Editorial

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Laboratory preparedness to face infectious outbreaks. Ebola and beyond

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Viral hemorrhagic fever (VHF), a term used to characterize a group of conditions caused by a number of different virus families, is frequently associated with severe multiorgan syndrome, up to death. The Ebola virus disease (EVD), previously known as Ebola hemorrhagic fever, is a member of this family and is responsible for a severe, an often fatal disease in humans, with a mean case fatality around 50% (7470 probable, confirmed and suspected cases as of October 1, 2014, with more than 3400 associated deaths) [1]. There is no effective treatment at present, but human vaccine trials have been promptly started. Although humans are not considered natural reservoirs for this and other viruses causing VHFs, contamination is possible from direct contact with animal sources, especially with blood and bodily fluids of infected animals, such as chimpanzees, gorillas, bats, monkeys, forest antelope and porcupines [2]. The viruses can then spread by human-to-human transmission via direct contact (through skin lesions or mucous membranes) with blood, secretions and bodily fluids of infected people, as well as by contaminated surfaces and materials. There is no evidence so far that the virus can be transmitted either by air or by casual contact [2]. Although science and medicine have long been challenged by VHFs, a sudden epidemic in the early 2014 has evolved into the largest, most severe and most complex outbreak since this pathogen was first discovered in 1976 [3]. The three most affected countries (i.e., Guinea, Liberia and Sierra Leone) are facing enormous difficulties in stopping transmission and providing patient care. Thus, the epidemic seems out of control, translating into a major challenge around the globe for potential expansion to other parts of Africa and beyond, due to the possibility that symptomatic persons boarding planes and unknowingly carrying the virus to other countries [4, 5].

Besides the huge efforts being put in place for outbreak control and patient care, the preparedness of the laboratory community is thus challenged by another natural hazard [6]. Indeed, the laboratory environment is only marginally involved in the direct diagnosis of EVD, which is reserved to highly specialized centers in most countries (i.e., typically Biosafety Level-4 laboratories), but may still be engaged in routine testing of samples from infected patients, especially from those who are considered 'suspect' EVD cases. It is thus theoretically possible that healthcare staff, including laboratory personnel, may come into contact and become regrettably infected while managing patients' specimens. This should be seen as a tangible threat, considering that the incubation period of the EVD is typically comprised between 2 and 21 days and blood samples usually begin to test positive on polymerase chain reaction (PCR) only 24 h before the onset of the symptoms.

In order to prevent any potential occasion of contamination and/or infection, clinical laboratories should adopt restrictive measures to handle biological materials, which are potentially contaminated with Ebola virus. Two important documents were recently made available by the World Health Organization (WHO; Infection prevention and control guidance for care of patients in healthcare settings, with focus on Ebola) [7] and by the Centers for Disease Control and Prevention (CDC; Interim guidance for specimen collection, transport, testing, and submission for persons under investigation for Ebola virus disease in the United States) [8, 9], the contents of which are briefly reviewed below (Table 1). Indeed, the two key issues entail the use of technological supports that may be effective to eliminate or limit the exposure to blood-borne pathogens, along with the adoption of appropriate (commercially available) and safe medical devices planned to eliminate or minimize occupational exposure. It is also clearly stated that phlebotomy and laboratory testing must be limited to the minimum necessary for essential diagnostic evaluation and patient care.

As specifically regards sample collection and shipment, it is recommended that phlebotomists should wear

Table 1 Summary of suggestions and recommendations to eliminate or minimize occupational exposure to Ebola virus (potentially)-bearing samples in clinical laboratories.

1. Sample collection:
a. Phlebotomists should always wear personal protective equipment (PPE)
b. Use closed collection (i.e., vacuum) systems
2. Sample transportation
a. Accurately identify samples and keep them separated from other samples
b. Place samples in durable, leak-proof secondary containers
c. Avoid pneumatic tube systems
3. Sample preparation and analysis
a. Limit phlebotomy and laboratory testing to the minimum necessary for essential diagnostic evaluation and patient care
b. The laboratory personnel should wear PPE
c. Manage samples under cabinets
d. Avoid manual pipetting and open centrifugation of samples
e. Manufacturer installed safety features for laboratory instruments should be used
f. Use disinfectants with higher potency for decontamination
g. Instrumental decontamination protocols appropriate for enveloped viruses are advisable
4. Sample waste
a. Eliminated in leak-proof containment or through sewerage system via a sealed drainage system
b. Discard as regulated medical waste

gloves, water-resistant gowns, full face shield or goggles, and masks to cover nose and mouth. Adjunctive personal protective equipment (PPE) (i.e., double gloving, overshoes or particulate respirators) may be required in certain situations, such as in the presence of copious amounts of body fluids in the environment. The specimens should be preferably collected using closed (i.e., vacuum) systems, must be accurately identified and kept separated from other samples so that they can be clearly recognized upon arrival in the laboratory. Diagnostic specimens should also be placed in a durable, leak-proof secondary container during transportation, avoiding pneumatic tube systems in order to limit the risk of breakage or leaks.

As regards the laboratory staff whose duty it is to test specimens from suspected EVD cases, it is recommended to wear gloves, water-resistant gowns, full face shield or goggles, and masks to cover all of the nose and mouth. As an added precaution, a certified class II biosafety cabinet or plexiglass splash guard usage is advocated to protect skin and mucous membranes when manipulating potentially infected biological material. No procedure should be performed on an open bench and activities, such as manual pipetting, and a centrifugation of open tubes should be avoided to prevent the generation of fine aerosols. Any contact between soiled items and the face area must be avoided when removing PPE, which should be safely discarded and not reused. The specimens should then be placed in clearly labeled, non-glass, leak-proof containers, and delivered directly to the designated area of testing. All manufacturer installed safety features for laboratory instruments should be used during sample analysis. These typically include operating with cap piercing (whenever possible), with covers or ports closed. Importantly, no specific mention to the exclusive use of point of care testing (POCT) is made in both WHO and CDC recommendations [7, 8]. In case of accidental contamination, a broad range of hospital disinfectants can be used, since enveloped viruses, such as Ebola, are more vulnerable to these agents than other pathogens (Figure 1). However, the use of disinfectants with higher potency than normally required for enveloped viruses (i.e., 3% acetic acid, 1% glutaraldehyde, alcohol-based products, calcium hypochlorite and dilutions from 1:10 to 1:100 of 5.25% sodium hypochlorite) may be considered as adjunctive precautions to disinfect potentially Ebola-contaminated materials [10]. Instrument decontamination protocols appropriate for enveloped viruses, such as HIV, influenza, or hepatitis C, are also encouraged. In particular, disinfection as recommended by the manufacturer or using sodium hypochlorite (1:100 dilution of household bleach) has recently been advocated by the Public Health Agency of Canada after diagnostic samples of (suspected) EDV cases have been processed [10]. This essentially implies that blood specimens should preferably be loaded alone in the analyzer, and no other specimens should be loaded until disinfection has been completed. Particular concern emerges from the treatment of waste generated during laboratory testing. This should preferably be placed in leak-proof containment and only discarded as regulated medical waste. Alternatively, the potentially contaminated drainage from machines used to process blood, serum or other body fluids should either

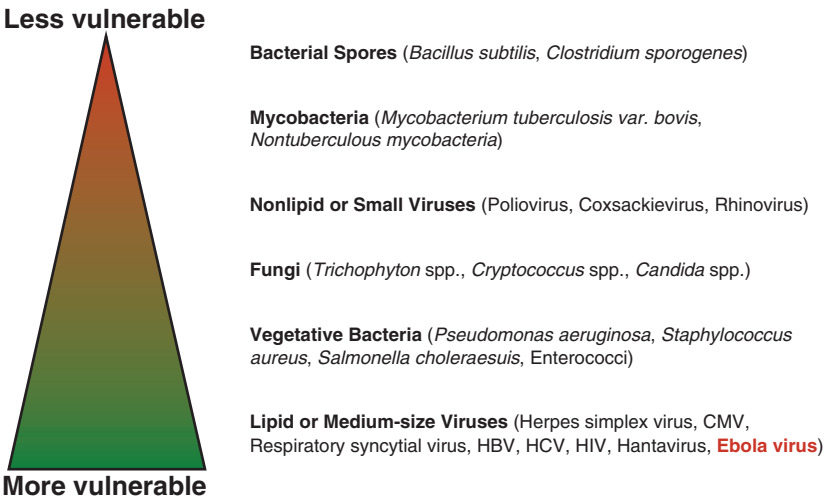

Figure 1 Order of resistance to germicidal chemicals.

pass into the sewerage system via a sealed drainage system or into a container via a sealed drainage system [11].

On August 8, the WHO has declared the West Africa Ebola crisis as a 'Public Health Emergency of International Concern (PHEIC) under the International Health Regulations (IHR)' [12]. Despite mindful efforts to safeguard operator safety, laboratory professionals who handle specimens from patients under investigation for EVD remain at risk of being infected as do the other healthcare staff [13]. Although we would all agree that each and every specimen received in the laboratory should be managed as if it is potentially infected, specific focus should be placed to eliminate or minimize the occupational risk of exposure to diagnostic samples of patients with known or suspected EVD or other VHFs.

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