Sites of Blood Collection and Topical Disinfectants Associated with Contaminated Cultures: An Ambidirectional Cohort Study

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Abstract

Background: We aimed to determine whether puncture sites for blood sampling and topical disinfectants are associated with rates of contaminated blood cultures in the emergency department (ED) of a single institution.

Methods: This single-center, ambidirectional cohort study of 548 consecutive patients ≥ 20 years old was performed in the ED of a university hospital in Japan over a 13-month period. Pairs of blood samples were collected for aerobic and anaerobic cultures from patients in the ED. Physicians selected puncture sites and topical disinfectants according to their personal preference.

Results: Potential contamination was identified in 110 of the 548 patients (20.1%). One hundred fourteen (20.8%) patients showed true-positive results for bacteremia and 324 (59.1%) patients showed true-negative results. Multivariate analysis revealed more frequent contamination when puncture sites were disinfected with povidone-iodine (PVI) than with alcohol/chlorhexidine (ACHX) (adjusted risk difference, 19.1%; 95% confidence interval [CI]), 15.7–22.6; P < 0.001). In terms of blood collection sites, femoral and central venous (CV) catheter with PVI disinfection showed more frequent contamination than venous sites with ACHX (adjusted risk differences: 26.6%, 95%CI 21.3–31.9, P < 0.001 and 41.1%, 95%CI 22.2–59.9, P < 0.001, respectively).

Conclusions: Rates of contaminated blood cultures were significantly higher when blood was collected from CV catheter or femoral sites with PVI as the topical disinfectant.

Background

Blood cultures are one of the most important tests to detect life-threatening bacteremia, which is associated with high mortality rates. Accurate diagnosis of cultured blood samples plays a crucial role in appropriate treatment. Contaminated blood cultures can result in unnecessary antibiotic use, unnecessarily long hospital stays, increased healthcare costs and, most importantly, an increased risk of antimicrobial resistance.[1,2] Several strategies have been proposed to reduce blood culture contamination. However, a meta-analysis has reported that only two methods can achieve this: sampling from a separate venipuncture site; or a well-trained phlebotomy team.[3] Although topical 1.0% alcohol/chlorhexidine gluconate (ACHX) reduces blood culture contamination more effectively than 10% aqueous povidone-iodine (PVI),[4,5] both agents are routinely applied at our institution as topical disinfectants before blood sampling. Rates of false-positive culture are significantly reduced when blood is sampled from various venipuncture sites compared with intravenous or central venous catheters.[6,7] Physicians at our institution may sample blood from various sites, such as intravenous and central venous catheters, as well as femoral arteries and veins, according to personal preference.

The emergency department (ED) is the frontline to investigate unwell patients, with blood culture contamination rates above the recommended 3%.[3,8] Our previous study for a period of 6 months revealed

that blood sampled from femoral arteries or veins and using PVI were associated with a significantly higher contamination rate in our ED.[9]

We thus aimed to investigate and validate in greater details which puncture sites for blood sampling and which topical disinfectants are associated with blood culture contamination in patients and samples from a single ED over a longer period.

Methods

Study design

This single-center, ambidirectional cohort study proceeded at the ED of a university hospital in Japan between August 1, 2018 and August 31, 2019. The hospital is an 882-bed university teaching hospital with 8,000 adults presenting to the ED annually. Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were used to design and report the results from this study.[10]

Ethics and Consent to Participate

The Institutional Review Board (IRB) at Osaka Medical College approved the study protocol (No. 675(2476)) and waived the need for written, informed consent. All investigations were carried out in accordance with relevant guidelines and regulations. The need for consent was waived by an IRB.

Patients

This study included 548 consecutive patients ≥ 20 years old from whom blood was sampled in the ED. Inclusion criteria were: age ≥ 20 years; and at least one pair of blood cultures collected in the ED. Patients were excluded if all blood samples were collected elsewhere. If one pair of blood samples was collected at our ED and another was collected elsewhere or no second pair was collected, then only the pair collected at our ED was analyzed. One or more of the following comorbidities of patients were recorded: malignancy, diabetes mellitus, hypertension, prior stroke, dementia, chronic renal insufficiency, liver cirrhosis and coronary artery disease.[11,12,13,14]

Death data were also analyzed in February 2021.

Blood cultures

Nurses and other medical staff at our institution are not permitted to collect blood for cultures. Only physicians, typically first- or second-year interns, are permitted to collect blood samples for blood culture in the ED.

Blood (14–20 mL) from peripheral veins or arteries was sampled for aerobic and anaerobic cultures (7–10 mL each) in BacT/Alert FA Plus and FN Plus resin bottles (bioMérieux Inc., Durham, NC, USA). Physicians selected the topical disinfectant such as 1% ACHX, 10% PVI, alcohol and others available in

the ED, according to their personal preferences. A blood culture was considered contaminated if one or more of the following organisms were identified in one of the two blood cultures: coagulase-negative staphylococci (CoNS), *Propionibacterium acnes*, *Micrococci*, *Corynebacteria*, *Bacillus* species other than *Bacillus anthracis*, or *Clostridium perfringens*.[7,15,16] Viridans group streptococci are regarded as contaminants based on the described criteria,[7,15] but are not considered as contaminants in our institute. Polymicrobial cultures showing a mixture of contaminant and true pathogens were regarded as contaminated.[14] A culture was defined as “negative” when bacterial growth was absent or when a bacterium was regarded by the attending microbiologist as having low pathogenicity. The source of infection was identified based on chart review with other cultures such as sputum, urine, ascites and so on, or with other modalities including ultrasonography, X-ray, computed tomography (CT), and magnetic resonance imaging (MRI). Details are described in Table 1.

Table 1
Characteristics of patients with blood cultures in the emergency department.

Characteristics of patients	True bacteremia		Contamination		True negative		P
	n = 114		n = 110		n = 324		
Mean age, y (SD)	72.6	(11.8)	74.3	(11.4)	67.3	(16.7)	< 0.001
Male sex, n (%)	64	(56.1)	75	(68.2)	189	(58.3)	0.126
Major comorbidities, n (%)							
Malignancy	50	(43.9)	40	(36.4)	124	(38.4)	0.473
Diabetes mellitus	26	(22.8)	25	(22.7)	58	(18.0)	0.383
Hypertension	41	(36.0)	43	(39.1)	80	(24.8)	0.005
Previous stroke	10	(8.8)	9	(8.2)	24	(7.4)	0.888
Chronic renal insufficiency	14	(12.3)	7	(6.4)	29	(9.0)	0.302
Liver cirrhosis	5	(4.4)	1	(0.9)	9	(2.8)	0.288*
Coronary artery disease	10	(8.8)	9	(8.2)	19	(5.9)	0.488
Dementia	7	(6.1)	13	(11.8)	21	(6.5)	0.153
Quick SOFA, n (%)							0.087
0	37	(32.5)	40	(36.4)	125	(38.6)	
1	33	(29.0)	41	(37.3)	114	(35.2)	
2	35	(30.7)	23	(20.9)	77	(23.8)	
3	9	(7.9)	6	(5.5)	8	(2.5)	
Origin of infection, n (%)							

SD, standard deviation; SOFA, sequential organ failure assessment

* Fisher's exact test was performed because of small numbers of patients in several cells. Other comparisons were analyzed using the χ^2 test and one-way analysis of variance.

Origin of infection means the cause of infection according to a medical chart review with several cultures and with diagnostic modalities.

Central nervous system includes meningitis, encephalitis and brain abscess. Pulmonary includes pneumonia, bronchitis, pleuritis and upper respiratory infection. Cardiovascular system includes endocarditis and pericarditis. Abdomen includes cholangitis, gastroenteritis, cancer of the gastrointestinal tract, hepatitis, cholecystitis, appendicitis and pancreatitis. Urinary tract includes pyelonephritis, cystitis and prostatitis. Skin includes decubitus, cellulitis, impetigo and erysipelas. Other or unknown includes febrile neutropenia, and cases where the source of infection cannot be identified.

Characteristics of patients	True bacteremia		Contamination		True negative		P
	n = 114		n = 110		n = 324		
Central nervous system	1	(0.9)	0	0.0	3	(0.9)	0.823*
Pulmonary	12	(10.5)	41	(37.3)	94	(29.0)	< 0.001
Cardiovascular system	6	(5.3)	0	0.0	2	(0.6)	0.003*
Abdomen	19	(16.7)	12	(10.9)	35	(10.8)	0.234
Urinary tract	47	(41.2)	13	(11.8)	53	(16.4)	< 0.001
Skin	6	(5.3)	9	(8.2)	9	(2.8)	0.283
Other or unknown	26	(22.8)	39	(35.5)	137	(42.3)	0.001
Death	37	(32.5)	35	(31.8)	99	(30.6)	0.92
Death within 30 days	11	(9.7)	5	(4.6)	34	(10.5)	0.169
SD, standard deviation; SOFA, sequential organ failure assessment							
* Fisher's exact test was performed because of small numbers of patients in several cells. Other comparisons were analyzed using the χ^2 test and one-way analysis of variance.							
Origin of infection means the cause of infection according to a medical chart review with several cultures and with diagnostic modalities.							
Central nervous system includes meningitis, encephalitis and brain abscess. Pulmonary includes pneumonia, bronchitis, pleuritis and upper respiratory infection. Cardiovascular system includes endocarditis and pericarditis. Abdomen includes cholangitis, gastroenteritis, cancer of the gastrointestinal tract, hepatitis, cholecystitis, appendicitis and pancreatitis. Urinary tract includes pyelonephritis, cystitis and prostatitis. Skin includes decubitus, cellulitis, impetigo and erysipelas. Other or unknown includes febrile neutropenia, and cases where the source of infection cannot be identified.							

Statistical analysis

Categorical variables are described as frequencies and percentages (%) and continuous variables are shown as mean with standard deviation (SD). Data were compared using one-way analysis of variance, the χ^2 test and Fisher's exact test, as appropriate. Differences in risk and robust 95% confidence intervals (CIs) of contamination according to sites and topical disinfectants were estimated using uni- and multivariate analyses with modified least-squares regression and a robust standard error estimator.[1718] The same patients were considered as a random effect in the above model. Age, sex and disease status were adjusted as confounders in multivariate analyses. Because blood can be sampled from few sites, we also included blood in five categories: CV catheter, blood sampled from a newly inserted central venous (CV) catheter; Femoral, blood sampled from the femoral artery or vein; Other, blood sampled from a newly inserted arterial catheter and implanted port; Venous, blood sampled from venipuncture without catheter insertion; and Venous catheter, blood sampled from a newly inserted venous catheter. Because

we did not have many topical disinfectants to assess, we included only PVI, ACHX and Other types (alcohol and benzalkonium) in analyses. We did not impute missing values. For all statistical investigations, values of $P < 0.05$ were taken as significant. All analyses were performed using STATA version 16.1 (Stata Corp., College Station, TX, USA).

Results

Baseline characteristics

We analyzed data from 548 patients and 1065 pairs of blood cultures between August 1, 2018, and August 31, 2019. A total of 155 (14.6%) potential contaminants from 110 patients (20.1%) were found in blood cultures, the most common of which was *Staphylococcus epidermidis* in 43 of the 155 blood samples (27.7%), followed by *S. hominis* in 20 samples (12.9%). Two patients (1.8%) had a mixture of true bacteremia and contaminating isolates. We identified true bacteremia in 114 patients (20.8%) and 226 blood samples (21.2%), with *Escherichia coli* as the most prevalent microorganism, in 57 of the 226 blood samples (25.2%). Cultured blood samples from 324 patients (59.1%) and 684 blood samples (64.2%) were identified as true negative. The most common source of infection in 47 patients (41.2%) with true bacteremia was urinary tract infection, whereas a pulmonary source was the most prevalent in 41 patients (37.3%) with contaminated cultures and 94 patients (29.0%) with true-negative cultures, respectively. These two sources significantly differed among the three groups (pulmonary and urinary tract; both $P < 0.001$). Only one pair of blood samples was cultured from 31 patients. Neither total number of deaths nor death within 30 days differed significantly between the three groups. Tables 1 and 2 show other baseline characteristics of the three groups of patients and blood cultures.

Table 2
Characteristics of blood cultures in the emergency department.

Characteristics of blood cultures	True bacteremia		Contamination		True negative		P
Site, n (%)	n = 226		n = 155		n = 684		
CV catheter	7	(3.1)	12	(7.7)	11	(1.6)	< 0.001
Venous catheter	11	(4.9)	1	(0.7)	45	(6.6)	0.004*
Other	9	(4.0)	3	(1.9)	19	(2.8)	0.512*
Venous	75	(33.2)	25	(16.1)	293	(42.8)	< 0.001
Femoral	124	(54.9)	114	(73.6)	316	(46.2)	< 0.001
Disinfectants, n (%)							
PVI	138	(61.1)	146	(94.2)	397	(58.0)	< 0.001
ACHX	84	(37.2)	8	(5.2)	261	(38.2)	< 0.001
Other types	4	(1.8)	1	(0.7)	26	(3.8)	0.054*
One pair	3	(1.3)	4	(2.6)	24	(3.5)	0.256*

ACHX, 1.0% alcohol/chlorhexidine gluconate; CV catheter, blood culture sample from a newly inserted central venous catheter; Femoral, blood culture sample from femoral artery or vein; Other types, alcohol and benzalkonium; Other (site), newly inserted arterial catheter or implanted port; PVI, 10% aqueous povidone-iodine; Venous, venipuncture without catheter insertion; Venous catheter, blood culture sample from newly inserted venous catheter.

* Fisher's exact test was performed because of small numbers of patients in several cells. Other comparisons were analyzed using the χ^2 test

Sites and topical disinfectants

Femoral arteries and veins tended to be sampled in most patients in all three groups, but at different ratios (Tables 1 and 2). Over 80% of blood samples from patients with contaminants were collected from femoral sites (mostly the femoral artery), whereas < 50% of blood samples from patients with negative cultures were collected from these sites. Blood sampled from a newly inserted central venous catheter conferred the greatest risk of contamination when taken as an independent factor. However, the number of samples was small (n = 31).

Topical disinfectants also differed significantly among groups (Table 2). Disinfection with PVI was performed for sites in > 90% of patients with contaminated blood cultures, compared with < 65% among patients in the other two groups. Other topical disinfectants comprising alcohol or benzalkonium are also shown in Table 2.

Proportion of contamination by sites and topical disinfectants

With reference to ACHX, univariate analysis using modified least-squares regression associated PVI and Other types with contamination (proportions of contamination associated with PVI, Other type or ACHX: 21.4% vs. 3.2% vs. 2.3%; risk difference, 19.1%; 95%CI 15.7–22.6, P < 0.001; 1.0%, 95%CI -5.5–7.4, P = 0.77, respectively). With reference to blood collected from venous catheters, univariate analysis using modified least-squares regression associated femoral sites, CV catheter, Other (including newly inserted arterial catheters as well as implanted ports), and venous venipuncture sites with contamination (proportions of contamination associated with femoral sites, CV catheter, Other, and venous venipuncture sites: 20.6%, 40.0%, 9.7% and 6.3%, respectively; risk difference, 18.8% (95%CI 14.0–23.6; P < 0.001), 38.2% (95%CI 20.3–56.2; P < 0.001), 9.7% (95%CI -3.1–18.9; P = 0.157), and 4.6% (95%CI 0.4–8.8; P = 0.032), respectively (Table 3).

Table 3
Univariate analysis using modified least-squares regression.

	Contaminants (%)	Risk difference	95%CI			P
Topical disinfectants						
PVI	21.4	19.1	15.7	–	22.6	< 0.001
Other types	3.2	1.0	-5.5	–	7.4	0.77
ACHX	2.3	Reference				
Blood sampling sites						
CV catheter	40.0	38.2	20.3	–	56.2	< 0.001
Other	9.7	7.9	-3.1	–	18.9	0.157
Femoral	20.6	18.8	14.0	–	23.6	< 0.001
Venous	6.3	4.6	0.4	–	8.8	0.032
Venous catheter	1.8	Reference				

ACHX, 1.0% alcohol/chlorhexidine gluconate; CI, confidence interval; CV catheter, blood culture sample from newly inserted central venous catheter; Femoral, blood culture sample from femoral artery or vein; Other, blood culture sample from newly inserted arterial catheter and implanted port; Other types, alcohol and benzalkonium; PVI, 10% aqueous povidone-iodine; Venous, venipuncture without catheter insertion; Venous catheter, blood culture sample from newly inserted venous catheter.

Using multivariate analysis, we assessed associations between sites and topical disinfectants with contamination. With reference to venous venipuncture sites and ACHX, PVI and femoral sites, and PVI and CV catheter were significantly associated with contamination (adjusted risk differences: 26.6% [95%CI 21.3–31.9; P < 0.001] and 41.1% [95%CI 22.2–59.9; P < 0.001], respectively). ACHX and Venous catheter, PVI and Venous catheter, and Other-type disinfectant and CV catheter were also associated with significantly decreased contamination, but the numbers of these combinations were 25, 29, and 1, respectively (Table 4).

Table 4
Multivariate analysis using modified least-squares regression.

	Risk difference	95% confidence interval			P
Explanatory Variable					
Disinfectants and blood sampling sites					
ACHX and Venous	Reference				
ACHX and Other	-0.2	-3.4	–	3.0	0.904
ACHX and Femoral	0.4	-3.1	–	3.9	0.815
ACHX and CV catheter	-2.4	-6.4	–	1.6	0.239
ACHX and Venous catheter	-2.7	-5.2	–	-0.2	0.035
PVI and Other	12.7	-3.2	–	28.6	0.118
PVI and Femoral	26.6	21.3	–	31.9	< 0.001
PVI and Venous	7.0	2.7	–	11.4	0.002
PVI and CV catheter	41.1	22.2	–	59.9	< 0.001
PVI and Venous catheter	0.6	-7.0	–	8.2	0.88
Other types and Other	-2.3	-5.7	–	1.1	0.194
Other types and Femoral	4.1	-9.4	–	17.6	0.55
Other types and Venous	-1.3	-4.8	–	2.2	0.457
Other types and CV catheter	-4.7	-7.9	–	-1.5	0.004
Other types and Venous catheter	-0.8	-5.7	–	4.0	0.736
Covariates					
Male (reference female)	1.2	-2.9	–	5.3	0.56
Age (per 10 years)	1.5	0.3	–	2.7	0.012

ACHX, 1.0% alcohol/chlorhexidine gluconate; CI, confidence interval; CV catheter, blood culture sample from newly inserted central venous catheter; Femoral, blood culture sample from femoral artery or vein; Other, blood culture sample from newly inserted arterial catheter and implanted port; Other types, alcohol and benzalkonium; PVI, 10% aqueous povidone-iodine; Venous, venipuncture without catheter insertion; Venous catheter, blood culture sample from newly inserted venous catheter.

Discussion

This single-center, ambidirectional cohort study found that blood samples collected from femoral areas and CV catheter insertion at the internal jugular vein disinfected with PVI were significantly associated

with contaminated blood cultures in the ED. As the previous study revealed, the most common source of infection among patients with true bacteremia was urinary tract infection, and most such patients had pyelonephritis.[9] In contrast, the most prevalent source of infection among patients with contamination was pulmonary disease, with most such patients having aspiration pneumonia, again similar to our previous study.[9] Mortality rates were not significantly different among contamination, true-negative results, and true bacteremia.

We also found that three combinations (femoral puncture site with PVI, CV catheter insertion at internal jugular vein with PVI, and venous venipuncture with PVI) comprised independent risk factors for blood culture contamination. Our previous study showed that the femoral site is unsuitable for blood cultures,[9] but this investigation suggested that the femoral site may be acceptable only if ACHX is used. Other disinfectants (alcohol or benzalkonium or both) might be effective to prevent contamination when blood samples were collected from the femoral site. However, the combination of the femoral site and ACHX should not be selected because this combination was only seen for 14 samples and the data were thus insufficient for reliable statistical analysis. Furthermore, as femoral sites are colonized more often than other sites[19], they are associated with catheter-related bloodstream infection.[20] Internal jugular sites were mostly chosen for CV catheter insertion at our hospital using PVI and this site has been confirmed to show a higher risk of contamination.[19,20] In addition, the CV catheter is not suitable as a route for blood culture sample compared with arterial lines or direct peripheral venipuncture.[21] The contamination rate in the present study was highest (40.0%) for the 30 blood samples collected from central catheters newly inserted into the internal jugular vein in the ED. However, this number was relatively low. Only one case of CV catheter insertion using alcohol was not contaminated and this combination was significantly less frequent than the combination of ACHX with venous venipuncture without catheter insertion. However, we should not use this combination, because only one case showed this combination and the data were thus insufficient for reliable statistical analysis. ACHX has been recommended when a CV catheter is inserted.[22]

Several reports have described associations between blood samples collected from newly inserted peripheral venous catheter and blood culture contamination.[23,24] According to those reports, collecting blood culture specimens through a newly inserted peripheral venous catheter increases the risk of contamination compared with venipuncture. Our results suggested that blood culture from a newly inserted peripheral venous catheter might be the best procedure to prevent blood culture contamination in the ED, and a review article also emphasized the need to balance the practical advantages of this method against the risk of increased contamination.[25]

Several reports have described associations between topical disinfectants and blood culture contamination.[26,27] A meta-analysis found that blood culture contamination was more significantly reduced by ACHX than by PVI.[4] However, physicians have tended to disinfect puncture sites with PVI more frequently than with ACHX at our hospital, for various reasons. First, physicians and ED staff are more familiar with PVI than with ACHX, because it has been applied as a skin disinfectant for many

years. Second, residents and medical students are not educated about blood culture procedures while at university.

Pneumonia was the most common illness among patients with contaminated and true-negative blood cultures. Several studies of patients with community-acquired pneumonia have found that blood cultures provide little diagnostic benefit.[28,29,30] One reason for the very high contamination rate at our hospital was the high proportion of blood samples collected from femoral areas disinfected with PVI. Blood samples should be cultured from selected immunocompromised patients, those with complicating urinary tract infection under antibiotic therapy at the time of blood collection, and patients with suspected endocarditis.[29,31]

Several strategies have been advocated to reduce rates of blood culture contamination. Sampling from various venipuncture sites, and reliance on a well-trained phlebotomy team can reduce these rates.[3] Furthermore, switching from PVI to ACHX or other topical disinfectants and informational intervention and feedback might reduce rates of blood culture contamination, even when physicians conduct phlebotomies.[32,33]

This study shows several limitations. Our patient cohort was not large and some parameters could not be conclusively determined. Nevertheless, specific injection sites and PVI were associated with significantly increased contamination rates. Some physicians were aware of this study proceeding within the ED and might have been more attentive when collecting blood than they might have been in wards. Physicians could select their preferred topical disinfectant for blood sampling, which also have represented a confounder, because many studies have associated contamination more with PVI than with ACHX. Blood collection sites prepared using the same disinfectant should be compared under the same conditions.

Conclusions

This single-center, ambidirectional cohort study found that femoral puncture sites and PVI as well as CV catheter insertion and PVI were independent risk factors for blood culture contamination. Newly inserted venous catheters with ACHX should be used to obtain blood samples to reduce culture contamination.

Abbreviations

ACHX
alcohol/chlorhexidine gluconate
ANOVA
one-way analyses of variance
CI
confidence interval
CT
computed tomography

CV
central venous
ED
emergency department
MRI
magnetic resonance imaging
PVI
povidone-iodine
SD
standard deviation
UTI
urinary tract infection

Declarations

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Authors' Contributions

Ko. O. designed the study and wrote the initial draft of the manuscript. Ka.O., D.N., Y.I., E.H., Y.S., and A.T. contributed to the analysis and interpretation of data and assisted in the preparation of the manuscript. All authors contributed to data collection and interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ICMJE Statement

All authors meet the ICMJE authorship criteria.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

We have no conflicts of interest to disclose.

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References

1. Dempsey C, Skoglund E, Muldrew KL, Garey KW. Economic health care costs of blood culture contamination: A systematic review. *Am J Infect Control*. 2019;000. doi:10.1016/j.ajic.2018.12.020
2. Alahmadi YM, Aldeyab MA, McElnay JC, et al. Clinical and economic impact of contaminated blood cultures within the hospital setting. *J Hosp Infect*. 2011;77(3):233–236. doi:10.1016/j.jhin.2010.09.033
3. Snyder SR, Favoretto AM, Baetz RA, et al. Effectiveness of practices to reduce blood culture contamination: a Laboratory Medicine Best Practices systematic review and meta-analysis. *Clin Biochem*. 2012;45(13–14):999–1011. doi:10.1016/j.clinbiochem.2012.06.007
4. Caldeira D, David C, Sampaio C. Skin antiseptics in venous puncture-site disinfection for prevention of blood culture contamination: systematic review with meta-analysis. *J Hosp Infect*. 2011;77(3):223–232. doi:10.1016/j.jhin.2010.10.015
5. Marlowe L, Mistry RD, Coffin S, et al. Blood culture contamination rates after skin antisepsis with chlorhexidine gluconate versus povidone-iodine in a pediatric emergency department. *Infect Control Hosp Epidemiol*. 2010;31(2):171–176. doi:10.1086/650201
6. Norberg A, Christopher NC, Ramundo ML, Bower JR, Berman SA. Contamination rates of blood cultures obtained by dedicated phlebotomy vs intravenous catheter. *JAMA*. 2003;289(6):726–729. http://www.ncbi.nlm.nih.gov/pubmed/12585951.
7. Hall KK, Lyman JA. Updated review of blood culture contamination. *Clin Microbiol Rev*. 2006;19(4):788–802. doi:10.1128/CMR.00062-05
8. Bool M, Barton MJ, Zimmerman PA. Blood culture contamination in the emergency department: An integrative review of strategies to prevent blood culture contamination. *Australas Emerg Care*. 2020;23(3):157–165. doi:10.1016/j.auec.2020.02.004
9. Ota K, Oba K, Fukui K, et al. Sites of blood collection and topical antiseptics associated with contaminated cultures: prospective observational study. *Sci Rep*. 2021;11(1):1–6. doi:10.1038/s41598-021-85614-7
10. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Int J Surg*. 2014;12(12):1495–1499. doi:10.1016/j.ijsu.2014.07.013
11. Schellevis FG, van der Velden J, van de Lisdonk E, van Eijk JT, van Weel C. Comorbidity of chronic diseases in general practice. *J Clin Epidemiol*. 1993;46(5):469–473. http://www.ncbi.nlm.nih.gov/pubmed/8501473.

12. García-Olmos L, Salvador CH, Alberquilla Á, et al. Comorbidity patterns in patients with chronic diseases in general practice. *PLoS One*. 2012;7(2):e32141. doi:10.1371/journal.pone.0032141
13. Prados-Torres A, Calderón-Larrañaga A, Hancco-Saavedra J, Poblador-Plou B, van den Akker M. Multimorbidity patterns: a systematic review. *J Clin Epidemiol*. 2014;67(3):254–266. doi:10.1016/j.jclinepi.2013.09.021
14. Lee C-C, Lee N-Y, Chuang M-C, Chen P-L, Chang C-M, Ko W-C. The impact of overcrowding on the bacterial contamination of blood cultures in the ED. *Am J Emerg Med*. 2012;30(6):839–845. doi:10.1016/j.ajem.2011.05.026
15. Bekeris LG, Tworek JA, Walsh MK, Valenstein PN. Trends in blood culture contamination: a College of American Pathologists Q-Tracks study of 356 institutions. *Arch Pathol Lab Med*. 2005;129(10):1222–1225. doi:10.1043/1543-2165(2005)129[1222:TIBCCA]2.0.CO;2
16. Lee CC, Lin WJ, Shih HI, et al. Clinical significance of potential contaminants in blood cultures among patients in a medical center. *J Microbiol Immunol Infect*. 2007;40(5):438–444. http://www.ncbi.nlm.nih.gov/pubmed/17932605.
17. Hagiwara Y, Fukuda M, Matsuyama Y. The Number of Events per Confounder for Valid Estimation of Risk Difference Using Modified Least-Squares Regression. *Am J Epidemiol*. 2018;187(11):2481–2490. doi:10.1093/aje/kwy158
18. Cheung YB. A modified least-squares regression approach to the estimation of risk difference. *Am J Epidemiol*. 2007;166(11):1337–1344. doi:10.1093/aje/kwm223
19. Gowardman JR, Robertson IK, Parkes S, Rickard CM. Influence of insertion site on central venous catheter colonization and bloodstream infection rates. *Intensive Care Med*. 2008;34(6):1038–1045. doi:10.1007/s00134-008-1046-3
20. Lorente L, Jiménez A, Iribarren JL, Jiménez JJ, Martín MM, Mora ML. The micro-organism responsible for central venous catheter related bloodstream infection depends on catheter site. *Intensive Care Med*. 2006;32(9):1449–1450. doi:10.1007/s00134-006-0266-7
21. Stohl S, Benenson S, Sviri S, et al. Blood cultures at central line insertion in the intensive care unit: comparison with peripheral venipuncture. *J Clin Microbiol*. 2011;49(7):2398–2403. doi:10.1128/JCM.02546-10
22. Marschall J, Mermel LA, Fakih M, et al. Strategies to Prevent Central Line–Associated Bloodstream Infections in Acute Care Hospitals: 2014 Update. *Infect Control Hosp Epidemiol*. 2014;35(7):753–771. doi:10.1086/676533
23. Norberg A, Christopher NC, Ramundo ML, Bower JR, Berman SA. Contamination Rates of Blood Cultures Obtained by Dedicated Phlebotomy vs Intravenous Catheter. *J Am Med Assoc*. 2003;289(6):726–729. doi:10.1001/jama.289.6.726
24. Self WH, Speroff T, McNaughton CD, et al. Blood culture collection through peripheral intravenous catheters increases the risk of specimen contamination among adult emergency department patients. *Infect Control Hosp Epidemiol*. 2012;33(5):524–526. doi:10.1086/665319

25. Ombelet S, Barbé B, Affolabi D, et al. Best Practices of Blood Cultures in Low- and Middle-Income Countries. *Front Med*. 2019;6(June):131. doi:10.3389/fmed.2019.00131
26. Benjamin RJ, Dy B, Warren R, Lischka M, Eder AF. Skin disinfection with a single-step 2% chlorhexidine swab is more effective than a two-step povidone-iodine method in preventing bacterial contamination of apheresis platelets. *Transfusion*. 2011;51(3):531–538. doi:10.1111/j.1537-2995.2010.02868.x
27. Yasuda H, Sanui M, Abe T, et al. Comparison of the efficacy of three topical antiseptic solutions for the prevention of catheter colonization: a multicenter randomized controlled study. *Crit Care*. 2017;21(1):320. doi:10.1186/s13054-017-1890-z
28. Benenson RS, Kepner AM, Pyle DN, Cavanaugh S. Selective use of blood cultures in emergency department pneumonia patients. *J Emerg Med*. 2007;33(1):1–8. doi:10.1016/j.jemermed.2006.12.034
29. Coburn B, Morris AM, Tomlinson G, Detsky AS. Does this adult patient with suspected bacteremia require blood cultures? *JAMA*. 2012;308(5):502–511. doi:10.1001/jama.2012.8262
30. Long B, Koyfman A. Best Clinical Practice: Blood Culture Utility in the Emergency Department. *J Emerg Med*. 2016;51(5):529–539. doi:10.1016/j.jemermed.2016.07.003
31. Spoorenberg V, Prins JM, Opmeer BC, de Reijke TM, Hulscher MEJL, Geerlings SE. The additional value of blood cultures in patients with complicated urinary tract infections. *Clin Microbiol Infect*. 2014;20(8):O476-9. doi:10.1111/1469-0691.12491
32. Roth A, Wiklund AE, Pålsson AS, et al. Reducing blood culture contamination by a simple informational intervention. *J Clin Microbiol*. 2010;48(12):4552–4558. doi:10.1128/JCM.00877-10
33. Gibb AP, Hill B, Chorel B, Brant R. Reduction in blood culture contamination rate by feedback to phlebotomists. *Arch Pathol Lab Med*. 1997;121(5):503–507. http://www.ncbi.nlm.nih.gov/pubmed/9167605.