防護具を一点ずつ取り外し，各操作の間には手袋表面を次亜塩素酸水で洗い流し，汚染を体表に残さないようにした．Cold zoneには，偶発的な汚染に備えて0.05%次亜塩素酸水の入った蛇口付バケツを各所に置き，必要に応じて手指を消毒できるようにした．使用済の個人防護具をはじめ，毎日大量の廃棄物が発生したが，地面に大きな穴を掘り，廃棄物を積み上げ，燃料をかけて焼却した．本来なら大型の焼却炉があればよかったが，燃え残りが堆積したり散乱したりして，理想的とは言えない状況であった．

治療は基本的にWHO「ウイルス性出血熱患者の臨床管理」ポケットガイドによった[6]．入院患者は多かれ少なかれ脱水があったが，患者一人あたりに使える診察時間は限られており，かつ医療者自身の針刺しリスクを最小化するため，比較的軽症の患者は経口補水液（oral rehydration solution：ORS）の摂取を励行し，重症患者はリンゲル液による経静脈輸液を行った．マラリア迅速診断キットで重複感染が見つかれば，マラリア治療を行った．重症例に広域抗菌薬を投与したこともあったが，効果は不明である．モノクローナル抗体製剤などの実験的治療薬は，筆者が派遣された時点で現地では入手不可能であり，患者への投与は考慮の対象外であった．

診療班は毎日2回の回診を行った．多数の重症患者がいたが，診療録の経過用紙はほぼ白紙であった．患者はhot zoneにいるが診療録はcold zoneにあり，個人防護具を装着してhot zoneに入り，50人前後の患者を診察してcold zoneに出てきたときに，どの患者にどんな所見があり，どんな治療をしたか思い出すのはほとんど不可能である．筆者が現地入りしたときの診療状況は，回診時に患者一人あたりに割く1分間ほどの，その場の診断と治療がすべてであり，患者ごとに一貫した治療方針が継続される保証はなかった．そこで，患者ごとに経過シート1枚を作成してhot zoneに置き，毎日の症状，身体所見，治療をごく簡潔に記入して，病状経過が次に回診した医師に分かるようにした．

確定患者の退院基準は，以下の4項目を条件とした[6]．

- 3日以上，発熱その他の症状がない
- 臨床症状が明らかに改善している
- 食事，保清，歩行などの日常生活動作が自立している
- 血液再検でPT-PCR法によりエボラウイルス陰性である

3. 臨床的特徴

Kenema国立病院では，入院時の担当看護師が各種症状の有無をチェックリストに記録し，診療録に残していた．7月13日時点で入院中の確定患者35名について，入院時の症状をTable 2に示す．

発熱が最も多く，次いで衰弱やめまいなどの全身症状，頭痛，下痢，嘔吐などが，よくみられる症状であった．家庭での体温計使用は一般的でなく，発熱の有無は体熱感の自己申告によることに留意されたい．出血症状については，入院時に症状があったのは歯肉出血の1名のみであった．病状が進行するにつれて吐下血

平成27年3月20日

Table 2 Symptoms on admission

Symptom	Yes	(%)	No	Not specified	Total
Fever	28	(80)	4	3	35
Weakness	26	(74)	6	3	35
Dizziness	24	(69)	8	3	35
Headache	21	(60)	6	8	35
Diarrhoea	19	(54)	12	4	35
Vomiting	16	(46)	14	5	35
Cough	14	(40)	9	12	35
Confusion	13	(37)	10	12	35
Sore throat	11	(31)	14	10	35
Abdominal pain	7	(20)	3	25	35
Conjunctival injection	6	(17)	18	11	35
Joint pain	3	(9)	7	25	35
Jaundice	2	(6)	14	19	35
Inflammation	2	(6)	16	17	35
Bleeding	1	(3)	7	27	35
Hearing loss	1	(3)	19	15	35
Facial oedema	1	(3)	21	13	35
Rash	0	(0)	12	23	35
Convulsion	0	(0)	20	15	35

Among 35 'confirmed' inpatients as of 13 July 2014.

などを起こす患者は増加するものの，筆者の観察では経過を通して出血傾向を呈するのは全体の2割程度であった．

重症患者の特徴として，3つのパターンが観察された．

1. 嘔吐や下痢を頻回に繰り返し，脱水に対する補液にもかかわらず，急速に衰弱が進行する
2. 口内炎，後胸骨痛，心窩部痛，腹部全体の著明な圧痛など，消化管に沿った部位に耐えがたい痛みがある
3. 入院時から意識障害がある

1について，深刻な看護師不足のため輸液パックを交換するスタッフも欠いていたことから，重症患者であっても1日の輸液量は最大1L程度にとどまった．診療要員が確保できれば，より積極的な輸液療法を行う余地はある．2について，水も飲めないほど，麻薬性鎮痛薬の投与を考えたいほど強い持続性の痛みであるが，現地ではこうした薬剤は入手できず，鎮静薬を投与するくらいしかできなかった．意識障害があり治療の協力が得られない場合，医療者の安全を考慮しながらの治療にならざるを得ない．上記3パターンに加えて消化管出血を起こした場合，現地の治療では救命の見込みはきわめて厳しくなる．

Kenema国立病院で7月1日から23日までの期間に退院した確定患者は，生存退院50名，死亡退院59名であった．入院と退院が定常状態に達していたと仮定すると，推定致死率＝59/(50＋59)＊100＝54%となる．

さらに，生存退院と死亡退院のうち，入退院日が確認できた患者の在院日数をFig. 2に示す．生存例では，解熱し，水が飲めるようになり，食事が摂れ，体力を回復して退院できるようになるまで，2〜3週間かかることが多かった．それに対して致死例は，入院当日から数日の間に次々と落命し，重症患者の病状進行は急速であった．

4. 医療従事者の感染

Kenema国立病院では，7月時点でエボラ治療センターに配属されていた看護師のうち実に11名がエボラ出血熱に感染し，うち5名が命を落としている(Table 3)．治療センターの責任医師も感染して死亡し，医療従事者が感染したニュースは国内外で大きく報道された．動揺して離職した看護師も分かっているだけで11名に上り，残されたスタッフにはさらに重い負担がかかった．

きわめて深刻な事態であったが，死亡した職員からの聞き取りは不可能であり，隔離中の職員からの聞き取りも様々な制約から困難で，感染の直接的原因の特定には至っていない．

John F. Kennedy記念病院では，筆者(加藤，古宮)がエボラ治療ユニットの開設に関わった8月から9月にかけては医療従事者の職業感染はなかったが[6]，10月に治療ユニットの医師を含む複数の職員が感染したとの報道がある[7]．現地を離れての情報収集には限界があり，職場での感染だったかどうかを含めて詳細は分かっていない．

ま と め

エボラ出血熱患者の臨床像については，今回の流行国4カ国(ギニア，リベリア，シエラレオネ，ナイジェリア)の症例全体で，各種症状の頻度や，出血を起こす患者は2割弱にとどまること，また意識障害，嚥下困難，咽頭痛，出血，下痢の5症状は，生存例に比べて致死例で有意に高い割合でみられており，筆者の観察と合致する結果が報告されている[8]．

Kenema国立病院における7月の致死率は54%前後と推定した．5月から6月にかけて確定診断された同病院の入院患者87名の致死率は74%との報告もあり[9]，いずれの数値もsituation reportから読み取れるシエラレオネにおける致死率29%とは大きな乖離がある．WHO対策チームが9月までの累積症例をまとめた報告では，シエラレオネの1,439例の致死率は32%であるが，最終的な転帰が確認されている445例に限ると致死率69%に上昇する[8]．Situation reportの速報値は，シエラレオネの死者数については明らかな過小報告であり，データ検証後に他国並みの高い致死率に修正されることが見込まれる．

現地の医療従事者が感染した直接的原因は特定され

Fig. 2　Days spent in hospital

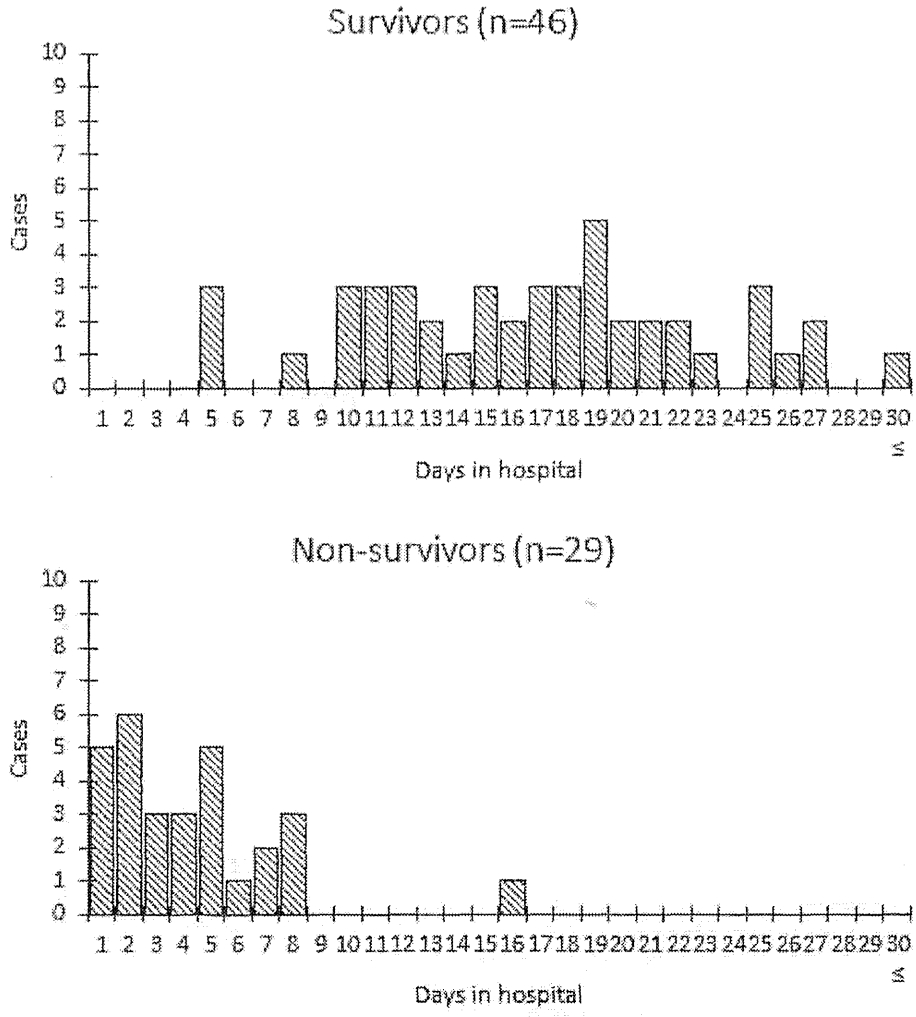


Table 3　Nursing staff at Kenema Government Hospital Ebola Treatment Centre

Status	Number
Well and present	20
Infected with EVD	11
(Died due to EVD)	(5)
Absent due to illness other than EVD	2
Absent due to non-illness reasons	11
Total	44

As of mid July 2014.

ていない．以下のような複合的要因が考えられている．

- 予測以上の流行規模，増え続ける患者数に対する，明らかな診療要員不足
- Hot zone で多数の患者に単独で対応したこと
- 厳重な個人防護具による身体活動制限と視界不良
- 頻発する個人防護具の在庫切れ
- 長期化するアウトブレイク対応で蓄積した身体的・精神的疲弊
- 治療センター責任者の感染と不在による指揮命令系統の機能不全

Kenema 国立病院では，経験年数の浅い看護師よりむしろ，看護師長をはじめとする熟練の看護師で感染が多発した[10]．6 月から 10 月までの期間にシエラレオネから報告された医療従事者の感染 199 例の分析では，単なる個人防護具装着手順の違反と言うより，職員訓練，物資調達，施設整備，患者トリアージ，厳格なゾーニング，廃棄物処理といった，感染対策の手法が全体として十分機能していなかったことが示唆されている[11]．現場の診療要員は決定的に不足していた一方で，患者は次々と運び込まれ，切迫した中で患者対応せざるを得なかった状況が，さらなる感染連鎖を生んだ構図と言える．

エボラ出血熱は，重篤な症状，高い致死率，二次感染の可能性から，感染対策には十分な注意が必要であるが，エボラウイルスの感染様式には既に分かっていた知見もある．

1995 年のコンゴ民主共和国 Kikwit における流行

平成27年 3 月20日

で，患者の同居家族173名の二次発病の有無とリスク因子を詳細に調査した研究によれば，潜伏期の患者の身体に直接接触しても感染リスクは増加せず，患者の発病後であっても身体や体液に直接触れていない同居家族には二次発病者はいなかった[13]．

2000年のウガンダGuluにおける流行で，患者由来のどの体液にエボラウイルス（*Sudan ebolavirus*）が存在するかを調査した研究によれば，急性期患者の唾液(67%)，便(50%)，皮膚(13%)からRT-PCR法でウイルス遺伝子が検出された．回復期患者の各種検体からは，母乳と精液を除き，いずれもウイルスは検出されなかった[13]．急性期患者は高率に嘔吐することを考慮すると，上記の唾液には嘔吐物が混入していた可能性はあるかもしれない．

同じく2000年のGuluの流行で，患者血清のエボラウイルスRNAを定量した研究によれば，生存例に比べて致死例のウイルスRNA量の増加は遥かに速く，RNAコピー数の違いは$2\log_{10}$に達した[9]．重症化するほどウイルスRNAが増加することから，重症患者は二次感染も起こしやすいと推測される．

これらの結果より，急性期，とりわけ重症患者の嘔吐物・下痢便・血液の取り扱いには特に注意が必要であり，また皮膚や粘膜への直接接触を避けるため適切に個人防護具を着用することが望ましい．一方，潜伏期の感染者と身体接触があったとしても二次感染リスクにつながるものではないし，回復期患者の体液からは急速にウイルスは消失して感染性は失われる．ただし，回復期であっても授乳と性行為は潜在的な感染リスクがあることは，患者への指導が必要である．

なお，我が国では行政上，確定患者の「急性期症状消失後，1週間以上の間隔を置いた2回の検査（血液および精液のウイルス分離）の結果，病原体が検出されなかった場合」，または「血液なら発病後8日，精液なら発病後61日を超えた後の場合にあっては，1回の検査の結果，病原体が検出されなかった場合」に，病原体を保有していないものと判断される[16]．感染症法によれば，都道府県知事は「一類感染症の病原体を保有していないことが確認されたときは，当該入院している患者を退院させなければならない」が[16]，症状消失後も精液にウイルスが長期残存する場合に入院継続すべきかどうかを定めた条文はない．WHOや各国基準との整合性や人権への配慮をふまえ，我が国の退院基準についても整理が必要と思われる．

流行国の対策から得られる教訓を，以下のようにまとめた．

1. 患者収容施設ではhot zoneとcold zoneを明確に区別する．
2. Hot zoneで個人防護具を着用している人は，患者対応に専念する．外回りスタッフはhot zoneにいる人を常にサポートし，孤立させない．
3. Hot zone/cold zone間の意思伝達手段を確保する．診療録をどうやって記録するか．
4. Hot zoneの医薬品・医療材料の在庫を切らさない．
5. 個人防護具は，手袋・ガウン・マスク・眼保護が基本形．視界がよいこと，作業しやすいことも重要．
6. 明確なトリアージ基準を持ち，患者トリアージと隔離を速やかに行う．
7. 急性期患者の嘔吐物・下痢便・血液を扱うときは，最大の注意を払う．できるかぎり複数のスタッフで対応する．
8. 医療従事者の士気を保つことは，きわめて重要．

エボラ出血熱は，我が国を含む先進国では，これまでどこか遠い国の謎めいた熱帯病と考えられてきた．今回の大規模な流行に際して，現地では多数の重症患者に適切な医療を提供しようとする努力と，臨床医学・疫学・ウイルス学の知見を集積して疾患の本質を解明するための試みが続いている．本稿が日本の関係者にとって，理にかなった疾患対策を実践する一助になることを願うものである．

免責事項：本論文の内容は筆者個人の意見に帰属する．本論文は各筆者の所属機関の公式見解を反映するものではない．

利益相反自己申告：申告すべきものなし．

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Ebola Virus Disease Outbreak Response in West Africa

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The largest ever outbreak of Ebola virus disease has been spreading in West Africa. The authors were deployed to Liberia and Sierra Leone as short-term consultants for the World Health Organization. Our mission was to ensure clinical management and infection prevention and control priorities in frontline treatment centres. This paper describes how the disease is spread, its symptoms and progression, measures currently taken to ensure both infection control and the best possible care, and the significance of infections among health care workers.

We adopted an approach which is detailed in the WHO Clinical Management of Patients with Viral Haemorrhagic Fever. Areas within the treatment centres were divided into either a "hot zone" or a "cold zone". Patients were interviewed, and those patients who met the criteria for suspected, probable or confirmed cases were moved to hot zones. All health care workers wore personal protective equipment when entering a hot zone and washed hands with a hypochlorite solution after each patient encounter.

Among the problems which we encountered was a fundamental mismatch in the numbers of patients and nurses. The nurses often had to work alone in hot zones in protective equipment which limited physical movement and blurred vision. These factors contributed to fatigue due to prolonged outbreak response and may have resulted in infections among the nursing staff.

In conclusion, we present the current situation in West Africa in regard to the recent outbreak of Ebola virus disease, specifically the clinical picture based on our observation. We further propose steps to be taken to handle the patient care safely and effectively. We hope our experience will contribute to national discussions on how to respond to the Ebola virus disease.

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