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MAJOR ARTICLE

Assessing Viral Transfer During Doffing of Ebola-Level Personal Protective Equipment in a Biocontainment Unit

Lisa M. Casanova,[1] Kimberly Erukunuakpor,[1] Colleen S. Kraft,[2] Joel M. Mumma,[3] Francis T. Durso,[3] Ashley N. Ferguson,[3] Christina L. Gipson,[3] Victoria L. Walsh,[4] Craig Zimring,[5] Jennifer DuBose,[5] and Jesse T. Jacob[4]; for the Centers for Disease Control and Prevention Epicenters Program, Division of Healthcare Quality Promotion

[1]Division of Environmental Health, School of Public Health, Georgia State University, [2]Department of Pathology and Laboratory Medicine, Emory University, [3]School of Psychology, Georgia Institute of Technology, [4]Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, and [5]School of Architecture, Georgia Institute of Technology, Atlanta

(See the Major Article by Mumma et al on pages 950–8.)

Background. Personal protective equipment (PPE) protects healthcare workers (HCWs) caring for patients with Ebola virus disease (EVD), and PPE doffing is a critical point for preventing viral self-contamination. We assessed contamination of skin, gloves, and scrubs after doffing Ebola-level PPE contaminated with surrogate viruses: bacteriophages MS2 and Φ6.

Methods. In a medical biocontainment unit, HCWs (n = 10) experienced in EVD care donned and doffed PPE following unit protocols that incorporate trained observer guidance and alcohol-based hand rub (ABHR). A mixture of Φ6 (enveloped), MS2 (nonenveloped), and fluorescent marker was applied to 4 PPE sites, approximating body fluid viral load (Φ6, 10^5; MS2, 10^6). They performed a patient care task, then doffed. Inner gloves, face, hands, and scrubs were sampled for virus, as were environmental sites with visible fluorescent marker.

Results. Among 10 HCWs there was no Φ6 transfer to inner gloves, hands, or face; 1 participant had Φ6 on scrubs at low levels (1.4×10^2). MS2 transfer (range, 10^1–10^6) was observed to scrubs (n = 2), hands (n = 1), and inner gloves (n = 7), where it was highest. Most (n = 8) had only 1 positive site. Environmental samples with visible fluorescent marker (n = 21) were negative.

Conclusions. Among experienced HCWs, structured, observed doffing using ABHR protected against hand contamination with enveloped virus. Nonenveloped virus was infrequent on hands and scrubs but common on inner gloves, suggesting that inner gloves, but not necessarily ABHR, protect against hand contamination. Optimizing doffing protocols to protect against all types of viruses may require reinforcing careful handling of scrubs and good glove/hand hygiene with effective agents.

Keywords. Ebola; personal protective equipment; occupational health; virus.

The 2014–2015 outbreak of Ebola virus disease (EVD) placed healthcare workers (HCWs) at high risk for acquiring EVD during patient care [1]. The potential for exposures to high volumes of bodily fluids containing high titers of virus [2, 3], and the lack of effective treatment options, leaves personal protective equipment (PPE) as the crucial barrier to HCW exposure while caring for those with EVD [4]. These high-risk, high-consequence exposures are mitigated through the use of multiple, layered barrier precautions [5, 6], including full body, fluid-resistant suits, fluid-resistant aprons or gowns, fluid-resistant footwear, N95 respirators or powered air-purifying respirators (PAPRs), inner and outer gloves, and face shields. While these extensive barrier precautions can prevent skin and mucous membrane contamination during patient care, effective barrier PPE can be contaminated with body fluids and infectious virus after a patient care encounter, and PPE items are handled during the doffing process. As previous studies assessing standard PPE have shown [7–10], PPE can become contaminated with infectious agents, making the doffing process a potential critical control point for preventing body fluid exposures and resulting viral self-contamination for the wearer [11].

Previous studies have found that following recommended PPE doffing methods and sequences is challenging, and practices are variable among HCW while using standard contact or respiratory isolation PPE [12, 13]. With complex EVD PPE, there are more numerous and high-stakes opportunities for error during the doffing process that may result in self-contamination. Detailed, structured protocols have been designed for doffing complex EVD PPE [5], with the goal of reducing the potential for error. An important error-reduction component is the presence of a trained observer (TO) who verbally guides the PPE wearer through a detailed doffing sequence. The TO's responsibilities include visually assessing PPE integrity and giving verbal instructions for what to do at each doffing step, how to touch and handle PPE items, and when to perform hand hygiene.

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Correspondence: L. M. Casanova, Georgia State University, PO Box 3995, Atlanta, GA 30303 (lcasanova@gsu.edu).

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EVD PPE doffing is a complex skill that most HCWs will rarely, if ever, perform outside of a training setting, yet when the skill is required, it is in a high-risk, high-stress patient care situation. This makes controlled observation for evidence-based evaluation and optimization of the doffing process extremely challenging. Simulation is playing an increasingly important role in training providers in clinical skills, and can also be applied to Ebola preparedness [14]. Simulation can be used to allow HCWs to practice the donning and doffing process, as well as patient care, while wearing EVD PPE in an environment that is not high-stress. It is possible to simulate not only the doffing process, but the process of self-contamination during doffing of contaminated PPE, using harmless surrogate viruses.

By incorporating close observation and artificial contamination with surrogate viruses, simulations can be designed to evaluate the effectiveness of the structured, observed doffing process in preventing errors and viral self-contamination. This approach has been used to determine the frequency and levels of self-contamination with viruses during doffing with standard PPE [7, 15] and in small groups of HCWs using EVD PPE [16, 17]. However, training, patient care experience, PPE selection, and PPE doffing protocols can vary across healthcare facilities. The artificial contamination/simulation approach can be expanded to assess doffing across a range of facilities with different doffing protocols, PPE elements, and levels of training and experience. The goal of this research was to assess viral self-contamination of skin, gloves, and scrubs during an EVD PPE doffing protocol performed by HCWs who have experience caring for EVD patients, using PPE artificially contaminated with 2 surrogate viruses: MS2 (a surrogate for nonenveloped human viruses) and bacteriophage Φ6 (a surrogate for enveloped viruses such as Ebola).

METHODS

All protocols were approved by the Emory University Institutional Review Board. Participants were members of the patient care team of a specialized biocontainment unit at a large tertiary care academic medical center. HCWs were excluded as team members if they were pregnant, immunocompromised, trainees, allergic to latex, or had nonintact skin on their hands or face. All participants had extensive training in the biocontainment unit in the donning, doffing, and use of EVD-specific PPE, and most had direct patient care experience with patients with confirmed EVD. All participants in this study, as a requirement of being a member of the biocontainment unit patient care team, had undergone quarterly training that included evaluation of their ability to don and doff their PPE.

The TO for all simulations was a physician who had provided direct care to patients with confirmed EVD. The TO had donned and doffed EVD PPE and observed the donning and doffing process for other providers multiple times during care of patients with EVD. The PPE doffing protocol used by the facility for care of patients with suspected or confirmed EVD (Table 1) was used in simulations.

Simulations took place in the anteroom and patient room of the biocontainment unit used for patient care, beginning with the donning process. First, the participant changed into disposable scrub shirt and pants and fluid-resistant shoes in the locker room, and then moved to the anteroom of the biocontainment unit. The TO then verbally guided them through the donning process using the biocontainment unit's checklist. When finished the participant wore a Tyvek suit, fluid-resistant apron, 1 pair of short inner gloves taped to the wrist of the Tyvek suit, 1 pair of long outer gloves covering the wrist completely, a PAPR, a PAPR hood, and fluid-resistant shoe covers. After donning of PPE, a mixture of MS2 and Φ6 suspended in phosphate-buffered saline containing a fluorescent tracer (GloGerm, Moab, Utah) was applied to 4 sites: the palm of the dominant hand, the shoulder of the gown opposite the dominant hand, the top side of the PAPR opposite the dominant hand, and the toe of the shoe cover opposite the dominant hand. A total of 25 μL was applied to each site in 5 drops of 5 μL each to simulate small droplet body fluid exposure that the HCW may not be aware of [15, 16]. Sites to be contaminated were chosen after consulting with clinicians with EVD patient care experience, who had observed PPE contamination in the patient care setting. The mean virus titer applied to each site in 25 μL was 2.3×10^5 for

Table 1. Ebola-Level Personal Protective Equipment Doffing Protocol Used at the Facility for Care of Suspected or Confirmed Ebola, and for All Simulations

Location	Step	Required Action
Patient room	Step 1	Remove apron
Patient room	Step 2	Remove 1 bootie, then step onto chemical mat
Patient room	Step 3	Remove other bootie, then step onto chemical mat
Patient room	Step 4	Sanitize gloves
Patient room	Step 5	Remove outer gloves using the beaking method
Patient room	Step 6	Sanitize inner gloves
Patient room	Step 7	Remove tape
Patient room	Step 8	Sanitize inner gloves
Patient room	Step 9	Remove biohazard coverall
Patient room	Step 10	Sanitize inner gloves
Patient room	Step 11	Enter anteroom
Anteroom	Step 12	Remove powered air-purifying respirator hood
Anteroom	Step 13	Sanitize inner gloves
Anteroom	Step 14	Remove inner gloves using the beaking method
Anteroom	Step 15	Wash hands with soap and water
Anteroom	Step 16	Remove belt, battery, and motor

All steps indicating "sanitize" use alcohol-based hand rub.

Φ6 and 5.70×10^6 for MS2, based on reports of viral load in body fluids during acute phases of EVD [2, 18, 19], as well as nonenveloped viruses such as norovirus that are shed in high titers in body fluids. There was no statistically significant difference between the inoculum of Φ6 and MS2 applied to each site ($P = .19$). Both participant and observer were instructed to close their eyes during application so they were not aware of the exact location of contamination.

To simulate actual tasks done while wearing PPE, the HCW then entered the patient room and emptied a urinary catheter bag attached to a mannequin, disposing of the contents in the toilet according to the biocontainment unit's protocol. The HCW then cleaned the room according to the biocontainment unit's standard protocols, including using disinfectant wipes on surfaces and mopping floors. After room cleaning, they began the PPE doffing process, which started in the patient room and proceeded through a door into the anteroom for the final step of removing the PAPR hood and PAPR. The TO verbally and visually (with gestures) guided them through the doffing process using the checklist in Table 1. Hand hygiene was frequently performed using alcohol-based hand rub (ABHR) except for step 15, where soap and water is used.

At the doffing step when inner gloves were removed (step 14), they were collected for sampling. The facility's protocol uses the "beaking" method for removing gloves, a glove-in-glove technique that results in the gloves coming off one inside the other, so gloves were sampled together. The entire simulation process was video recorded from multiple angles using 4 stationary cameras and 1 hand-held camera for human factors analysis (Mumma et al, manuscript in preparation).

After the doffing process concluded (step 16), 3 sites were examined under ultraviolet light for fluorescent tracer and sampled for virus: bare hands, face, and scrubs worn under PPE. The face was swabbed on each cheek for virus using a polyester swab dipped in eluent. Hands were sampled for virus using whole-hand sampling [20]. Scrubs were collected for sampling by complete immersion in eluent after removal [16]. Samples were placed on ice and immediately transported back to the laboratory for analysis using previously described methods [21]. High-touch surfaces in the patient room and doffing area were examined under ultraviolet light for the presence of fluorescent tracer, including door handles, toilet handles, and bedrails. Any sites that appeared to have any fluorescent tracer were sampled using macrofoam swabs. A 1-cm^2 surface surrounding the tracer was defined and swabbed 10 times in a back-and-forth motion. Swabs were eluted in 1.5% beef extract containing 0.1% Tween 80 by shaking at 100 rpm for 20 minutes. All samples were assayed for MS2 and Φ6 using the single agar layer assay. Virus recovered from each site was expressed as plaque-forming units (PFU).

RESULTS

A total of 10 HCWs participated (9 registered nurses and 1 physician). Participants were 60% female, with at least 3 years of healthcare experience (range, 3 to >25 years); most (n = 9) had donned and doffed EVD PPE during care of a confirmed EVD patient. All had >1 year of training with EVD PPE, and 9 of 10 had trained within the last 4 months prior to participation.

No detectable transfer of enveloped bacteriophage Φ6 to inner gloves, hands, or face for any participants was observed. There was transfer of Φ6 to scrubs for 1 participant (~140 PFU, 0.002% of original inoculum). Detectable transfer of nonenveloped bacteriophage MS2 (Table 2) was observed in 7 of 10 HCWs. Sites of contamination with MS2 included scrubs, hands, and inner gloves, but not face. MS2 was detected on the inner gloves for most participants (7/10; mean, 8.8×10^5 PFU; 7% of original inoculum), and on scrubs (2/10; mean, 1.5×10^3 PFU; 0.004% of original inoculum) and hands (1/10; ~100 PFU; <0.00003% of the original inoculum) for the minority of participants. Most (n = 8) had detection of MS2 at only 1 site, while 2 had virus at 2 sites (inner gloves and either scrubs or hands).

Fluorescent tracer was not detected on PPE, skin, or scrubs under ultraviolet (UV) light. A total of 21 surface sites were sampled because fluorescent tracer was visible by examination under UV light, including door handles, toilet handles, and bed rails. No bacteriophage was detected on any of these sites.

DISCUSSION

Our study is the first to experimentally evaluate viral self-contamination during EVD PPE doffing under controlled conditions in HCWs who have cared for patients with EVD. Although the integrity and effectiveness of PPE during patient care is crucial for HCW protection from contamination, doffing is a

Table 2. Detection of Nonenveloped Bacteriophage MS2 After Doffing Ebola-Level Personal Protective Equipment in 10 Simulation Studies

HCW	Nondominant Hand, PFU	Dominant Hand, PFU	Gloves, PFU	Face	Scrubs, PFU
1	ND	ND	ND	ND	ND
2	ND	ND	2.50×10^1	ND	ND
3	ND	ND	3.42×10^4	ND	1.33×10^4
4	ND	ND	1.44×10^3	ND	ND
5	ND	ND	ND	ND	ND
6	144	96	8.64×10^6	ND	ND
7	ND	ND	1.30×10^5	ND	ND
8	ND	ND	ND	ND	1.27×10^3
9	ND	ND	4.60×10^4	ND	ND
10	ND	ND	3.00×10^2	ND	ND
Arithmetic mean	144	96	8.82×10^5	…	1.46×10^3
SD	…	…	2.72×10^6	…	4.18×10^3

Abbreviations: HCW, healthcare worker; ND, not detected; PFU, plaque-forming units; SD, standard deviation.

critical point for assessing contamination risk, due to the necessity of touching and handling contaminated PPE at multiple points in the process. Previous simulation research has shown that hand contamination with a nonenveloped virus is common with standard contact isolation PPE [7], where doffing is often not structured. Using a structured, observed EVD PPE doffing protocol in a population of providers who were trained but had no direct EVD patient care experience, prior simulations studies found no transfer of an enveloped surrogate for Ebola virus to hands, face, or inner gloves [16]. The time from contamination with virus to scrub removal was <1 hour; negligible inactivation of virus is expected to take place during this time [22]. The results of this study suggest that current structured, observed doffing protocols, including the use of ABHR for sanitizing gloves, are protective against hand contamination with an enveloped virus when used by HCWs with differing levels of training and experience.

However, other simulations of structured observed doffing have found transfer of nonenveloped virus to inner gloves, scrubs, and hands [16, 17]. In this study, there was low but detectable transfer of nonenveloped MS2 to hands (1 participant) and scrubs. The fact that most participants had detectable MS2 on their inner gloves but not on their hands suggests that inner gloves are playing a vital role in protection against direct hand contamination. Because gloves are repeatedly touching PPE during the doffing process, even use of ABHR on the outside of gloves between doffing steps may not completely prevent inner glove contamination with a nonenveloped virus. Human factors analyses (Mumma et al, manuscript in preparation) suggest that the mishandling of certain items of PPE during doffing contributes considerably to the probability that a HCW's gloves, scrubs, and hands become contaminated. For example, when ABHR does not have adequate time to dry after application, it may make gloves slippery and harder to manipulate. This in turn may contribute to accidental glove "snapping" due to loss of grip on the glove during removal, potentially leading to hand contamination.

If contamination occurs, hand hygiene plays a vital role; human factors analysis suggests that the hand hygiene steps present multiple opportunities for error during the doffing process. Human factors analyses suggest room for improvement in hand hygiene technique with ABHR, including taking adequate time that allows for coverage of all hand surfaces as well as adequate drying before proceeding to the next step. Hand hygiene agents may play an important role in the differences in how lipid-enveloped and nonenveloped viruses survive during PPE doffing. Enveloped Φ6 was not detected on inner gloves, but MS2 was. This is an expected result, as evidence supports that ABHR is more effective against enveloped viruses such as Ebola than against nonenveloped viruses [23–26]. To minimize viral load on inner gloves, both careful doffing and control measures such as stronger glove sanitizing agents (such as hypochlorite or povidone-iodine) may be needed, particularly if nonenveloped viruses emerge as high-risk pathogens. However, whether units use ABHR or other hand sanitizers with demonstrated in vitro effectiveness against viruses, contact time, and technique are still important [27]. These results highlight the fact that even when wearing PPE that provides whole body coverage, hand hygiene after doffing is still critical, with hand hygiene agents that are effective against a range of organisms. Defects in hand hygiene may be an important risk factor for HCWs to acquire EVD [28]. While the Centers for Disease Control and Prevention guidelines do not specify the hand hygiene product, the World Health Organization and Médecins Sans Frontières recommend use of 0.5% chlorine for all hand hygiene events, which has been supported by some data using Φ6 [29].

Opportunities for unintentional contact with PPE with hands, wrists, neck, and scrubs underscores the need for close observation during the complex doffing process. Postsimulation viewing of video recording suggested that there may be contact and contamination events that are not recognized by the doffer or the TO during the process. In this and other doffing protocols, scrubs are touched with bare hands and may be removed and handled after exiting the patient care area. The detection of virus on scrubs suggests that disposable scrubs that are carefully handled and disposed of after doffing may be safest. Improved PPE designs that allow for easier removal without touching the outside of PPE items may also mitigate this risk, as well as reduce the risk of virus transfer to the TO by eliminating any need for them to physically assist with doffing.

These simulations of PPE doffing have applications for biocontainment units beyond Ebola. Enveloped bacteriophage Φ6 was chosen as a surrogate because it serves as a model not only for Ebola, but other high-consequence pathogens, such as the Lassa, Marburg, and smallpox viruses. Imported cases of Lassa fever are an emerging problem; biocontainment units in the United States and elsewhere have also cared for suspected and actual cases of Lassa infection [30–32]. Recent high-consequence emerging pathogens such as the coronaviruses causing severe acute respiratory syndrome and Middle East respiratory syndrome, and Ebola, are enveloped viruses, but the possibility of emerging nonenveloped pathogens exists as well. The use of MS2 not only provides a model for possible nonenveloped viral threats, but serves as a very conservative surrogate for measuring the effectiveness of disinfection and hand hygiene steps in PPE doffing.

Our findings with complex PPE may be directly applicable to HCWs outside biocontainment units. All US acute care hospitals are required to be prepared to triage a patient with potential or suspected Ebola and may encounter an unknown or emerging pathogen. "Rule-out" scenarios are much more common than care for a patient with known infection, but both require the appropriate and safe use of PPE to protect HCWs. Furthermore, the more typical PPE used by HCWs in other clinical settings

may be contaminated in a similar method, though more studies are needed with these types of PPE and markers that mimic bacterial pathogens that remain significant public health concerns, including those that are multidrug resistant.

Previous studies of complex PPE doffing using fluorescent tracers as markers of contamination found contamination of hands after PPE removal [10, 17, 33]. PPE removal studies using both fluorescent markers and infectious viruses simultaneously have been done with MS2; in one study, rates of self-contamination with fluorescent tracer and MS2 were similar [7], but in others they were not [8, 17]. These types of studies have not yet been done using enveloped viruses, and our findings suggest that fluorescent tracers alone may not be a reliable indicator of self-contamination with infectious viruses as none were found despite clear evidence of virologic transfer. Variation in the type and use of these markers may explain some of these observed differences, and standardization of these approaches is needed.

A structured doffing protocol using a trained observer, double gloves, and multiple glove sanitizing steps appears to protect against self-contamination with enveloped viruses. There was a low risk of self-contamination with a nonenveloped virus, possibly due to these viruses' higher resistance to agents used to sanitize gloves. Improved doffing protocols that are highly protective against all types of viruses may need to incorporate changes in the removal process, reinforcement of hand hygiene, careful handling of scrubs, and highly effective glove sanitizing and hand hygiene agents.

Notes

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