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High-Containment Pathogen Preparation in the Intensive Care Unit



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KEYWORDS

- Preparedness • Supportive critical care • High-containment pathogens
- Biocontainment unit

KEY POINTS

- Providing state-of-the-art critical care to patients with highly infectious diseases presents unique challenges to health care providers and hospitals.
- Specialized biocontainment units or modification of existing care environments are needed to facilitate the delivery of safe and effective high-containment care.
- Multidisciplinary teams, protocol development, appropriate staffing, and training optimize the likelihood of a successful clinical outcome, including prevention of health care worker infections.
- Coordination at the local, state, regional, and national level is required to care for patients infected with high-containment pathogens.

INTRODUCTION

The recent Ebola virus disease (EVD) outbreak in West Africa in 2014 to 2016 highlighted the capabilities of dedicated biocontainment units (BCUs) at the National Institutes of Health (NIH), Emory University, and the Nebraska Medical Center to provide care for patients with highly infectious diseases.¹⁻³ In order to increase national capacity, the Centers for Disease Control and Prevention (CDC) called for the creation

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of a tiered network of US hospitals, including frontline hospitals, assessment hospitals, and Ebola Treatment Centers (ETCs).⁴ The Office of the Assistant Secretary for Preparedness and Response (ASPR) also funded the creation of 10 Regional Ebola and Special Pathogen Treatment Centers (RESPTCs).⁵

There are no definitive guidelines outlining the optimal environment of care for patients with highly infectious diseases.⁵ Several of the RESPTCs and some of the ETCs built new stand-alone BCUs.⁶ Other hospitals, such as Bellevue Health Center in New York City, transitioned existing intensive care unit (ICU) or other patient-care space into high-containment areas to be used on an as-needed basis.⁷ Regardless of the chosen solution, there are several core principles that underlie the creation of containment areas that can provide care for patients with highly infectious diseases^{3,8} (Box 1). In this article, the authors review the key aspects of high-containment care and provide a framework for successful critical care in this environment.

THE ENVIRONMENT

The physical structure of the care space is critical to ensuring health care worker, staff, and patient safety in the context of highly infectious diseases. The European Network of Infectious Diseases as well as a group from US centers with experience in highly infectious diseases have published consensus guidelines on the design and operation of BCUs.^{3,8} Lessons learned from the 2014 to 2016 EVD outbreak have further informed design considerations.⁶

Location of the Unit

The ideal containment area should be located away from other clinical areas with secured entry and exit points. This location will limit unnecessary traffic through the space. There should also be clearly identifiable transport routes into and out of the unit to allow entry of new patients and to evacuate patients and staff in the event of an emergency.³

Layout of the Care Space

The layout of the unit needs to support infection control practices, such as the donning and doffing of personal protective equipment (PPE) as well as the prevention of cross-contamination of clean areas. At a minimum, each patient room should have an

Box 1

Common features of biocontainment units

- Secure entry and exit points
- Onsite laboratory
- Advanced air-handling system for airborne and droplet transmission
- Highly trained nurse and clinician provider team
- Critical care capabilities
- Onsite portable radiology and ultrasound
- Advanced telecommunication capabilities
- Pass-through autoclaves for waste management
- Dedicated donning and doffing areas
- Unidirectional flow of staff through patient care areas where possible

anteroom for donning and doffing. Some facilities include an anteroom for donning and then a separate exit-room for doffing.⁶ Although an exit-room is not necessary for an airborne pathogen, this design allows for unidirectional flow of patients, staff, and materials through the care space to limit the possibility of cross-contamination, particularly in the context of contact-transmitted pathogens, such as Ebola virus (EBOV) or other viral hemorrhagic fevers. This principle of unidirectional flow is a cornerstone of Ebola Treatment Centers in Africa.⁹ Each unit should have an exit space where staff can shower after their care shift and change into clean clothing before exiting the unit. The unit should be equipped to provide critical care services and, depending on the local need, should anticipate caring for additional patient populations, including children and pregnant women.⁶

In addition to the care space, there should also be a staff break area for personnel to gather before and after their shift. This space needs to be separate from the rest of the unit and ideally should be on a separate air-handling system to ensure safety.

Fig. 1 shows the layout of the Johns Hopkins BCU, which was built in response to the 2014 to 2016 EVD outbreak.

Air Handling

In order to support the care of patients with diseases transmitted by droplet and airborne routes, the containment space should have an air-handling system that provides a negative pressure environment for contaminated areas. Such a system also protects health care workers and other patients in situations whereby infectious particles might be aerosolized (eg, coughing, sneezing, procedures, such as endotracheal intubation, and so forth).¹⁰ There are no existing regulations for air-handling

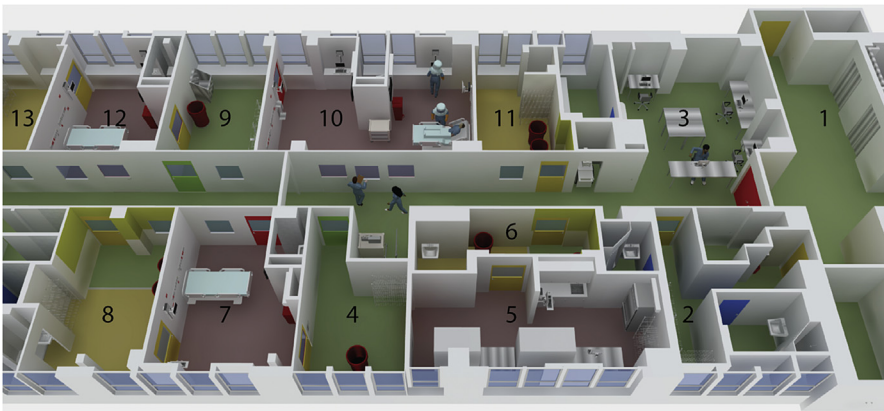


Fig. 1. General layout of the Johns Hopkins BCU. Patient rooms and the laboratory have dedicated space for donning and doffing PPE. This space allows unidirectional flow to reduce the risk of cross-contamination. Green indicates clean space, red indicates contaminated space, and yellow indicates doffing rooms. (1) Off-unit area with dedicated elevators, locker room, changing area, and lounge for staff; (2) clean entry and exit space for staff; (3) nurse station; (4) shared donning room for laboratory and patient room 3; (5) laboratory; (6) doffing room for laboratory; (7) patient room 3; (8) doffing room for patient room 3; (9) shared donning room for patient rooms 1 and 2; (10) patient room 1 with 2 ICU headwalls; (11) doffing room for patient room 1; (12) patient room 2; (13) doffing room for patient room 2. (*Reprinted from Garibaldi BT, Kelen GD, Brower RG, et al. The creation of a biocontainment unit at a tertiary care hospital. The Johns Hopkins medicine experience. Ann Am Thorac Soc 2016;13(5):603; with permission from American Thoracic Society.*)

systems in an entire containment unit. Guidelines for airborne infection isolation (AII) rooms from the CDC, American Society of Heating, Refrigerating, and Air-Conditioning Engineers, American National Standards Institute, and American Society for Healthcare Engineering can inform the design of the air-handling system for an entire unit.^{6,11}

For example, the entire Johns Hopkins BCU is negative pressure relative to the rest of the hospital. Each contaminated area is designed to have a pressure differential of at least -0.02 -in water gauge to adjacent areas (twice the requirement for an AII). This design ensures that air does not travel from a contaminated to a clean space. All intake air is filtered using a minimum efficiency reporting value 16 filter that captures 99% of $1.0\ \mu\text{m}$ particles; no air is recirculated. The anteroom air is changed at least 10 times per hour, whereas the patient room air is changed 12 to 15 times per hour, in accordance with AII guidelines. The air intake is on the ceiling, whereas the exhaust ports are on the wall close to the floor. This location creates laminar flow, away from a health care worker's face. The negative pressure for the unit is maintained by 2 rooftop fans, each equipped with high-efficiency particulate air (HEPA) filters that capture 99.99% of particles with a size of $0.3\ \mu\text{m}$. Each fan can maintain the negative pressure for the entire unit in the case of a single fan failure or the need for maintenance.⁶ Such redundancies improve the safety of the care space but may not be possible in all environments.

Decontamination of the Environment

Decontamination of the environment is an important consideration when designing an isolation unit. Floors and walls must be constructed of materials that can resist breakdown from hospital disinfectants, such as bleach and quaternary ammonium. Where possible, floor and wall seams should be sealed, or heat-welded, to prevent leakage of infectious materials into adjacent areas.^{3,6}

The use of either UV light or vaporized hydrogen peroxide to decontaminate the health care environment after patients are discharged may require additional design considerations, such as UV reflective paint or special exhaust covers for the air-handling system.^{12,13}

Equipment

In addition to the standard medical equipment required to care for critically ill patients, there are several equipment issues that are unique to the containment environment.

Imaging and other diagnostic technology Because patients are often not able to be transported outside of the containment environment for diagnostic testing or invasive procedures, it is necessary to provide advanced imaging and procedural capabilities onsite.⁸ Portable ultrasound devices allow for chest, abdomen, cardiac, and obstetric imaging as well as facilitate procedures, such as central venous catheter and chest tube insertion. Other point-of-care devices, such as digital stethoscopes, can overcome some of the limitations of PPE and enhance the diagnostic yield of the physical examination.⁶ Portable digital x-ray devices also allow for chest and abdominal imaging, although the need to process the plate and decontaminate the equipment presents additional logistical problems.¹⁴

Communication Communication is critical in a BCU environment, both for staff and for patients and their families. It can be difficult for providers to hear one another while wearing powered air purifying respirators (PAPRs), and visibility and facial recognition may be constrained by visors or PAPR hoods. Visitors are usually not allowed in the unit, which can contribute to a sense of isolation. There are several potential solutions,

ranging from less expensive choices (eg, smartphones and tablets) to advanced telecommunications systems that could include PAPP-integrated microphones and headsets. The goal of these devices is to allow patients and staff to effectively communicate with each other in the unit but also with individuals outside of the containment environment. This communication can facilitate consultation by health care providers and other ancillary services that do not need to enter into the contaminated space as well as allow patients to spend time with family and friends in a more intimate environment.

Reusing equipment and supplies In addition to the equipment mentioned earlier, there is a need to develop policies and procedures surrounding the reuse of specific critical care devices, such as mechanical ventilators and continuous renal replacement therapy machines. The CDC has published interim guidance on the decontamination of dialysis machines, but individual manufacturers may need to provide specific instructions on how best to clean a device after use.¹⁵ If there is any doubt as to the ability to safely decontaminate a device, the device should be discarded or, at the very least, kept out of clinical circulation until an effective decontamination strategy is developed.

Waste management

The safe handling of highly infectious waste is one of the most challenging issues in a containment environment.^{16–19} Category A infectious substances, defined as substances that can cause life-threatening or permanent injury on exposure to humans, have strict federal regulations surrounding their packaging, transport, and disposal.²⁰ Only a handful of civilian facilities process category A substances, and the cost of transport and disposal is substantial.²¹ The potential high volume of waste, both in the form of patient secretions and disposable products, such as PPE, present additional challenges.^{18,19,21,22} The CDC and ASPR recommend that facilities planning to care for patients with EVD consider installing steam sterilizers, or autoclaves, to sterilize waste before transport out of the containment facility.¹⁷ It is critical that facilities using onsite autoclaves validate their protocols using simulated patient waste and biological indicators to ensure successful sterilization.²¹ In a recent survey of 43 ETCs, 10 had onsite autoclave capabilities. The remaining centers had alternative plans that included packaging waste according to Department of Transportation's guidelines and transporting it to a certified processing facility. Onsite incineration is also a possibility but not currently planned by any ETC.²³

In addition to waste that is packaged for transport, facilities must have a plan to dispose of liquid waste from patient secretions (eg, urine, feces, vomit, and so forth) and procedures, such as dialysis. Specific protocols will vary depending on municipal regulations and water treatment facilities, but most call for the addition of a disinfectant for a designated period of time before allowing waste water to enter the sewage system.^{17–19}

Transportation

Transportation is a critical issue in the care of patients with highly infectious diseases. Guidelines and recommendations for the aeromedical transport of patients exist but are beyond the scope of this current review.^{24–26} Although some facilities have their own dedicated ground transport units,^{6,27–29} every facility with biocontainment capabilities should be prepared to accept the handoff of patients from a ground transport team.

Ground transportation requires careful coordination of local and state agencies, including law enforcement, public health, and emergency medical services.²² There is no clear consensus on how best to prepare an ambulance for transport. Many

US centers recommend wrapping the ambulance in impermeable material, such as plastic, to aid in ambulance decontamination,^{28,29} although this practice is not universally followed. Although some countries in Europe have invested in specially designed ambulances with HEPA filtration,⁸ it is likely sufficient to separate the driver's compartment from the care bay to limit the potential for exposure to aerosolized or airborne pathogens.²⁹ Ambulance staff should be properly trained in the use of appropriate PPE.³⁰ Patients can be placed in PPE to prevent excessive spillage of contaminated bodily fluids.^{28,29} A transport isolation system can also be used, although this might limit access to patients if the need for interventions during transport arises.⁸

On arrival to the biocontainment facility, a facility-specific transport team can take over the care of patients, while the ambulance team prepares to decontaminate their equipment in a dedicated and secure area.²⁷⁻²⁹ Once inside the facility, there should be a clearly delineated path from the point of entry to the BCU. This path should be easily securable and ideally would not pass through other clinical areas.⁸

CLINICAL CARE

State-of-the-art critical care can be provided to patients with highly infectious diseases while maintaining staff safety and preventing nosocomial transmission.⁷ Success in this setting is defined both by achieving the desired clinical outcome of patient survival with limited morbidity and by preventing secondary infections among hospital staff and patients.³¹ Critical care planning for high-containment pathogens benefits from a detailed understanding of disease natural history including routes of pathogen transmission, infectious period, and expected time course of organ dysfunction.³²⁻³⁵ Although some of these data are incomplete for emerging or re-emerging pathogens, available information can be used to guide likely resources (staff, space, equipment, supplies) needed to facilitate the desired clinical outcome while maintaining staff safety. A prior knowledge of disease natural history will also assist in predicting the supportive care procedures and interventions that may be required during illness, so that risks associated with these interventions may be mitigated through planning and practice.^{35,36}

Experiences from the care of patients infected with severe acute respiratory syndrome coronavirus (SARS-CoV), middle east respiratory syndrome coronavirus (MERS-CoV), and EBOV emphasize the need for multidisciplinary coordination before, during, and after the care of these patients.^{37,38} **Fig. 2** summarizes some of the essential planning and intervention elements required during this care continuum. In this section, the authors summarize recommendations for effective multidisciplinary team building, staffing, use of PPE, development of clinical protocols, clinical laboratory testing, and training to facilitate the delivery of safe and effective critical care in high-containment environments.

Multidisciplinary Teams

Developing and maintaining multidisciplinary teams is an essential first step to plan for and deliver care to patients infected with high-containment pathogens.³¹ Intensive care teams include critical care physicians, nurses, therapists, consulting providers, pharmacists, dietitians, technicians, ethicists, and administrative staff.^{39,40} Additional close partnerships with hospital administrators, facilities engineers, infection control specialists, waste management experts, laboratory and radiology staff, and others are also required.⁶

Beyond internal stakeholders, external stakeholders should be identified and engaged. External stakeholders might include local, state, and federal public health

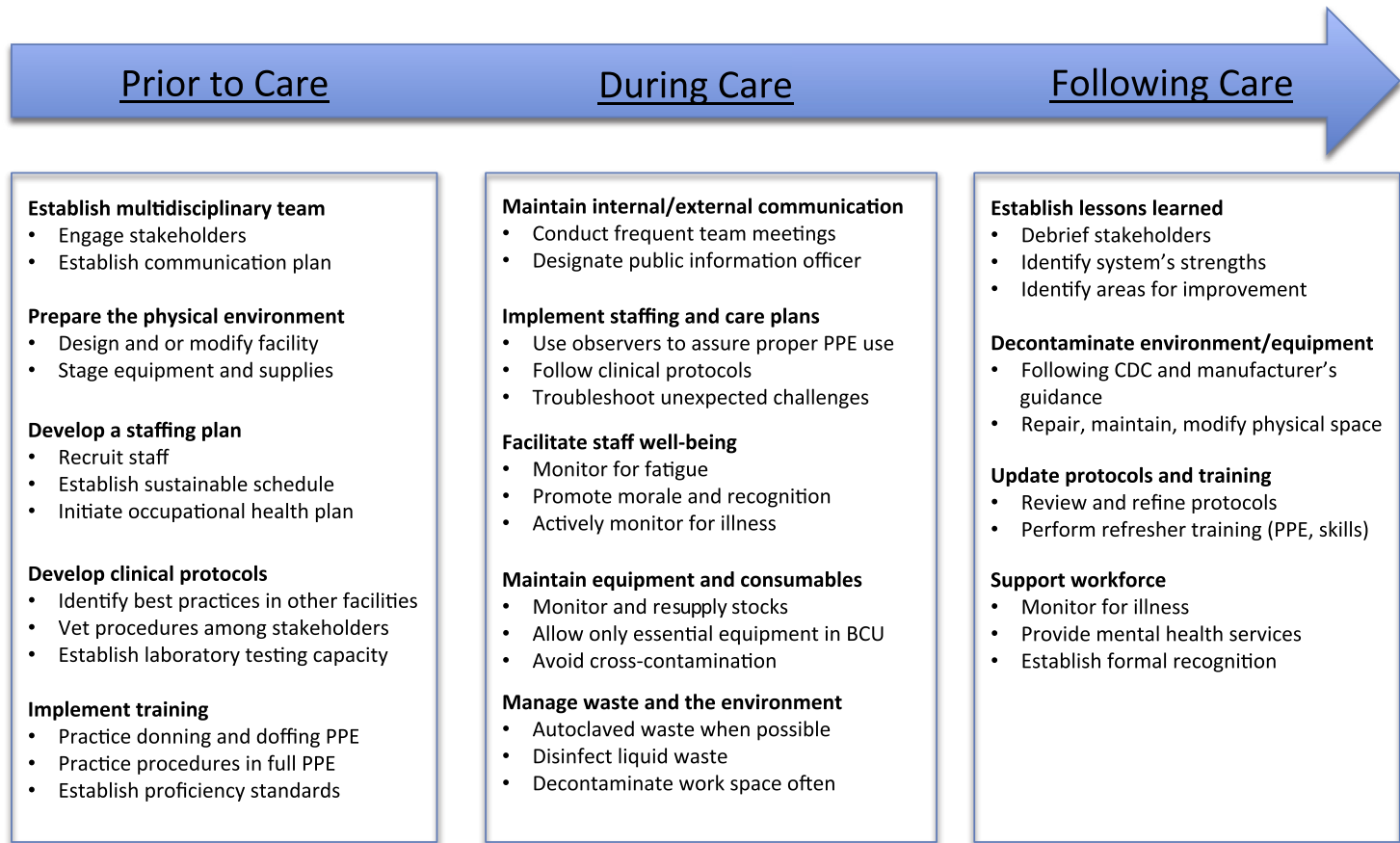


Fig. 2. Timeline of activities caring for patients infected with high-containment pathogens.

officials; local community members and government representatives; medical waste management providers; and emergency medical transportation providers, among others.^{41,42} These stakeholders should be engaged by a designated spokesperson with a clear communication plan and well-defined objectives to facilitate exchange of ideas and expertise, maintain transparency, and provide a platform to troubleshoot operational challenges as they arise. Establishing points of contact and a collaborative approach will allow for standardization of protocols and common training and drilling in advance of patient care.

Staffing

Staffing of BCUs must take into account the need for first-line and backup personnel, the role of consultants, volunteer versus mandatory staff participation, and impact on patient care units elsewhere in the hospital. Staff members likely to provide direct patient care include critical care and infectious diseases physicians, medical and intensive care nurses, respiratory therapists, and radiology technicians.³⁹ Clinical consultants, including nephrologists, neurologists, ophthalmologists, surgeons, and other subspecialists, may also be called on to provide direct patient care.^{43,44} Support staff that are likely to be involved include infection control observers and dedicated laboratory, housekeeping, and administrative staff. The ability of care teams to deliver specialized obstetric, pediatric, or complicated surgical care would need to be defined in advance with appropriate facilities, staffing, and care protocols in place.^{45,46}

Staffing models should take into account excess physical demand placed on health care workers related to prolonged use of PPE^{39,47} and excess emotional demand associated with caring for critically ill patients who may be highly infectious.⁴⁸ During the 2014 to 2016 EVD outbreak, health care workers were on occasion stigmatized in the workplace and in their communities, exacerbating emotional strain.^{39,49} Backup providers should be identified and formalized backup schedules established when possible to provide redundancy if first-line providers become unavailable.

The decision to request volunteer or required staff participation must allow adequate time for staff recruitment, education, and training as staffing levels needed to care for patients infected with high-containment pathogens exceed those of routine care.³¹ A single critically ill patient infected with EBOV cared for at NIH required 4 nurses (2 ICU nurses and 2 medical floor nurses) per 8-hour shift and 2 physicians (1 ICU and 1 infectious diseases physician) per 12-hour shift to participate in direct patient care. Multiple additional support staff per shift was needed.⁴³ The decision to cohort staff to the care of patients on BCUs will also increase staffing demands on other clinical care units.

Personal Protective Equipment

The US Department of Labor Occupational Safety and Health Administration regulates the availability and use of PPE to assure proper fit and function among health care workers (29 CFR 1910.132 and 29 CFR 1910.134). Recommendations for the use of PPE are pathogen dependent with detailed guidance for US health care facilities provided by the CDC.⁵⁰ Specific guidance on the use of PPE for EVD is available.⁵¹ Standard universal precautions mandate hand hygiene on entering and exiting patient rooms; contact precautions recommend use of gloves and gowns; droplet precautions require use of a surgical mask; and airborne precautions require the use of a respirator, such as an N-95 mask or PAPR. Under routine circumstances, compliance with these precautions is less than 100%, and so added emphasis and oversight is needed in the care of patients with highly infectious diseases.

Although some pathogens are thought to primarily spread via large respiratory droplets (eg, influenza virus, MERS-CoV), added precautions, including use of a respirator and eye protection, are needed during aerosol-generating procedures. Procedures associated with increased risk of health care worker exposure include endotracheal intubation and noninvasive positive pressure mechanical ventilation.⁵² Other procedures, including bronchoscopy and high-flow oxygen delivery, may also increase risk.⁵³ External surfaces of PPE and the environment may become contaminated, emphasizing the need for caution in removing PPE and the need for frequent environmental decontamination.^{54,55}

The low infectious dose of EBOV⁵⁶ and prior examples of inadvertent health care worker exposures contributed to the CDC's recommendation that PPE cover all exposed skin and mucous membranes and that trained observers facilitate donning and doffing PPE.³⁷ EBOV has been shown to survive on inanimate surfaces for days to weeks at temperature and humidity observed in hospital settings, further emphasizing the need for caution in removing PPE and frequent environmental decontamination.⁵⁵ Detailed recommendations for environmental decontamination in the care of patients infected with EBOV are available.⁵⁷ Educational videos and training materials on the use of PPE from facilities with experience in the care of EBOV-infected patients are also available online.^{58–60}

Hospitals should take into account the type and amount of PPE required to maintain on hand for training, drills, and actual patient care and how often these supplies need to be replaced or replenished. Shortages of PPE may occur during outbreak situations or during periods of perceived increased risk. Local health officials may guide PPE availability when supplies are limited, with preference given to facilities designated as specialized treatment centers.

Clinical Protocols

Development of written protocols facilitates identification of care processes that might place health care workers at increased risk of exposure. These processes can then be modified to mitigate risks.⁴⁰ Outlining individual steps of otherwise routine procedures allows clinical stakeholders to closely review and vet processes, standardizes expectation among staff, and provides a template for staff training and proficiency testing.

Although few data exist to mandate specific clinical protocols in the care of patients in BCUs, practical suggestions may be derived from best practice among organizations with experience caring for patients with EVD. Practice modifications should take into account risks associated with invasive procedures (blood-borne exposures), aerosol-generating procedures (small or large droplet exposures), and procedures that result in significant environmental contamination (indirect fomite exposures).

Although safe sharp practices are routinely recommended in all care settings (eg, use of smart sharp devices, avoiding recapping needles), additional considerations might further reduce the risk of needle sticks in the care of patients in BCUs. For example, procedures for placement of central venous catheters in EBOV-infected patients may require that all catheters be placed under ultrasound guidance and that only one sharp be placed on the sterile procedural field at a time.

Aerosol-generating procedures in patients with acute respiratory infections have been associated with increased risk of secondary health care worker infection.⁵² Therefore, consideration should be given to modifying routine respiratory care practices, such as limiting the use of noninvasive positive pressure ventilation and avoiding discontinuity of the respiratory circuit during invasive positive-pressure ventilation. Additional research is needed in this area to better guide practice.

Box 2 provides a list of procedures that might benefit from the development of detailed standardized protocols.

Laboratory Testing

Accurate and timely laboratory testing is essential for effective management of patients in BCUs. Common point-of-care tests might include comprehensive chemistry panels, arterial blood gas analyses, complete blood counts with differential, coagulation studies, blood cultures, and microscopy (eg, thick and thin blood smear).⁶¹ A recent survey of the 55 hospitals in the United States designated as ETCs revealed that 87% of responding hospitals planned to provide point-of-care testing within the isolated patient room and 91% had biosafety level 3 laboratory support through their clinical laboratory or jurisdictional public health laboratory.⁶²

Adequate planning and preparation is required to successfully implement laboratory testing in BCUs. This planning must take into account the timing and availability of specific tests and protocols for handling, transporting, and evaluating specimens.⁶³ The CDC provides guidance for the management of clinical specimens when there is a concern for EVD.⁶⁴

Training

Training is required to assure staff familiarity and proficiency in use of PPE, clinical protocols, and waste and environmental management. When caring for patients with EVD, the use of trained observers is recommended to assure proper donning and doffing of PPE. Although high-quality studies are limited, stepwise and orchestrated removal of PPE seems to significantly reduce the risk of self-contamination.⁶⁵ Training may be implemented via online learning, video presentations, in-person didactics, and experiential hands-on sessions. Multiple existing training materials are publically available, including clear and concise videos for the safe donning and doffing of PPE as noted earlier.

It is prudent for staff to practice routine ICU procedures (eg, central venous catheter placement, endotracheal intubation) in simulated care scenarios while wearing full PPE, as PPE may alter manual dexterity as well as tactile, auditory, and visual cues.⁶⁶ Training should familiarize staff with limitations imposed by PPE and provide an opportunity to assess and improve procedural proficiency while prioritizing safety.⁶⁷ Multidisciplinary training for complex tasks, such as delivering advanced cardiac life support in a code blue scenario or extraction of an impaired health care worker, facilitates team building and effective communication and provides a common venue to clearly define processes and parameters of care.

All designated team members should undergo initial training. Given that care of patients infected with high-containment pathogens is likely to be a rare event, recurrent training to maintain baseline proficiency is also prudent and rational. Ideal frequency of

Box 2

Standardized protocols for a high-containment environment

- Invasive procedures (eg, central line placement)
- Advanced respiratory care (eg, endotracheal intubation, invasive mechanical ventilation)
- Renal replacement therapy
- Advanced cardiac life support (ie, code blue response)
- Extraction of an impaired health care worker
- Health care worker infectious exposure (ie, occupational medicine plan)

repeat training has not been established and requires objective, prospective evaluation. While just-in-time training should not be relied on as a primary approach, it does offer the opportunity to rapidly refresh competencies of previously trained providers or to establish baseline competencies of newly recognized providers.

DISCUSSION

During the 2014 to 2016 EVD outbreak, 40% mortality was observed among more than 28,000 Ebola cases in West Africa.⁶⁸ Twenty-seven patients were treated in Europe and the United States. Most of these patients (82%) survived, largely because they received high-quality, supportive critical care.⁷ Planning and delivering care to these patients was labor and resource intensive and took place in a few specialized centers. The cost to establish an Ebola treatment center in the United States has been estimated to be \$1,200,000, whereas the cost to care for a single patient in this setting may be as high as \$30,000 per day.^{69,70} Secondary transmission of EBOV to health care workers in a community hospital in Texas served as a stark reminder of the risks associated with caring for patients with EVD and the need for adequate resources, planning, and training to mitigate risk.⁷¹

Although EVD is the most recent example of a highly infectious disease necessitating ICU care, SARS-CoV and MERS-CoV serve as other important examples. The 2003 to 2004 SARS-CoV epidemic resulted in more than 8000 infections and 700 deaths worldwide. In Toronto, Canada, 375 probable and suspected cases of SARS-CoV occurred, with 72% related to a health care exposure.^{72,73} Similarly, MERS-CoV has resulted in large nosocomial outbreaks in Saudi Arabia and Korea. During an August-September 2015 nosocomial outbreak of MERS-CoV in Saudi Arabia, 63 patients, including 8 health care workers, were admitted to 3 MERS-CoV-designated ICUs. Hospital mortality among these patients was 63%.³⁵

Given existing and emerging serious infectious disease threats, including the ever-looming threat of a severe influenza pandemic, it seems prudent to continue to build capacity to provide high-quality ICU level care for affected patients under safe conditions. An important step forward in this process was the establishment of the National Ebola Training and Education Center (NETEC) through the ASPR and CDC.⁷⁴ This collaboration provides funding to Emory University, University of Nebraska, and Bellevue Hospital Center, all centers with a successful track record of caring for patients with EVD, to train and prepare other US health care facilities for emerging threats. NETEC will work with the other federally funded RESPTCS as well as the NIH Special Clinical Studies Unit, to advance the clinical science behind high-containment care and to ensure the safety of patients, health care workers, and their surrounding communities.

Hospitals must take stock of existing capacity to care for patients with highly infectious diseases. Although not all facilities will be called on to provide ICU-level care, all hospitals must have protocols, plans, and training in place to identify, isolate, and provide short-term care for patients infected with high-containment pathogens. Hospitals designated to provide definitive ICU care must maintain staff and facility readiness through ongoing training and pursuit of best practices. Improved coordination and communication among existing centers as well as with local, state, and federal health officials will further the goal of establishing a sustainable infrastructure to address the persistent threat of severe infectious disease outbreaks.

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REFERENCES

1. Connor MJ Jr, Kraft C, Mehta AK, et al. Successful delivery of RRT in Ebola virus disease. *J Am Soc Nephrol* 2015;26:31–7.
2. Johnson DW, Sullivan JN, Piquette CA, et al. Lessons learned: critical care management of patients with Ebola in the United States. *Crit Care Med* 2015;43:1157–64.
3. Smith PW, Anderson AO, Christopher GW, et al. Designing a biocontainment unit to care for patients with serious communicable diseases: a consensus statement. *Biosecur Bioterror* 2006;4:351–65.
4. Interim guidance for preparing Ebola treatment centers. Available at: <http://www.cdc.gov/vhf/ebola/healthcare-us/preparing/treatment-centers.html>. Accessed February 2, 2017.
5. HHS selects nine regional Ebola and other special pathogen treatment centers. Available at: <http://www.hhs.gov/about/news/2015/06/12/hhs-selects-nine-regional-ebola-and-other-special-pathogen-treatment-centers.html>. Accessed February 2, 2017.
6. Garibaldi BT, Kelen GD, Brower RG, et al. The creation of a biocontainment unit at a Tertiary Care Hospital. The Johns Hopkins Medicine Experience. *Ann Am Thorac Soc* 2016;13:600–8.
7. Uyeki TM, Mehta AK, Davey RT Jr, et al, Working Group of the U.S.–European Clinical Network on Clinical Management of Ebola Virus Disease Patients in the U.S. and Europe. Clinical Management of Ebola Virus Disease in the United States and Europe. *N Engl J Med* 2016;374:636–46.
8. Bannister B, Puro V, Fusco FM, et al. Framework for the design and operation of high-level isolation units: consensus of the European Network of Infectious Diseases. *Lancet Infect Dis* 2009;9:45–56.
9. Manual for the care and management of patients in Ebola care units/community care centres: interim emergency guidance. Available at: <http://www.who.int/csr/resources/publications/ebola/patient-care-CCUs/en/>. Accessed February 2, 2017.
10. Kortepeter MG, Kwon EH, Hewlett AL, et al. Containment care units for managing patients with highly hazardous infectious diseases: a concept whose time has come. *J Infect Dis* 2016;214:S137–41.
11. ASHRAE position document on airborne infectious diseases. Available at: <https://www.ashrae.org/about-ashrae/position-documents>. Accessed February 2, 2017.
12. Boyce JM, Havill NL, Moore BA. Terminal decontamination of patient rooms using an automated mobile UV light unit. *Infect Control Hosp Epidemiol* 2011;32:737–42.
13. Weber DJ, Rutala WA, Anderson DJ, et al. Effectiveness of ultraviolet devices and hydrogen peroxide systems for terminal room decontamination: focus on clinical trials. *Am J Infect Control* 2016;44:e77–84.
14. Mollura DJ, Palmore TN, Folio LR, et al. Radiology preparedness in Ebola virus disease: guidelines and challenges for disinfection of medical imaging equipment for the protection of staff and patients. *Radiology* 2015;275:538–44.
15. Recommendations for safely performing acute hemodialysis in Patients with Ebola virus disease (EVD) in U.S. hospitals. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/hospitals/acute-hemodialysis.html>. Accessed February 2, 2017.

16. Safe handling, treatment, transport and disposal of Ebola-contaminated waste. Available at: https://www.osha.gov/Publications/OSHA_FS-3766.pdf. Accessed February 2, 2017.
17. Ebola-associated waste management. Available at: <http://www.cdc.gov/vhf/ebola/healthcare-us/cleaning/waste-management.html>. Accessed February 2, 2017.
18. Lowe JJ, Gibbs SG, Schwedhelm SS, et al. Nebraska Biocontainment Unit perspective on disposal of Ebola medical waste. *Am J Infect Control* 2014;42:1256–7.
19. Lowe JJ, Olinger PL, Gibbs SG, et al. Environmental infection control considerations for Ebola. *Am J Infect Control* 2015;43:747–9.
20. Transporting infectious substances safely. US Department of Transportation. Pipeline and Hazardous Materials Safety Administration. Available at: http://www.phmsa.dot.gov/staticfiles/PHMSA/DownloadableFiles/Files/Transporting_Infectious_Substances_brochure.pdf. Accessed February 2, 2017.
21. Garibaldi BT, Reimers M, Ernst N, et al. Validation of autoclave protocols for successful decontamination of category a medical waste generated from care of patients with serious communicable diseases. *J Clin Microbiol* 2017;55:545–51.
22. Hewlett AL, Varkey JB, Smith PW, et al. Ebola virus disease: preparedness and infection control lessons learned from two biocontainment units. *Curr Opin Infect Dis* 2015;28:343–8.
23. Herstein JJ, Biddinger PD, Kraft CS, et al. Current capabilities and capacity of Ebola treatment centers in the United States. *Infect Control Hosp Epidemiol* 2016;37:313–8.
24. Guidance on air medical transport (AMT) for patients with Ebola virus disease (EVD). Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/emergency-services/air-medical-transport.html>. Accessed February 2, 2017.
25. Christopher GW, Eitzen EM Jr. Air evacuation under high-level biosafety containment: the aeromedical isolation team. *Emerg Infect Dis* 1999;5:241–6.
26. Withers MR, Christopher GW. Aeromedical evacuation of biological warfare casualties: a treatise on infectious diseases on aircraft. *Mil Med* 2000;165:1–21.
27. Isakov A, Jamison A, Miles W, et al. Safe management of patients with serious communicable diseases: recent experience with Ebola virus. *Ann Intern Med* 2014;161:829–30.
28. Isakov A, Miles W, Gibbs S, et al. Transport and management of patients with confirmed or suspected Ebola virus disease. *Ann Emerg Med* 2015;66:297–305.
29. Lowe JJ, Jelden KC, Schenarts PJ, et al. Considerations for safe EMS transport of patients infected with Ebola virus. *Prehosp Emerg Care* 2015;19:179–83.
30. Interim guidance for emergency medical services (EMS) systems and 9-1-1 public safety answering points (PSAPs) for management of patients under investigation (PUIs) for Ebola virus disease (EVD) in the United States. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/emergency-services/ems-systems.html>. Accessed February 2, 2017.
31. Decker BK, Sevransky JE, Barrett K, et al. Preparing for critical care services to patients with Ebola. *Ann Intern Med* 2014;161:831–2.
32. de Wit E, van Doremalen N, Falzarano D, et al. SARS and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol* 2016;14:523–34.
33. Yildirimak T, Tulek N, Bulut C. Crimean-Congo haemorrhagic fever: transmission to visitors and healthcare workers. *Infection* 2016;44:687–9.
34. Baseler L, Chertow DS, Johnson KM, et al. The pathogenesis of Ebola virus disease. *Annu Rev Pathol* 2016;12:387–418.

35. Al-Dorzi HM, Aldawood AS, Khan R, et al. The critical care response to a hospital outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) infection: an observational study. *Ann Intensive Care* 2016;6:101.
36. Sampathkumar P, Temesgen Z, Smith TF, et al. SARS: epidemiology, clinical presentation, management, and infection control measures. *Mayo Clin Proc* 2003;78:882–90.
37. Cummings KJ, Choi MJ, Esswein EJ, et al. Addressing infection prevention and control in the first U.S. community hospital to care for patients with Ebola virus disease: context for national recommendations and future strategies. *Ann Intern Med* 2016;165:41–9.
38. Booth CM, Stewart TE. Severe acute respiratory syndrome and critical care medicine: the Toronto experience. *Crit Care Med* 2005;33:S53–60.
39. Johnson SS, Barranta N, Chertow D. Ebola at the National Institutes of Health: perspectives from critical care nurses. *AACN Adv Crit Care* 2015;26:262–7.
40. Torabi-Parizi P, Davey RT Jr, Suffredini AF, et al. Ethical and practical considerations in providing critical care to patients with Ebola virus disease. *Chest* 2015;147:1460–6.
41. Kabore HJ, Desamu-Thorpe R, Jean-Charles L, et al. Monitoring of persons with risk for exposure to Ebola virus - United States, November 3, 2014–December 27, 2015. *MMWR Morb Mortal Wkly Rep* 2016;65:1401–4.
42. Zucker HA, Whalen D, Raske KE. Lessons from New York State's preparedness efforts for Ebola. *Disaster Med Public Health Prep* 2016;10:1–6.
43. Chertow DS, Nath A, Suffredini AF, et al. Severe meningoencephalitis in a case of Ebola virus disease: a case report. *Ann Intern Med* 2016;165:301–4.
44. Sueblinvong V, Johnson DW, Weinstein GL, et al. Critical care for multiple organ failure secondary to Ebola virus disease in the United States. *Crit Care Med* 2015;43:2066–75.
45. DeBiasi RL, Song X, Cato K, et al, CNHS Ebola Response Task Force. Preparedness, evaluation, and care of pediatric patients under investigation for Ebola virus disease: experience from a pediatric designated care facility. *J Pediatr Infect Dis Soc* 2016;5:68–75.
46. Kamali A, Jamieson DJ, Kpaduwa J, et al. Pregnancy, labor, and delivery after Ebola virus disease and implications for infection control in obstetric services, United States. *Emerg Infect Dis* 2016;22:1156–61.
47. Chertow DS, Kleine C, Edwards JK, et al. Ebola virus disease in West Africa - clinical manifestations and management. *N Engl J Med* 2014;371:2054–7.
48. Gershon R, Dernehl LA, Nwankwo E, et al. Experiences and psychosocial impact of West Africa Ebola deployment on US health care volunteers. *PLoS Curr* 2016;8:1–29.
49. Lewis JD, Enfield KB, Perl TM, et al. Preparedness planning and care of patients under investigation for or with Ebola virus disease: a survey of physicians in North America. *Am J Infect Control* 2017;45:65–8.
50. 2007 guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Available at: <https://www.cdc.gov/hai/pdfs/isolation2007.pdf>. Accessed February 2, 2017.
51. Infection prevention and control recommendations for hospitalized patients under investigation (PUIs) for Ebola virus disease (EVD) in U.S. hospitals. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/hospitals/infection-control.html>. Accessed February 2, 2017.

52. Tran K, Cimon K, Severn M, et al. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One* 2012;7:e35797.
53. Thompson KA, Pappachan JV, Bennett AM, et al, EASE Study Consortium. Influenza aerosols in UK hospitals during the H1N1 (2009) pandemic—the risk of aerosol generation during medical procedures. *PLoS One* 2013;8:e56278.
54. Kim SH, Chang SY, Sung M, et al. Extensive viable Middle East respiratory syndrome (MERS) coronavirus contamination in air and surrounding environment in MERS isolation wards. *Clin Infect Dis* 2016;63:363–9.
55. Fischer R, Judson S, Miazgowiec K, et al. Ebola virus stability on surfaces and in fluids in simulated outbreak environments. *Emerg Infect Dis* 2015;21:1243–6.
56. Franz DR, Jahrling PB, Friedlander AM, et al. Clinical recognition and management of patients exposed to biological warfare agents. *JAMA* 1997;278:399–411.
57. Interim guidance for environmental infection control in hospitals for Ebola virus. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/cleaning/hospitals.html>. Accessed February 2, 2017.
58. Personal protective equipment (PPE) training. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/ppe/training.html>. Accessed February 2, 2017.
59. Ebola courses for the general public & clinicians. Available at: <http://www.nebraskamed.com/biocontainment-unit/ebola>. Accessed February 2, 2017.
60. Ebola preparedness protocols. Available at: <http://www.emoryhealthcare.org/ebola-protocol>. Accessed February 2, 2017.
61. Hill CE, Burd EM, Kraft CS, et al. Laboratory test support for Ebola patients within a high-containment facility. *Lab Med* 2014;45:e109–11.
62. Jelden KC, Iwen PC, Herstein JJ, et al. U.S. Ebola treatment center clinical laboratory support. *J Clin Microbiol* 2016;54:1031–5.
63. Iwen PC, Garrett JL, Gibbs SG, et al. An integrated approach to laboratory testing for patients with Ebola virus disease. *Lab Med* 2014;45:e146–51.
64. Guidance for U.S. laboratories for managing and testing routine clinical specimens when there is a concern about Ebola virus disease. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/laboratories/safe-specimen-management.html>. Accessed February 2, 2017.
65. Verbeek JH, Ijaz S, Mischke C, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. *Cochrane Database Syst Rev* 2016;(4):CD011621.
66. Grillet G, Marjanovic N, Diverrez JM, et al. Intensive care medical procedures are more complicated, more stressful, and less comfortable with Ebola personal protective equipment: a simulation study. *J Infect* 2015;71:703–6.
67. Wiechmann W, Toohey S, Majestic C, et al. Intubating Ebola patients: technical limitations of extensive personal protective equipment. *West J Emerg Med* 2015;16:965.
68. World Health Organization. Situation report. Ebola virus disease 10 June 2016. Available at: Interim guidance for environmental infection control in hospitals for Ebola virus. Available at: <https://www.cdc.gov/vhf/ebola/healthcare-us/cleaning/hospitals.html>. Accessed May 1, 2017.
69. Herstein JJ, Biddinger PD, Kraft CS, et al. Initial costs of Ebola treatment centers in the United States. *Emerg Infect Dis* 2016;22:350–2.
70. Sun LH. Cost to treat Ebola in the U.S.: \$1.16 million for 2 patients. Available at: https://www.washingtonpost.com/news/post-nation/wp/2014/11/18/cost-to-treat-ebola-in-the-u-s-1-16-million-for-2-patients/?utm_term=.894ccd9d6105. Accessed May 1, 2017.

71. Wallis L. First U.S. nurse to contract Ebola sues Texas health resources. *Am J Nurs* 2015;115:16.
72. Skowronski DM, Petric M, Daly P, et al. Coordinated response to SARS, Vancouver, Canada. *Emerg Infect Dis* 2006;12:155–8.
73. McDonald LC, Simor AE, Su IJ, et al. SARS in healthcare facilities, Toronto and Taiwan. *Emerg Infect Dis* 2004;10:777–81.
74. National Ebola Training and Education Center (NETEC). Available at: <http://netec.org/>. Accessed February 2, 2017.