

Another part of the estimates consisted of the difference between the costs of a patient being admitted to the hospital for *C. difficile* and the costs of a patient with a different disease but a similar comorbidity set.

ACKNOWLEDGMENTS

Financial support: Support for this study was received from the German Research Foundation (grant no. WO 1746/1-2 to M.W. and grant no. KA 4199/1-1 to T.H.). Additional funding was received from the Innovative Medicines Initiative Joint Undertaking (grant no. 115737-2 to K.K., Combatting bacterial resistance in Europe—molecules against gram-negative infections [COM-BACTE-MAGNET]). The funders had no role in the preparation of this manuscript.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

**Thomas Heister, Dipl-Econ;
Martin Wolkewitz, PhD;
Klaus Kaier, PhD**

Affiliations: Division Methods in Clinical Epidemiology, Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center, University of Freiburg, Freiburg, Germany.

Address correspondence to Dr. rer. pol. Klaus Kaier, Institut für Medizinische Biometrie und Statistik - Universitätsklinikum Freiburg, Stefan-Meier-Str. 26, 79104 Freiburg, Germany (kaier@imbi.uni-freiburg.de).

Infect Control Hosp Epidemiol 2018;39:759–760

© 2018 by The Society for Healthcare Epidemiology of America. All rights reserved. 0899-823X/2018/3906-0024. DOI: 10.1017/ice.2018.42

REFERENCES

- Mehrotra P, Jang J, Gidengil C, Sandora TJ. Attributable cost of *Clostridium difficile* infection in pediatric patients. *Infect Control Hosp Epidemiol* 2017;38:1472–1477.
- Nanwa N, Kwong JC, Krahn M, et al. The economic burden of hospital-acquired *Clostridium difficile* infection: a population-based matched cohort study. *Infect Control Hosp Epidemiol* 2016;37:1068–1078.
- Schumacher M, Allignol A, Beyersmann J, Binder N, Wolkewitz M. Hospital-acquired infections—appropriate statistical treatment is urgently needed! *Int J Epidemiol* 2013;42:1502–1508.
- Heister T, Kaier K, Wolkewitz M. Estimating the burden of nosocomial infections. Time dependency and cost clustering should be taken into account. *Am J Infect Control* 2017;45:94–95.
- Resch A, Wilke M, Fink C. The cost of resistance: incremental cost of methicillin-resistant *Staphylococcus aureus* (MRSA) in German hospitals. *Eur J Health Econ* 2009;10:287–297.
- Andersen PK, Keiding N. Interpretability and importance of functionals in competing risks and multistate models. *Stat Med* 2012;31:1074–1088.
- Miller AC, Polgreen LA, Cavanaugh JE, Polgreen PM. Hospital *Clostridium difficile* infection rates and prediction of length of stay in patients without *C. difficile* infection. *Infect Control Hosp Epidemiol* 2016;37:404–410.

Got GAS? Ease the Bloat with Real-Time Whole-Genome Sequencing

To the Editor—Annually, more than 10,000 patients in the United States acquire an infection caused by invasive group A *Streptococcus* (GAS). The fatality rate of this illness is 11.7%, and many infections are transmitted person to person.^{1,2} Outbreak investigations of postsurgical group A *Streptococcus* (GAS) infections can substantially disrupt surgical throughput if staff require furloughing, and they can be extremely labor intensive when surgeons practice at multiple facilities.³ One benefit that has received little attention is the labor-saving potential that whole-genome sequencing (WGS) offers infection preventionists (IPs) when the turnaround time is sufficiently rapid to inform investigations and mitigation efforts.⁴ Here, we highlight an outbreak involving 22 surgical staff, several of whom practice at multiple facilities that often care for the same patients within a regional care network.

On day 0, patient A underwent a procedure at community hospital X, performed by surgeon I who also practices at referral hospital Y (Table 1). On day 5, patient A developed an invasive GAS surgical wound infection while at hospital X. On day 7, patient B underwent a procedure performed by surgeon II at hospital X. On day 8, patient B developed a complication requiring escalation of care to hospital Y for follow-up surgery, again performed by surgeon II. On day 13, GAS was isolated from the surgical wound of patient B while at hospital Y. The 2 GAS isolates were sent for WGS, using methods described previously.^{4,5} Simultaneously, IP staff initiated a retrospective review of all laboratory results beginning 6 months prior to the first surgery. Involved surgical staff at all facilities were contacted to have their throats and groins swabbed. Mitigation planning was begun in case staff furloughing would be required pending decolonization.

The core genome sequences of the 2 isolates differed by ~40,000 nucleotide changes, indicating that they were genetically unrelated.⁵

The WGS results were available within a week, before all staff had been swabbed and before any culture results of those that had been swabbed were available. On other occasions, results have been available in <50 hours.⁴ For this event, WGS permitted earlier termination of the investigation and faster resumption to full surgical capacity, saving time, labor, and money (Table 1). The costs in Table 1 were calculated based on material and labor costs in this region⁶ for screening all involved operating room staff (n = 22). If WGS had determined that the isolates were related, the cost would have been \$80.00 more for the WGS approach compared to the conventional approach (not using WGS). When WGS revealed that the isolates were unrelated, the cost savings were substantial because surgical throughput was not slowed or disrupted, and IPs were able to devote their time and efforts

TABLE 1. Potential Impact of an Outbreak Investigation for Surgical Site Infection due to Group A *Streptococcus*

Day and Event	Patient / Hospital	Surgeon / No. of Support Staff
Day 0, Surgical procedure	Patient A / Hospital X	Surgeon I / 1 Staff
Day 5, GAS infection	Patient A / Hospital X	
Day 7, Surgical procedure	Patient B / Hospital X	Surgeon II / 9 Staff
Day 8, Surgical procedure	Patient B / Hospital Y	Surgeon II / 10 Staff
Day 13, GAS infection	Patient B / Hospital Y	
		Total of 22 Possible Carriers
Costs	Conventional approach	Real-time sequencing approach
Direct		
Laboratory	\$175.00	\$80.00
Infection preventionist labor ^a	10 RN+hours = \$500.00	\$0.00
Employee health labor ^a	8 RN+hours = \$400.00	\$0.00
Indirect		
Lost revenue due to time surgical staff not operating due to specimen collection or on furlough if screened positive and awaiting genotyping and/or decolonization	Potentially \$1,000–100,000 depending on number of staff involved and time line	\$0.00

^aRN+, registered nurse at 90% effort with Advanced Practitioner or Physician Oversight at 10% effort.

to other issues. Currently, WGS has become faster, less expensive, and more informative than pulsed-field gel electrophoresis (PFGE). Furthermore, PFGE has been suggested to lead to erroneous conclusions regarding genetic relatedness among strains.⁷ However, such timely feedback is not yet available to most hospitals; thus, IPs, surgical facilities, and patients would benefit from wider access to real-time, genome-based support.

ACKNOWLEDGMENTS

The views expressed in this article are those of the authors and do not reflect the official policies of the Department of the Army, Navy, or Air Force, the Department of Defense, or the US government.

Financial support: No financial support was provided relevant to this article.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

Emil P. Lesho, DO;¹
Erik Snesrud, BS;²
Melissa Bronstein, MPA;³
Margaret Pettis, RN;⁴
Ana Ong, BS;²
Rosslyn Maybank, BA;²
Yoon Kwak, MS;²
Anthony Jones, PhD;²
Kelly Vore, PhD;⁴
Patrick McGann, PhD;²
Mary Hinkle, MD²

Affiliations: 1. Infectious Diseases Unit, Rochester Regional Health, Rochester, New York; 2. Multidrug-resistant Organism Repository and Surveillance Network, Walter Reed Army Institute of Research, Silver Spring, Maryland; 3. Quality Safety Institute, Rochester Regional Health, Rochester, New York; 4. Infection Prevention, Rochester Regional Health, Rochester, New York.

Address correspondence to Emil Lesho, 1425 Portland Avenue, Rochester, NY 14621 (carolinelesho@yahoo.com).

Infect Control Hosp Epidemiol 2018;39:760–762

© 2018 by The Society for Healthcare Epidemiology of America. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited. All rights reserved. 0899-823X/2018/3906-0025. DOI: 10.1017/ice.2018.73

REFERENCES

- Flores AR, Luna RA, Runge JK, Shelburne SA, Baker CJ. Cluster of fatal group A Streptococcal emm87 infections in a single family: molecular basis for invasion and transmission. *J Infect Dis* 2017;215:1648–1652.
- Nelson GE, Pondo T, Toews KA, et al. Epidemiology of invasive group A Streptococcal infections in the United States, 2005–2012. *Clin Infect Dis* 2016;63:478–486.
- The Prevention of Invasive Group A Streptococcal Infections Workshop Participants. Prevention of invasive group A Streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: recommendations from the Centers for Disease Control and Prevention. *Clin Infect Dis* 2002;35:950–959.
- McGann P, Bunin J, Snesrud E, et al. Real time application of whole genome sequencing for outbreak investigation—What is an achievable turnaround time? *Diagn Microbiol Infect Dis* 2016; 85:277–282.
- Jacob KM, Spilker T, LiPuma JJ, Dawid SR, Watson ME Jr. Complete genome sequence of emm4 *Streptococcus pyogenes* MEW427, a throat isolate from a child meeting clinical criteria for pediatric autoimmune neuropsychiatric disorders associated with Streptococcus (PANDAS). *Genome Announc* 2016;4:e00127–16.
- Landers T, Davis J, Crist K, Malik C. APIC MegaSurvey: methodology and overview. *Am J Infect Control* 2017;45: 584–588.

7. Salipante SJ, SenGupta DJ, Cummings LA, Land TA, Hoogstraal DR, Cookson BT. Application of whole-genome sequencing for bacterial strain typing in molecular epidemiology. *J Clin Microbiol* 2015;53:1072–1079.

Bacteriophage M13 May Be Used for the Assessment of Viral Transfer during Doffing of Ebola-Level Personal Protective Equipment

To the Editor—Extensive barrier precautions can prevent skin and mucous membrane contamination during the patient care. However, personal protective equipment (PPE) can be contaminated with body fluids and infectious virus after a patient care encounter.^{1,2} We read with interest the articles by Casanova et al³ and Kwon et al,⁴ which reported a certain level of self-contamination with nonenveloped viruses and a much lower rate of self-contamination with enveloped viruses, with contamination limited to inner gloves. Recently, Casanova et al⁵ and Mumma et al⁶ (from the Centers for Disease Control and Prevention Epicenters Program, Division of Healthcare Quality Promotion, United States) further assessed the contamination of skin, gloves, and scrubs after doffing Ebola-level PPE. In these studies, they assessed self-contamination risks using 2 surrogate viruses, bacteriophages MS2 and $\Phi 6$, to represent nonenveloped and enveloped viruses, respectively. However, given that both MS2 and $\Phi 6$ are spherical bacteriophages and are much smaller than the filamentous Ebola virus, their adhesion capabilities on PPE are much different. Thus, the reported contamination rates after doffing Ebola-level PPE may be inaccurate.

Ebola virus is an enveloped RNA virus with a filamentous appearance and a uniform diameter of ~ 80 nm, but Ebola virus particles vary greatly in length. In general, the median particle length of Ebola viruses ranges from 974 to 1,086 nm.⁷ In contrast, bacteriophage $\Phi 6$ has a pleomorphic appearance and a uniform diameter of ~ 80 nm,⁸ which is almost 10 times shorter than the average length of an Ebola virus particle (Figure 1). In microbial fermentations, small increases in hyphal length (eg, the formation of pellets or clumps) can cause large increases in broth viscosity because filamentous bioparticles have higher adhesion forces than spherical bioparticles.⁹ Thus, the adhesion capability of $\Phi 6$ on PPE may be much lower than that of Ebola virus. Thus, the bacteriophage $\Phi 6$ might not be an ideal surrogate virus.

In detailed studies, Casanova et al⁵ found that no $\Phi 6$ transfer to inner gloves, hands, or face among 10 healthcare workers. Only 1 healthcare worker had $\Phi 6$ on scrubs at low levels (1.4×10^2). This contamination rate was much lower than that of nonenveloped bacteriophage MS2: 2 healthcare worker had MS2 on scrubs, 1 had it on hands, and 7 had it on inner gloves (at 10^1 – 10^6). Despite these differences, the fault

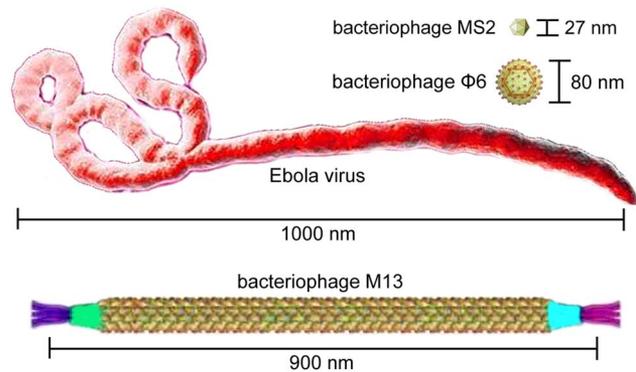


FIGURE 1. Lengths and shapes of Ebola virus and bacteriophages MS2, $\Phi 6$, and M13.

trees for MS2 and $\Phi 6$ contamination suggested similar pathways.⁶ Similarly, very low levels of $\Phi 6$ contamination (much lower than those of MS2) have also been reported in previous studies.^{3,4} However, for the aforementioned reason, the risk the doffing protocol for Ebola-level PPE may be underestimated when $\Phi 6$ is selected as the surrogate virus. Also, the risk that the doffing protocol for Ebola-level PPE may be overestimated when MS2 is selected as the surrogate virus must be considered.

Different from $\Phi 6$ and MS2, M13 is a filamentous bacteriophage with a ~ 900 nm particle length,¹⁰ which is very close to the average length of Ebola viruses (Figure 1). The M13 bacteriophage can be easily cultured and detected with the visible fluorescent marker, making it an ideal surrogate virus for the biocontainment study on the Ebola-level PPE. Presumably, a more accurate contamination rate after doffing Ebola-level PPE could be achieved using the surrogate virus M13. Nevertheless, we agree with the authors that the doffing protocols should be improved for better protections against all types of viruses, especially the filamentous Ebola viruses with high adhesion capabilities.

ACKNOWLEDGMENTS

Financial support: No financial support was provided relevant to this article.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

Shu Yuan, PhD;¹
Zhong-Wei Zhang, PhD;¹
Zi-Lin Li, MD²

Affiliations: 1. College of Resources, Sichuan Agricultural University, Chengdu, China; 2. Xijing Hospital, Medical University of the Air Force, Xi'an, China.

Address correspondence to Shu Yuan, College of Resources, Sichuan Agricultural University, Chengdu 611130, China (roundtree318@hotmail.com). *Infect Control Hosp Epidemiol* 2018;39:762–763

© 2018 by The Society for Healthcare Epidemiology of America. All rights reserved. 0899-823X/2018/3906-0026. DOI: 10.1017/ice.2018.74