*Infection Control & Hospital Epidemiology* (2018), **39**, 1125–1132
doi:10.1017/ice.2018.154

## Research Briefs

# Trends in "usual care" for septic shock

Patrick S. Hume MD, PhD[1], Jack Varon MD[1,2], Joshua A. Englert MD[1,2], Shelley Hurwitz PhD[1], Michael Klompas MD, MPH[1,3], Rebecca M. Baron MD[1,2,a] and Chanu Rhee MD, MPH[1,3,a]

[1]Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, [2]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts and [3]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts

(Received 6 May 2018; accepted 7 June 2018; electronically published July 19, 2018

Sepsis is the focus of hospital performance improvement initiatives and national quality measures, but controversy remains regarding the importance and optimal delivery of bundled care.[1,2] Early goal-directed therapy (EGDT) was initially reported in 2001 to significantly lower mortality rates in septic shock, catalyzing the Surviving Sepsis Campaign and EGDT protocols in hospitals around the world.[3] However, 3 subsequent large, multicenter trials conducted from 2008 to 2014 showed no benefit with EGDT versus usual care.[4–6] The discrepancy may be due to changes in usual care for septic shock over the past two decades.[7] In particular, increasing emphasis on early antibiotic and fluid administration may have made usual care and EGDT more similar over time.

Understanding changes in usual care for septic shock may shed light on the importance of early antibiotic and fluid administration, on the observed declines in septic shock mortality over time, and on how best to improve the quality of sepsis care.[8,9] Therefore, we examined changes in treatment patterns for septic shock in the emergency department (ED) of a large academic hospital.

## Methods

We screened all adult patients (≥18 years) admitted to a medical service at Brigham and Women's Hospital from 2003 to 2013 for possible septic shock based on orders for antibiotics, blood cultures, and vasopressors on admission. We reviewed medical records of patients chosen by a random generator in alternating calendar years to confirm septic shock criteria (at least 15 patients per year), and we assessed changes in care. We defined septic shock as suspected or confirmed infection, ≥2 systemic inflammatory response syndrome criteria, and hypotension (systolic blood pressure <90 mmHg or mean arterial pressure <65 mmHg) while in the ED and vasopressor requirement within 24 hours. We excluded patients transferred from outside hospitals and those for whom the goals of care prohibited aggressive resuscitation. We abstracted time to fluid boluses and intravenous antibiotics relative to onset of hypotension. Interventions given before hypotension were considered zero minutes to care. We examined trends using the Exact Jonkheere-Terpstra test and general linear models using SAS version 9.4 software (SAS Institute, Cary, NC). The Partners Healthcare Institutional Review Board approved this study.

## Results

We screened 478 patients with markers of possible septic shock, and we identified 98 patients for inclusion. The mean age of the study participants was 63 ± 1.7 years; 50 of the participants were male. The most common infection sources were pulmonary (43%), genitourinary (28%), and intra-abdominal (11%). Chronic comorbidities were common, including congestive heart failure (21%), cancer (21%), and pulmonary disease (17%). The mean Sequential Organ Failure Assessment score on presentation was 8.5 ± 0.3 and did not significantly change across the study period.

The mean time from hypotension onset to antibiotic administration decreased from 122 ± 44 min in 2003 to 49 ± 17 min in 2013 ($P = .02$ for trend) (Fig. 1a). The mean time from hypotension onset to 1-L fluid bolus also decreased over the study period (128 ± 54 min in 2003 to 38 ± 14 min in 2013; $P = .03$) (Fig. 1b). No significant changes occurred in time to completion of 2-L fluids or total volume of fluid administered by 6, 24, and 72 hours (Fig. 1c). Over the study period, the proportion of patients who received antibiotics prior to hypotension onset increased from 20% in 2003 to 40% in 2013 ($P = .047$), and the proportion of patients who received the first 1-L fluid bolus prior to hypotension onset increased from 27% to 47% ($P = .04$) (Fig. 1d). The mean hospital length of stay decreased from 11 days in 2003 to 7 days in 2013 ($P = .02$). The overall in-hospital mortality rate was 21% and did not significantly change during the study period.

## Discussion

We detected significant decreases in average time from hypotension onset to fluids and antibiotics in ED patients with septic shock from 2003 to 2013. We also observed more fluids and antibiotics being administered prior to hypotension onset. Our findings

**Author for correspondence:** Chanu Rhee MD, MPH, Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, 401 Park Drive, Suite 401, Boston, MA 02215. E-mail: crhee@bwh.harvard.edu

[a] Authors of equal contribution.

**Cite this article:** Hume PS, *et al.* (2018). Trends in "usual care" for septic shock. *Infection Control & Hospital Epidemiology* 2018, 39, 1125–1126. doi: 10.1017/ice.2018.154

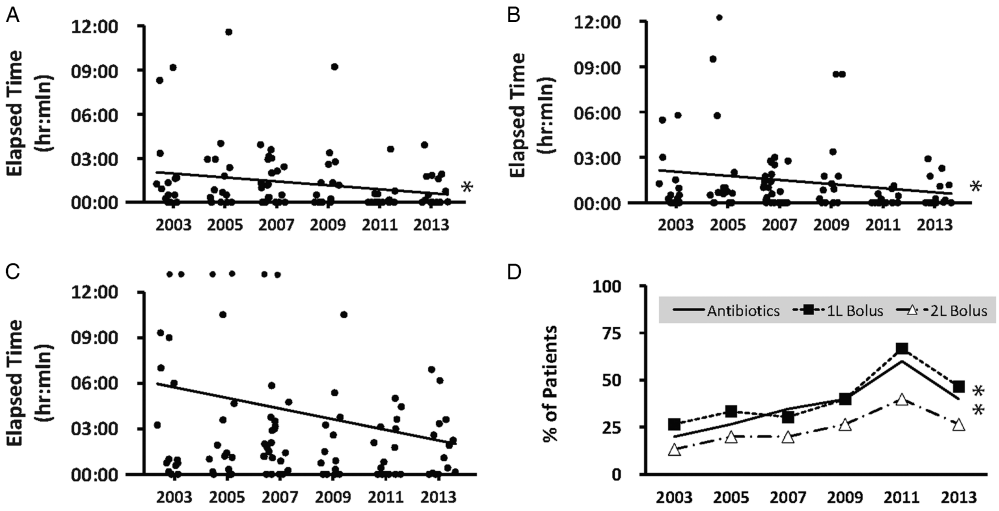


**Fig. 1.** Trends in septic shock care, 2003–2013. (A) Time from hypotension onset to initial intravenous antibiotic administration. (B) Time from hypotension onset to completion of 1-L fluid bolus. (C) Time from hypotension onset to completion of 2-L fluid bolus. (D) Percentage of septic shock patients receiving treatment in the emergency department prior to the onset of hypotension. All data points represent individual patients and trend lines represent a linear regression. *Denotes a significant ($P < .05$) reduction from 2003 to 2013.

suggest that usual care changed substantially between the time when EGDT was first reported to lower mortality and the time that 3 more recent trials reported no mortality benefit with EGDT.[3–6]

In our cohort, patients received the first liter of fluids earlier over time, but the total volume administered at 6, 24, or 72 hours did not change significantly, suggesting that most of the practice changes occurred during the very early stages after ED presentation. Most patients in the recent EGDT trials also received antibiotics and fluids early, even before study enrollment.[4–6] These rapid measures may be partially responsible for the global improvements in septic shock outcomes reported in the recent EGDT trials versus the original 2001 study, as EGDT following early fluids and antibiotics does not appear to confer additional benefit.[8,9]

Our study has several limitations. First, the sample size was small. Nonetheless, we detected significant trends. Second, we studied only 1 hospital, which limits the generalizability of our findings. Third, we were unable to ascertain whether the observed trends were already occurring before publication of the first EGDT trial in 2001. Fourth, despite the decreased time to antibiotic and fluid administration, we did not observe a significant improvement in mortality in our cohort. This may be due to our small sample size; other population-level analyses in our study hospital have suggested decreases in septic shock mortality over the same time period.[9,10] We also only included patients that received vasopressors; thus, we could have missed hypotensive patients in whom the need for vasopressors might have been averted by earlier antibiotics and fluids.

In conclusion, from 2003 to 2013, we observed significant reductions in time to antibiotics and fluids for patients with septic shock in the ED, underscoring the evolution of "usual care" over time. These findings may explain why EGDT is not beneficial in the current era and may help inform ongoing deliberations regarding best practices for sepsis care.

**Acknowledgments.** We wish to thank Brianna Triplett for her assistance with the initial screening of patients for exclusion criteria.

**Financial support.** This work was supported in part by the Agency for Healthcare Research and Quality (grant no. K08HS025008 to C.R.) and by the National Institutes of Health (grant no. 1-R01-HL112747-01 to R.M.B). The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality or the National Institutes of Health.

**Conflicts of interest.** All authors report no conflicts of interest relevant to this article.

## References

1. Klompas M, Rhee C. The CMS sepsis mandate: right disease, wrong measure. *Ann Intern Med* 2016;165:517–518.
2. Pepper DJ, Jaswal D, Sun J, Welsh J, Natanson C, Eichacker PQ. Evidence underpinning the US government-mandated hemodynamic interventions for sepsis: a systematic review. *Ann Intern Med* 2018;168:558–568.
3. Rivers E, Nguyen B, Havstad S, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368–1377.
4. Peake SL, Delaney A, Bailey M, *et al.* Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2015;371:1496–1506.
5. Yealy DM, Kellum JA, Huang DT, *et al.* A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370:1683–1693.
6. Mouncey PR, Osborn TM, Power GS, *et al.* Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med* 2015;372:1301–1311.
7. Levy MM.. Early goal-directed therapy: what do we do now? *Crit Care* 2014;18:705.
8. Castellanos-Ortega A, Suberviola B, Garcia-Astudillo LA, *et al.* Impact of the Surviving Sepsis Campaign protocols on hospital length of stay and mortality in septic shock patients: results of a three-year follow-up quasi-experimental study. *Crit Care Med* 2010;38:1036–1043.
9. Kadri SS, Rhee C, Strich JR, *et al.* Estimating ten-year trends in septic shock incidence and mortality in United States Academic medical centers using clinical data. *Chest* 2017;151:278–285.
10. Rhee C, Kadri S, Huang SS, *et al.* Objective sepsis surveillance using electronic clinical data. *Infect Control Hosp Epidemiol* 2015;37:163–171.

https://doi.org/10.1017/ice.2018.154 Published online by Cambridge University Press

# Penicillin allergy and association with ciprofloxacin coverage in community-onset urinary tract infection

Courtney M. Dewart MPH, RN[1], Yuan Gao MS[2], Protiva Rahman BS[3], Awa Mbodj MS[4], Erinn M. Hade PhD[4], Kurt Stevenson MD, MPH[1,5] and Courtney L. Hebert MD, MS[4,5]

[1]Division of Epidemiology, The Ohio State University College of Public Health, Columbus, Ohio, [2]Division of Biostatistics, The Ohio State University College of Public Health, Columbus, Ohio, [3]Department of Computer Science and Engineering, The Ohio State University College of Engineering, Columbus, Ohio, [4]Department of Biomedical Informatics, The Ohio State University College of Medicine, Columbus, Ohio and [5]Division of Infectious Diseases, The Ohio State University College of Medicine, Columbus, Ohio

(Received 15 March 2018; accepted 28 May 2018; electronically published July 23, 2018

The prevalence of patients with a documented penicillin allergy is >10% in many healthcare settings in the United States.[1,2] Though up to 90% of these patients may safely tolerate penicillin, the presence of an allergy label is associated with increased use of broad-spectrum antimicrobials including fluoroquinolones, glycopeptides, and carbapenems.[2–4] In the treatment of urinary tract infections (UTIs), recent fluoroquinolone use is a demonstrated risk factor for ciprofloxacin resistance among *Escherichia coli* UTIs.[5] As part of a study aimed at developing predictive models for empiric antibiotic prescribing, we investigated the relationship between a documented penicillin-class allergy and ciprofloxacin-resistant community-onset UTIs in adult hospitalized patients. Our analysis is inclusive of all urinary pathogens.

## Methods

Using electronic health record (EHR) data from a 1,300-bed teaching hospital, we established a retrospective cohort of adult patients admitted to an inpatient unit from November 1, 2011, to June 30, 2016, with a UTI diagnosis and a positive urine culture in the first 48 hours. Only the first encounter during the study period was included. We defined the exposure as presence of a penicillin-class allergy label (eg, penicillin, amoxicillin, piperacillin) documented in the EHR, and we defined the outcome as a UTI not covered by ciprofloxacin. We included all urinary pathogens for infections where multiple pathogens were present. For UTIs with unreported ciprofloxacin susceptibilities, subject matter experts inferred susceptibility according to previously reported methods.[6]

We used modified Poisson regression with stabilized inverse probability weights (IPW) to estimate the adjusted relative risk of resistance.[7,8] Inverse probability weighting adjusted for potential measured confounders: sex, age, Elixhauser score, number of inpatient and emergency department admissions in the past year, and indicator variables for transfer from a nursing home and presence of a cephalosporin or carbapenem allergy label. We adjusted for cephalosporin and carbapenem allergy to isolate the effect of a penicillin-class allergy label. Stabilized IPW were estimated via boosted logistic regression, and covariate balance between exposure groups after weighting was evaluated by standardized differences between exposure groups using the *twang* package version 1.5 in R.[8] Analyses were conducted in Stata version 15 software (StataCorp, College Station, TX) and R version 3.4.2 software (R Foundation for Statistical Computing, Vienna, Austria).

Additionally, we examined the potential mediation effect of recent fluoroquinolone use in the relationship between a penicillin-class allergy label and lack of ciprofloxacin coverage. We estimated the total, direct, and indirect effects of prior fluoroquinolone use, adjusted by IPW, through the *mediation* package (version 4.4.6) in R.[9] This study was approved by the Institutional Review Board of the Office of Responsible Research Practices at The Ohio State University.

## Results

Among 6,361 patients admitted with community-onset UTI, 1,252 (19.7%) had a penicillin-class allergy label documented in the EHR. A total of 7,431 isolates representing 75 organisms were included in the analysis. The most prevalent organisms, which accounted for 75.9% of all isolates, were *Escherichia coli* (n = 2,797), *Enterococcus faecalis* (n = 1,281), *Klebsiella pneumoniae* (n = 876), *Pseudomonas aeruginosa* (n = 391), and *Enterococcus faecium* (n = 292). Prior to IPW, exposure groups were notably imbalanced on sex, age, and cephalosporin allergy. After IPW, all standardized differences between exposure groups were < 10%. Patients with a penicillin-class allergy label were 1.13 times more likely to have a ciprofloxacin-resistant UTI (707 of 1,252, 56.5%) compared to those without a penicillin-class allergy label (2,601 of 5,109, 50.9%; aRR, 1.13; 95% CI, 1.06–1.19). Mediation analysis revealed that 24% of the total effect of a penicillin-class allergy label on ciprofloxacin-resistant UTI was explained by fluoroquinolone use in the past 90 days, as documented in our EHR at least 24 hours prior to culture (95% CI, 0.08–0.49) (Fig. 1).

A major assumption in the development of susceptibilities for this cohort was that enterococci were not covered by ciprofloxacin if susceptibilities were not reported. However, because enterococci may be susceptible to ciprofloxacin, we reevaluated our models assuming that enterococci with missing susceptibilities were susceptible to ciprofloxacin (21% of encounters affected). Overall inference in the association of interest and mediation effect by

**Author for correspondence:** Courtney L. Hebert, Department of Biomedical Informatics, The Ohio State University College of Medicine, 220S Lincoln Tower, 1800 Cannon Drive, Columbus, OH 43210. E-mail: Courtney.Hebert@osumc.edu

**Cite this article:** Dewart CM, *et al.* (2018). Penicillin allergy and association with ciprofloxacin coverage in community-onset urinary tract infection. *Infection Control & Hospital Epidemiology* 2018, 39, 1127–1128. doi: 10.1017/ice.2018.155

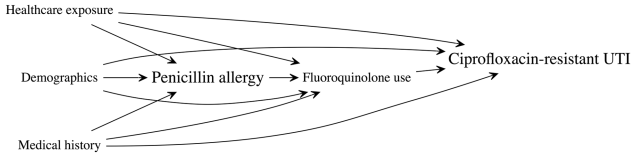


**Fig. 1.** Directed acyclic graph of the proposed association between penicillin-class allergy label and ciprofloxacin-resistant urinary tract infection (UTI), including partial mediation by recent fluoroquinolone use. Potential confounding variables accounted for in our analysis are also presented: demographics (sex and age), healthcare exposure (nursing home transfer, emergency department admissions, inpatient admissions), and medical history (Elixhauser score, cephalosporin allergy, carbapenem allergy).

fluoroquinolone use in this sensitivity analysis did not substantially change (aRR, 1.20; 95% CI, 1.09–1.31; average proportion mediated: 17%; 95% CI, 0.06–0.37).

## Discussion

Among patients presenting with a UTI, those with a penicillin-class allergy label may be at a slightly increased risk of not being covered by ciprofloxacin. Recent fluoroquinolone use partially contributes to this effect, suggesting additional mechanisms behind this association. Because we were limited to evaluating antibiotic exposures that occurred within our healthcare system, the proportion of the total effect mediated by fluoroquinolone use may have been higher than 24% if similar patterns of recent fluoroquinolone use by allergy status occurred outside of our health system. Additional mediators could include recent exposure to other antimicrobial classes that were not evaluated in this study.

Targeting areas of antibiotic overuse is key to combating resistance and improving patient outcomes through appropriate antibiotic prescribing. With respect to penicillin-class allergy labels, antimicrobial stewardship initiatives have focused on allergy confirmation through skin testing and oral challenge.[10] In many cases, patients with a documented but unconfirmed penicillin-class allergy can be de-labeled following appropriate testing.[10] Our finding that nearly 20% of patients in this cohort had a documented penicillin-class allergy highlights the potential for more accurate classification and labeling of allergies to support antimicrobial stewardship. We show that a penicillin-class allergy is a modest risk factor for ciprofloxacin resistance, which may be due in part to increased use of fluoroquinolones. This finding suggests that one possible solution to fluoroquinolone overuse would be to reassess the veracity of penicillin allergy labels at the point of care.

**Acknowledgments.**

**Financial support.** This research reported here was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health (grant no. R01AI116975) and The Ohio State University Center for Clinical and Translational Science (National Center for Advancing Translational Sciences, grant no. 8UL1TR000090-05). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**Conflict of interest.** All authors report support from NIH grants during this study.

## References

1. Shah NS, Ridgway JP, Pettit N, Fahrenbach J, Robicsek A. Documenting penicillin allergy: the impact of inconsistency. *PLoS One* 2016;11: e0150514.
2. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol* 2014;133:790–796.
3. Sogn DD, Evans R, Shepherd GM, *et al.* Results of the National Institute of Allergy and Infectious Diseases Collaborative Clinical Trial to test the predictive value of skin testing with major and minor penicillin derivatives in hospitalized adults. *Arch Intern Med* 1992;152:1025–1032.
4. Trubiano JA, Chen C, Cheng AC, Grayson ML, Slavin MA, Thursky KA. Antimicrobial allergy "labels" drive inappropriate antimicrobial prescribing: lessons for stewardship. *J Antimicrob Chemother* 2016;71:1715–1722.
5. Killgore KM, March KL, Guglielmo BJ. Risk factors for community-acquired ciprofloxacin-resistant *Escherichia coli* urinary tract infection. *Ann Pharmacother* 2004;38:1148–1152.
6. Hebert C, Ridgway J, Vekhter B, Brown EC, Weber SG, Robicsek A. Demonstration of the weighted-incidence syndromic combination antibiogram: an empiric prescribing decision aid. *Infect Control Hosp Epidemiol* 2012;33:381–388.
7. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;159:702–706.
8. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Statist Med* 2015;4:3661–3679.
9. Tingley D, Yamamoto T, Hirose K, Imai K, Keele L. Mediation: R package for causal mediation analysis. *J Statist Soft* 2014;59:1–38.
10. Bourke J, Pavlos R, James I, Phillips E. Improving the effectiveness of penicillin allergy de-labeling. *J Allerg Clin Immunol Pract* 2015;3: 365–374.

https://doi.org/10.1017/ice.2018.154 Published online by Cambridge University Press

# Spiking of intravenous bags does not cause time-dependent microbial contamination: a preliminary report

John G. Brock-Utne MD, PhD[1], Sara C. Smith MD[1], Niaz Banaei MD[2], Shao-Ching Chang MT[2], Diane Alejandro-Harper Cer AT, BS[1] and Richard A. Jaffe MD, PhD[1]

[1]Department of Anesthesiology, Stanford University School of Medicine, Stanford, California and [2]Department of Pathology, Stanford University School of Medicine, Stanford, California

(Received 18 January 2018; accepted 19 May 2018; electronically published July 2, 2018

As the result of an apparent misinterpretation of the United States Pharmacopeia (USP) Chapter 797 Standards for Pharmaceutical Compounding[1] by the Association for Professionals in Infection Control and Epidemiology (APIC),[2] the Joint Commission, without scientific evidence, is requiring that intravenous (IV) solution bags must be spiked no sooner than 1 hour before being connected to a patient to avoid contamination.

Recent studies have shown no growth in normal saline (NS) over a 4-hour period[3] and in lactated Ringer's (LR) over an 8-hour period[4] after spiking. Unfortunately, these short time intervals could not be used to support our longstanding hospital policy, which had permitted 24 hours of storage before discard or use. In addition, we wanted to extend the observation period to 9 days to maximize the probability of detecting even low-level microbial contamination. Finally, we wanted to verify that our protocol was sufficiently sensitive to detect a low level of contamination (0.1 CFU/mL) because previous studies have demonstrated that low levels of contamination can be difficult to detect.[5]

## Methods

Our anesthesia technologists spiked IV bags in the anesthesia workroom using our standard protocol. The technician removed each IV administration set (Codan US, Santa Ana, CA) from its sterile packaging using clean gloves, without masks or gowns. The plastic outer covering of the IV bags (Hospira, Lake Forest, IL) was removed, and the bags were hung on IV poles. Each IV bag administration port cover was removed, and the administration set spike was inserted into the IV bag in the usual manner. The end cap of the IV administration set was removed, and the roller clamp was opened. When fluid was seen emerging from the distal tip of the IV set, after all air bubbles had been removed, the fluid was stopped with the roller clamp and the end cap of the IV tubing was replaced. To avoid affecting standard procedure, the technologists were not informed about the study prior to bag spiking.

In the first part of the study, 25 one-liter bags of normal saline (NS) were spiked and placed in storage at room temperature in the anesthesia workroom. At 1 hour, 24 hours, 48 hours, 5 days, and 9 days, 5 bags were randomly selected and sampled for microbial contamination. At each time interval, 20-mL samples were collected after thorough mixing by repeatedly squeezing each bag immediately before sampling. All samples were taken from the rubber stopper on the IV bag after it was cleaned with alcohol. The stopper was allowed to dry completely before a sample was taken. Each 20-mL sample was divided equally and placed into 2 BACTEC Plus Aerobic/F blood culture vials (Becton Dickinson, Sparks, MD). The sample vials were transported to the clinical microbiology laboratory and incubated in the BACTEC FX blood culture system (Becton Dickinson). The vials were monitored for 5 days for growth of bacteria and fungi. Each culture vial contained a fluorescent chemical sensor to detect increases in carbon dioxide produced by the growth of microorganisms, including bacteria and fungi. Each vial was monitored every 10 minutes for an increase in fluorescence. A positive reading would indicate the presence of microorganisms. To confirm microbial growth in positive vials detected by the BACTEC system, smears were obtained and Gram stained. A subculture on media for isolation (ie, blood agar and chocolate agar) was used to identify any microbes detected by the BACTEC system. In the second part of the study, we added an additional 3 groups. Group 2 consisted of 5 bags of 5% dextrose in lactated Ringer's (D5LR), a chemically complex solution more vulnerable to microbial contamination and sustained growth, for comparison to NS group 1. We also wanted to have positive controls to verify that both NS and D5LR solutions could support readily detectable bacterial growth following low-level contamination (0.1 CFU/mL). Group 3 consisted of 5 bags of NS contaminated with *E. coli*, and group 4 consisted of 5 bags of D5LR contaminated with *E. coli*. Both groups 3 and 4 were inoculated with *E. coli* at time zero. *Escherichia coli* was selected as the positive control based on microbiology recommendation. Sampling protocol for part 2 was identical to the one used in part 1 described above. The contaminated bags were stored at room temperature in a private locked office in the hospital to eliminate any chance of cross-contamination.

## Results

At 1 hour and after 1, 2, 3, and 9 days in storage, no growth of bacteria or fungi was observed in any sample of group 1 (NS) or group 2 (D5LR) following 5 days of incubation under standard blood-culture conditions (Table 1). The positive control groups of NS (group 3) and D5LR (group 4) that were inoculated with *E. coli* all grew confirmed *E. coli* colonies at all sample times (Table 1). No other microorganisms were detected in either group. Unfortunately, the samples from group 3 (NS with *E. coli*) from day 9 were lost.

**Address for correspondence:** John G Brock-Utne MD, PhD, Stanford University Medical Center, 300 Pasteur Drive, Room H3580, Stanford, CA 94305-5640. E-mail: brockutn@stanford.edu

**Cite this article:** Brock-Utne JG, *et al.* (2018). Spiking of intravenous bags does not cause time-dependent microbial contamination: a preliminary report. *Infection Control & Hospital Epidemiology* 2018, 39, 1129–1130. doi: 10.1017/ice.2018.143

**Table 1.** Results of Microbial Growth for Each Study Group

| Study Group | Day 0 | Day 1 | Day 2 | Day 5 | Day 9 |
|---|---|---|---|---|---|
| Group 1 (NS) | No growth | No growth | No growth | No growth | No growth |
| Group 2 (D5LR) | No growth | No growth | No growth | No growth | No growth |
| Group 3 (NS with 100 CFU/L *E. coli*) | + Growth | + Growth | + Growth | + Growth | Lost data |
| Group 4 (D5LR with 100 CFU/L *E. coli*) | + Growth | + Growth | + Growth | + Growth | + Growth |

NOTE. NS, normal saline; D5LR, 5% dextrose in lactated Ringer's; CFU, colony-forming units; *E. coli, Escherichia coli.*

## Discussion

The widespread misinterpretation of USP 797 regarding contamination of IV bags 1 hour after spiking would mean that any sterile solution (and its administration set) would have to be disposed of every 60 minutes, a clearly untenable situation. In operating rooms and many other areas of the hospital, IV bags are spiked and readily available for prompt patient care and hospital efficiency. Indeed, requiring that a sterile solution be connected to a patient within one hour after spiking and then allowing that solution to be administered over many hours seems illogical unless connection to a patient somehow prevents contamination.

The USP chapter 797 is not vague regarding the context under which its standards apply. In the introduction to USP 797 it clearly states, "The standards in this chapter do not pertain to the *clinical administration* of compounded sterile preparations to patients …" Because clinical administration of a commercially prepared IV or arterial line flush solution requires spiking, USP 797 standards do not pertain in that circumstance (confirmed by personal communication from the USP Liaison Officer for Chapter 797).

Although our study was not powered to detect a truly rare event, it does demonstrate that under the standard nonsterile anesthesia workroom conditions in which our 40 NS and D5LR bags were spiked and stored, no unanticipated growth of bacteria or fungi could be detected at any time up to 9 days after spiking and nonsterile storage. A subsequent study of 400 spiked containers has been proposed that will provide sufficient power $(1-\beta=0.8)$ to detect a 0.5% contamination rate. More than 16,000 samples would be required to detect a 1 in 10,000 contamination rate, emphasizing the difficulty of proving no effect.

This study emphasizes the need for evidence-based decisions in all aspects of hospital management to ensure that the efficient delivery of high-quality healthcare is the highest priority. Arbitrary and unfounded time limitations on spiked intravascular fluids are an unnecessary compromise of efficiency without any evidence of improved patient safety. Although these non–evidence-based measures are well intentioned, in acute-care settings when timely intravascular access is crucial, these policies may not only be inefficient but, in fact, may also be detrimental to patient care.

**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.

## References

1. Pharmaceutical compounding—sterile preparations. In: *US Pharmacopeia*, chapter 797. Rockville, MD: The United States Pharmacopeia Convention; 2011.
2. Dolan SA, Felizerda G, Barnes S, *et al*. APIC position paper: safe injection, infusion, and medication vital practices in health care. *Am J Infect Control* 2010;38:167–172.
3. Stedman JL, Yarmush JM, Joshi MC, Kamath S, Schianodicola J. How long is too long? The prespiked intravenous debate. *Anesth Analg* 2017; 124:1564–1568.
4. Haas R, Beitz E, Reed A, *et al*. No bacterial growth found in spiked intravenous fluids over an 8-hour period. *Am J Infect Control* 2017;45:448–450.
5. Guynn JB, Poretz DM, Duma RJ. Growth of various bacteria in a variety of intravenous fluids. *Amer J Hosp Pharm* 1973;30:321–325.

https://doi.org/10.1017/ice.2018.154 Published online by Cambridge University Press

# Near-patient environmental contamination of an intensive care unit with Vancomycin-resistant Enterococci (VRE) and Extended-Spectrum Beta-Lactamase–Producing Enterobacteriaceae (ESBL-E) before and after the introduction of chlorhexidine bathing for patients

Hélène McDermott MD[1], Mairead Skally MSc[2], James O'Rourke FFARCSI[3], Hilary Humphreys MD[1,2] and Deirdre Fitzgerald-Hughes PhD[1]

[1]Department of Clinical Microbiology, Royal College of Surgeons in Ireland, Education and Research Centre, Beaumont Hospital, Dublin, Ireland, [2]Department of Microbiology, Beaumont Hospital, Dublin, Ireland and [3]Department of Anaesthesia, Beaumont Hospital, Dublin, Ireland

(Received 22 February 2018; accepted 24 May 2018; electronically published June 28, 2018

In the intensive care unit (ICU), prior room contamination by patients with, for example, vancomycin-resistant Enterococci (VRE), and extended-spectrum β-lactamase–producing Enterobacteriaceae (ESBL-E) is predictive for the acquisition of infections.[1] However, while daily chlorhexidine bathing reduces infection rates due to multidrug-resistant pathogens,[2] the effect of this practice on environmental contamination rates are largely unknown. Surveillance of the healthcare environment is usually only conducted in response to outbreaks along with other infection prevention and control (IPC) investigations and interventions.[3] This is largely due to resource constraints, the transient nature of environmental contamination, low yields from environmental screening, and culture delays, all of which preclude rapid decision making based on these results. In an observational study in a 12-bed adult medical/surgical ICU during non-outbreak periods, we assessed the overall bacterial contamination of near-patient surfaces of occupied beds, including VRE and ESBL-E, before and after the introduction of a chlorhexidine bathing protocol.

A total of 1,703 swabs (Copan E-swabs, Copan Diagnostics, Murrieta, CA) were taken from the immediate environment (within a ~1-m radius) of 157 ICU patients in seven 3-week intervals between October 2012 and June 2014. A chlorhexidine bathing protocol was introduced after period 4 (October 2013). For patient washing, 2% chlorhexidine gluconate cloths, (Sage Products, Cary IL) were universally adopted for use with 100% of ICU patients following a 1-month staff training period. In each 3-week period, 6 'high-touch' sites in occupied beds (Figure 1A) were swabbed twice weekly, as described previously.[4] For some patients, their environment was sampled more than once because their ICU stay exceeded 48 h and because some patients moved beds. Swabs were processed for identification of VRE and ESBL-E among Enterococci and Enterobacteriaceae as described previously.[4]

**Author for correspondence:** Dr Deirdre Fitzgerald-Hughes, Department of Clinical Microbiology, RCSI Education and Research Centre, Smurfit Building, Beaumont Hospital, Dublin 9, Ireland. E-mail: dfitzgeraldhughes@rcsi.ie

**Cite this article:** McDermott H, *et al.* (2018). Near-patient environmental contamination of an intensive care unit with Vancomycin-resistant Enterococci (VRE) and Extended-Spectrum Beta-Lactamase–Producing Enterobacteriaceae (ESBL-E) before and after the introduction of chlorhexidine bathing for patients. *Infection Control & Hospital Epidemiology* 2018, 39, 1131–1132. doi: 10.1017/ice.2018.146



Of 1,703 environmental swabs, 1,186 (70%) were positive for bacterial growth. In total, 176 of 1,186 (14.8%) were positive for *Enterococcus* spp, of which 61% were VRE, and 49 of 1,186 (4.1%) were Enterobacteriaceae, of which 20% were ESBL-E. Of the 1,703 sites sampled, 745 (43.7%) were taken before chlorhexidine bathing was introduced and 958 (56.3%) were taken after chlorhexidine bathing was introduced.

Following the introduction of chlorhexidine cloths for patient bathing, we observed a statistically significant reduction in overall contamination of the environment (74% before vs 62% after; $P = .0005$, Fisher's exact test) and in VRE/ESBL-E contamination (9.4% vs 5.0%; $P < .0001$). The distribution of VRE/ESBL-E between the surfaces sampled before and after chlorhexidine introduction is shown in Figure 1B. A statistically significant reduction in VRE/ESBL-E was observed for handwashing basins only. Cleaning practices, which involved sequential cleaning of patient bed spaces and general ICU areas with 1000 ppm sodium dichloroisocyanurate (Presept®, GS Medical, Dublin, Ireland), were unchanged before and after chlorhexidine bathing was introduced. Hand hygiene audits conducted over the periods in which sampling took place averaged $80.3 \pm 10.5\%$ before chlorhexidine bathing was introduced versus $85.5 \pm 6.5\%$ after chlorhexidine introduction, and the difference was not statistically significant ($P = .52$, unpaired $t$ test). Data from an ICU annual audit revealed a 15% increase in the number of patients admitted to the unit over the study period; bed-space occupancy increased from 98% to 110% and mean length of stay decreased from 7.0 to 6.3 days. Higher bed occupancy is reported to positively correlate with HCAI rates.[5,6] Therefore, the reduction in environmental contamination observed following the introduction of chlorhexidine bathing, despite increased pressure on the unit in terms of bed occupancy, is notable. Other potential confounders that may have affected ward activity in the 2 phases included ambient temperature (as a measure of seasonal alterations) and antibiotic consumption. The mean ambient monthly temperature recorded by the nearest weather station (<6 km) over the 2 sampling phases and available from the Irish meteorological service MetEireann[7] was lower after chlorhexidine bathing was introduced, but not significantly so ($7.9 \pm 0.47$°C vs $8.5 \pm 0.37$°C; $P = .70$). The ICU ambient temperature was constant between study phases (temperature, 22–24°C; humidity 30–60°C). In addition, ICU antibiotic

https://doi.org/10.1017/ice.2018.154 Published online by Cambridge University Press

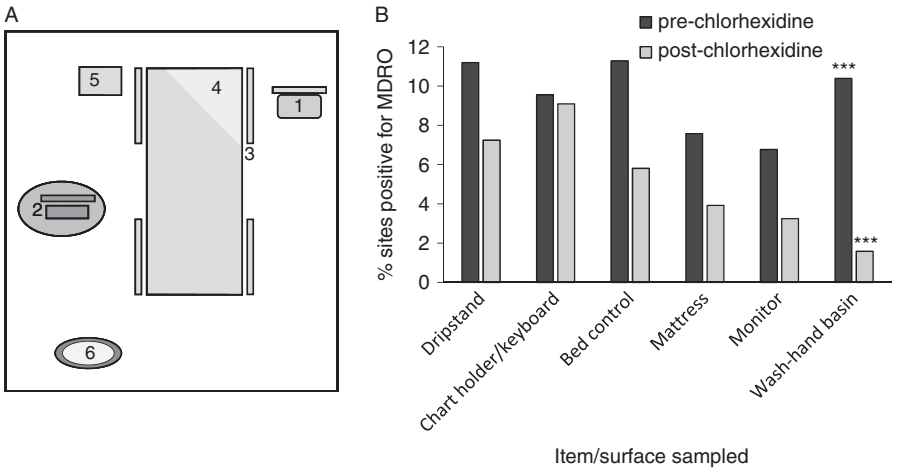


**Fig. 1.** Surface contamination with multidrug-resistant organisms (MDROs): vancomycin-resistant Enterococci or extended-spectrum β-lactamase–producing Enterobacteriaceae (VRE/ESBL-E). (A) Schematic of patient representative bed space indicating the 6 sampling points: (1) drip stand, (2) chart-holder/keyboard, (3) bed control, (4) mattress, (5) monitor, and (6) handwashing basin. For sampling of handwashing basins, those located in isolation rooms were sampled or the unit handwashing basin, if in the open plan area. (B) Percentage of sampled sites positive for VRE/ESBL-E, before and after the introduction of chlorhexidine wipes for patient bathing. Number of sites sampled = 745 before chlorhexidine bathing was introduced (63 VRE-positive, 7 ESBL-positive) and 958 after chlorhexidine introduction (45 VRE-positive, 3 ESBL-E positive). *** indicates statistical significance; *P* value <.005.

consumption, measured by total defined daily dose (DDD) over the 2 periods, indicated a 16% increase in the post-chlorhexidine phase (from 6,023 to 6,982), but the difference was not statistically significant ($P = .176$).

The microbiome of the ICU may be affected by factors including the patient cohort, changes in staff, the nature of and compliance with cleaning regimens, IPC policies, and seasonal changes in ward activity. The sampling periods investigated here can be regarded as 'snapshots' in time over 20 months based on environmental sampling of high-touch ICU surfaces.

Our study has several limitations. It was a single-center study, and the results may not be generalizable to other locations or populations. The before-and-after study design lacked a control for comparison. Also, we did not use molecular typing to characterize recovered bacteria, and the identification of environmental contamination was not linked to individual patients (eg, patients with incontinence/diarrhea) and their specific flora.

Patient chlorhexidine bathing has been reported to reduce acquisition of VRE, MRSA, and coagulase-negative staphylococcal bloodstream infection rates,[2] but few studies have investigated its potential impact on the healthcare environment. Of the 7 MDR organisms of major public health importance, VRE and ESBL-E were investigated here as target gram-positive and gram-negative MDR-pathogens due to the relatively high VRE rates in Ireland and the growing ESBL-E rates.[8] The small but significant reduction in contamination overall of the healthcare environment, but particularly the significant reduction in environmental VRE/ESBL-E found here, warrants further investigation.

**Acknowledgments.** The authors thank Ms Leah Gaughan, Antimicrobial Pharmacist, Beaumont Hospital, for providing antibiotic consumption data.

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

**Potential conflicts of interest.** H.H. has received research support from Pfizer and Astellas in recent years. He has also recently received lecture and other fees from Pfizer and AstraZeneca. All other authors report no conflicts of interest relevant to this article.

## References

1. Mitchell BG, Dancer SJ, Anderson M, Dehn E. Risk of organism acquisition from prior room occupants: a systematic review and meta-analysis. *J Hosp Infect* 2015;91:211–217.
2. Climo MW, Sepkowitz KA, Zuccotti G, *et al.* The effect of daily bathing with chlorhexidine on the acquisition of methicillin-resistant *Staphylococcus aureus,* vancomycin-resistant Enterococcus, and healthcare-associated bloodstream infections: results of a quasi-experimental multicenter trial. *Crit Care Med* 2009;37:1858–1865.
3. Dancer SJ. The role of environmental cleaning in the control of hospital-acquired infection. *J Hosp Infect* 2009;73:378–385.
4. McDermott H, Skally M, O'Rourke J, Humphreys H, Fitzgerald-Hughes D. Vancomycin-resistant Enterococci (VRE) in the intensive care unit in a nonoutbreak setting: identification of potential reservoirs and epidemiological associations between patient and environmental VRE. *Infect Control Hosp Epidemiol* 2018;39:40–45.
5. Borg MA, Waisfisz B, Frank U. Quantitative assessment of organizational culture within hospitals and its relevance to infection prevention and control strategies. *J Hosp Infect* 2015;90:75–77.
6. Humphreys H. Controlling the spread of vancomycin-resistant Enterococci. Is active screening worthwhile? *J Hosp Infect* 2014;88:191–198.
7. The Irish meterological service. MetEireann website. http://www.met.ie/climate. Accessed May 30, 2018.
8. Antimicrobial resistance surveillance in Europe 2015. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). European Centre for Disease Prevention and Control website. https://ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2015. Published 2016. Accessed May 30, 2018.

https://doi.org/10.1017/ice.2018.154 Published online by Cambridge University Press