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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE TRADEMARK TRIAL AND APPEAL BOARD

Proceeding	91206212
Party	Plaintiff Carefusion 2200, Inc.
Correspondence Address	JOSEPH R DREITLER DREITLER TRUE LLC 19 E KOSSUTH STREET COLUMBUS, OH 43206 UNITED STATES mtrue@ustrademarklawyer.com, jdreitler@ustrademarklawyer.com, ttro-fino@ustrademarklawyer.com
Submission	Opposition/Response to Motion
Filer's Name	Joseph R. Dreitler
Filer's e-mail	jdreitler@ustrademarklawyer.com, mtrue@ustrademarklawyer.com, ttro-fino@ustrademarklawyer.com
Signature	/Joseph R. Dreitler/
Date	06/25/2015
Attachments	Amended Notice of Reliance with Motion and attachments (part 1).pdf(4545878 bytes) Amended Notice of Reliance with Motion and attachments (part 2) (compressed).pdf(1622902 bytes) Art25.pdf(56694 bytes)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE TRADEMARK TRIAL AND APPEAL BOARD

IN THE MATTER OF Trademark Application Serial Nos. 85/499349; 85/499345; 85/499337 and 85/499332

DATE OF PUBLICATION: May 29, 2012

CareFusion 2200, Inc., **Opposer,** **v.** **Entrotech Life Sciences, Inc.,** **Applicant.**	**Combined Opposition No. 91206212**

RESPONSE TO APPLICANT'S MOTION TO STRIKE OPPOSER'S NOTICE OF RELIANCE ON CERTAIN PRINTED PUBLICATIONS AND MOTION FOR LEAVE TO FILE AMENDED NOTICE OF RELIANCE

Opposer CareFusion 2200, Inc. ("Opposer"), by and through counsel, responds to Applicant's Motion to Strike [Dkt. 60] Opposer's Notice of Reliance [Dkt. 42] by seeking leave to file the attached Amended Notice of Reliance that corrects the procedural defects raised in Applicant's Motion to Strike.

Dated: June 25, 2015

Respectfully submitted,

/Joseph R. Dreitler/
Joseph R. Dreitler
Mary R. True
Dreitler True LLC
19 E. Kossuth St.
Columbus, OH 43206
Telephone: 614-449-6677
jdreitler@ustrademarklawyer.com
mtrue@ustrademarklawyer.com

Attorneys for Opposer

CERTIFICATE OF SERVICE

I hereby certify that on June 25, 2015, a copy of the foregoing was served both via email at hickey@fr.com and via First Class U.S. Mail upon the following attorney for Applicant:

Erin M. Hickey, Esq.
Fish & Richardson
12390 El Camino Real
San Diego, CA 92130

/Joseph R. Dreitler/
Joseph R. Dreitler

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
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AMENDED NOTICE OF RELIANCE

Pursuant to Rule 704.08 of the Trademark Trial and Appeal Board Manual of Procedure and 37 C.F.R. § 2.122(e), Opposer CareFusion 2200, Inc. ("Opposer"), by and through counsel, hereby gives notice of its intention to rely upon the attached articles, clinical study and trial results, and bibliographies, all of which are available to the general public, in support of its case:

1. Chambers CE, Eisenhauer MD, McNicol LB, Block PC, Phillips WJ, Dehmer GJ, Heupler FA, Blankenship JC. "Infection Control Guidelines for the Cardiac Catheterization Laboratory: Society Guidelines Revisited." Catheterization and Cardiovascular Interventions 67:78-86 (2006)
2. Garcia, Robert, Gayle K. Mulberry, Ann R. Brady, John S. Hibbard. "Comparison of ChloraPrep and Betadine as preoperative skin preparation antiseptics." Poster presented at: 40th Annual Meeting of the Infectious Disease Society of America, Chicago, IL (October 25, 2002)

3. Bhutta, Adnan, Craig Gilliam, Michele Honeycutt, Stephen Schexnayder, Jerril Green, Michele Moss, KJS Anand. “Reduction of bloodstream infections associated with catheters in paediatric intensive care unit: stepwise approach.” BMJ 334:362-65 (17 February 2007)
4. Weinstein, Robert A. “Nosocomial Infection Update.” Emerging Infectious Diseases Volume 4, Number 3 (July-September 1998)
5. Crosby, Cynthia T., Alicia K. Mares. “Skin Antisepsis Past, Present, and Future.” Journal of Vascular Access Devices 1-6 (Spring 2001)
6. Ryder, Marcia. “Evidence-Based Practice in the Management of Vascular Access Devices for Home Parenteral Nutrition Therapy.” Journal of Parenteral and Enteral Nutrition Vol. 30, No. 1, Supplement:82-93 (2006)
7. Tepus, Dwayne, Sandra R. Cox, Susan Hazelett. “The Effectiveness of Chloraprep™ in the Reduction of Blood Culture Contamination Rates in the Emergency Department.” Journal of Nursing Care Quality Vol. 23, No. 3:272-6 (July-September 2008)
8. Garcia R., L. Jendresky, S. Landesman, A. Maher, F. Nicolas. “Three Years Experience in Implementing Hicpac Recommendations for the Reduction of Central Venous Catheter-Related Bloodstream Infections.” Managing Infection Control 10:42-49 (2003)
9. Hibbard, John S., Gayle K. Mulberry, Ann R. Brady. “A Clinical Study Comparing the Skin Antisepsis and Safety of ChloraPrep, 70% Isopropyl Alcohol, and 2% Aqueous Chlorhexidine.” Journal of Infusion Nursing Vol. 25, No. 4:244-49 (July/August 2002)
10. Onder, Ali Mirza, Jayanthi Chandar, Anthony Billings, Rosa Diaz, Denise Francoeur, Carolyn Abitbol, Gaston Zilleruelo. “Chlorhexidine-based antiseptic solutions effectively reduce catheter-related bacteremia.” Pediatric Nephrology 24:1741-47 (2009)

11. “ChloraPrep highly effective for presurgical pathogen removal.” Law & Health Weekly (2005)
12. “ChloraPrep provides non-linting application.” Pharma Law Weekly (2005)
13. “Availability of preoperative antibacterial skin preparation announced.” Food & Drug Law Weekly (2005)
14. Scales, Katie. “Correct use of chlorhexidine in intravenous practice.” Nursing Standard Vol. 24, No. 8:41-46 (Oct 28-Nov 3, 2009)
15. Zinn, Jennifer, Jeanne B. Jenkins, Vangela Swofford, Beverly Harrelson, Sharon McCarter. “Intraoperative Patient Skin Prep Agents: Is There a Difference?” Association of Perioperative Registered Nurses Journal Vol. 92, No. 6:662-74 (December 2010)
16. “Superior antibacterial activity in surgical skin preparation.” Critical Care Nurse Vol. 26, No. 4:56-57 (August 2006)
17. Shaffer, Virginia Oliva, Caitlin D. Baptiste, Yuan Liu, Jahnavi K. Srinivasan, John R. Galloway, Patrick S. Sullivan, Charles A. Staley, John F. Sweeney, Joe Sharma, Theresa W. Gillespie. “Improving Quality of Surgical Care and Outcomes: Factors Impacting Surgical Site Infection after Colorectal Resection.” The American Surgeon Vol. 80, No. 8:759-63 (August 2014)
18. Darouiche, Rabih O., Matthew J. Wall, Jr., Kamal M.F. Itani, Mary F. Otterson, Alexandra L. Webb, Matthew M. Carrick, Harold J. Miller, Samir S. Awad, Cynthia T. Crosby, Michael C. Mosier, Atef AlSharif, David H. Berger. “Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis.” The New England Journal of Medicine 362, 1:18-26 (January 2010)

19. Adams, D., M. Quayum, T. Worthington, P. Lambert, T. Elliott. “Evaluation of a 2% chlorhexidine gluconate in 70% isopropyl alcohol skin disinfectant.” Journal of Hospital Infection 61, 287-290 (2005)
20. Barenfanger, Joan, Cheryl Drake, Jerry Lawhorn, Steven J. Verhulst. “Comparison of Chlorhexidine and Tincture of Iodine for Skin Antisepsis in Preparation for Blood Sample Collection.” Journal of Clinical Microbiology Vol. 42, No. 5:2216-2217 (May 2004)
21. Berenholtz, Sean M., Peter J. Pronovost, Pamela A. Lipsett, Deborah Hobson, Karen Earsing, Jason E. Farley, Shelley Milanovich, Elizabeth Garrett-Mayer, Bradford D. Winters, Haya R. Rubin, Todd Dorman, Trish M. Perl. “Eliminating catheter-related bloodstream infections in the intensive care unit.” Critical Care Medicine Vol. 32, No. 10:2014-2020 (2004)
22. Fauerbach, LL, C Ruse, MA Gross, R Kelly, D Danek, L Larson, J Janelle. “Continuing Evolution of Multidisciplinary Approach to Prevention of Central Line-Associated Bacteremias.” American Journal of Infection Control Vol. 32, No.3:40-41 (May 2004)
23. Taylor, Beth A. “Cutting surgical-site infection rates for pacemakers and ICDs.” Nursing2006 Vol. 36, No. 3:18-19 (March 2006)
24. Wilkins, Mona, Sheryl Kempin, Linda Laukaitis. “2% Chlorhexidine Gluconate in 70% Isopropyl Alcohol Donor Arm Scrub Validation.” Presented at: The American Association of Blood Banks Annual Meeting; Abstract No. SP57, Baltimore, MD (October 22-26, 2004)

The foregoing are being submitted and relied upon to show the widespread recognition of ChloraPrep within the national medical community, the unique advantages of using ChloraPrep, with its active ingredient of chlorhexidine, prior to, during, and after medical procedures, and the great value of and goodwill associated with the ChloraPrep product.

Dated: June 25, 2015

Respectfully submitted,

/Joseph R. Dreitler/
Joseph R. Dreitler
Mary R. True
Dreitler True LLC
19 E. Kossuth St.
Columbus, OH 43206
Telephone: 614-449-6677
jdreitler@ustrademarklawyer.com
mtrue@ustrademarklawyer.com

Attorneys for Opposer

Catheterization and Cardiovascular Interventions 67:78–86 (2006)

Core Curriculum

Infection Control Guidelines for the Cardiac Catheterization Laboratory: Society Guidelines Revisited

Writing Committee Members: Charles E. Chambers,*† MD, FSCAI, Michael D. Eisenhauer,† MD, FSCAI, Lynn B. McNicol, BSN, MPH, Peter C. Block,† MD, FSCAI, William J. Phillips, MD, FSCAI, Gregory J. Dehmer, MD, FSCAI, Frederick A. Heupler,† MD, James C. Blankenship,† MD, FSCAI, and the Members of the Catheterization Lab Performance Standards Committee for the Society for Cardiovascular Angiography and Interventions

In the early years of diagnostic cardiac catheterization, strict sterile precautions were required for cutdown procedures. Thirteen years ago, when the original guidelines were written, the brachial arteriotomy was still frequently utilized, femoral closure devices were uncommon, "implantables," such as intracoronary stents and PFO/ASD closure devices, were in their infancy, and percutaneous valve replacement was not a consideration. In 2005, the cardiac catheterization laboratory is a complex interventional suite with percutaneous access routine and device implantation standard. Despite frequent device implantation, strict sterile precautions are often not observed. Reasons for this include a decline in brachial artery cutdown, limited postprocedure follow-up with few reported infections, limited use of hats and masks in televised cases, and lack of current guidelines. Proper sterile technique has the potential to decrease the patient infection rate. Hand washing remains the most important procedure for preventing infections. Caps, masks, gowns, and gloves help to protect the patient by maintaining a sterile field. Protection of personnel may be accomplished by proper gowning, gloving, and eye wear, disposal of contaminated equipment, and prevention and care of puncture wounds and lacerations. With the potential for acquired disease from blood-borne pathogens, the need for protective measures is as essential in the cardiac catheterization laboratory as is the standard Universal Precautions, which are applied throughout the hospital. All personnel should strongly consider vaccination for hepatitis B. Maintenance of the cardiac catheterization laboratory environment includes appropriate cleaning, limitation of traffic, and adequate ventilation. In an SCAI survey, members recommended an update on guidelines for infection control in the cardiac catheterization laboratory. The following revision of the original 1992 guidelines is written specifically to address the increased utilization of the catheterization laboratory as an interventional suite with device implantation. In this update, infection protection is divided into sections on the patient, the laboratory personnel, and the

This document was approved by the Society for Cardiovascular Angiography and Interventions Executive Committee in September 2005.

*Correspondence to: Dr. Charles E. Chambers, Hershey Medical Center, 500 University Drive H047, Division of Cardiology Hershey, PA 17033. E-mail: cchambers@psu.edu

†In accordance with the policy of the Journal, the designated authors disclose a financial or other interest in the subject discussed in this article.

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laboratory environment. Additionally, specific CDC recommendation sections highlight recommendations from other published guidelines.

Key words: cardiac catheterization; coronary intervention; adverse effects; quality control; laboratory infection; device infection

INTRODUCTION

In the evolving environment of the cardiac catheterization laboratory, the sterile techniques of the 1970s, typical of those in an operating suite, became less prevalent in the 1990s. Rigorous postprocedure follow-up to track infectious complications is now uncommon and only catastrophic events are noted. Brachial artery cutdown is rarely performed, disposable one-time use equipment is standard, and major symposia often broadcast physicians as moderators on camera rather than surgeons operating in a sterile field. However, as advances in technology are made, there are reasons to believe more rigorous sterile techniques are necessary. Implantable devices such as percutaneous heart valves, septal closure devices, femoral access closure devices, and vascular stent grafts are making it difficult to distinguish a cardiac catheterization suite and a surgical suite. With these advances, a reevaluation of infection control guidelines in the cardiac catheterization laboratory is appropriate.

The Laboratory Performance Standards Committee of the Society for Cardiovascular Angiography and Interventions (SCAI) published the first guidelines for infection control in the cardiac catheterization laboratory in 1992 [1]. To reassess the need for updated guidelines, SCAI conducted a survey of its membership regarding infection control issues in the cardiac catheterization laboratory. Approximately 20% of the membership responded, with the majority being directors of catheterization laboratories (Table I). Significant infections requiring extended admission, readmission, surgical procedure, or death were reported by 36% of the respondents. Only 60% had written infection control policies in place, and nearly 80% of responders requested publication of revised infection control guidelines for the cardiac catheterization laboratory infection control.

When the last guidelines were published, there were limited data describing the frequency, prevention, and outcome of nosocomial infections in the cardiac catheterization laboratory. The reported incidence of all catheter-related infections was $< 1\%$, but this assessment was based only on retrospective studies [2]. A major problem with tracking the incidence of such events is the 5- to 10-day delay between the procedure and the development of common signs or symptoms of infection. Therefore, such retrospective studies may, and likely do, underestimate the incidence of infectious complications.

Since the publication of the last guidelines, several studies have addressed the occurrence of infection in the cardiac catheterization laboratory. In a series of over 22,000 patients undergoing invasive, nonsurgical, coronary procedures from 1991 to 1998, bacterial infections occurred in 0.11% at a median of 1.7 days after the procedure [3]. In over 4,000 patients undergoing coronary intervention, bacterial infections occurred in 0.64% and septic complications occurred in 0.24% [4]. Ramsdale et al. [5] obtained blood cultures in 147 consecutive patients undergoing complex PCI. Positive blood cultures were found in 18% immediately after the procedure and in 12% at 12 hr after the procedure, but no clinical sequela was seen. Case reports have described both intracoronary stent and vascular closure device infection, with both significant morbidity and mortality reported [6,7].

Despite these reports, recommendations for specific sterile techniques in the cardiac catheterization laboratory are still hampered by the lack of supporting prospective trials. With the potential for acquired diseases such as HIV and hepatitis, the use of protective measures by all cardiac catheterization laboratory personnel is required by the standard Universal Precautions applied throughout the hospital [8]. Additionally, standard precautions applicable for infection prevention in surgical wounds may logically be applied to wounds produced in the cardiac catheterization laboratory. Among the types of procedures currently performed in the cardiac catheterization laboratory, most can be classified somewhere between the initial insertion of a central line and an actual surgical incision with primary closure.

The limited published literature as well as the other credible sources utilized in revising these recommendations will be referenced when appropriate. Specifically, several articles deserve notation for their specific value. In 2003, the AHA published a scientific statement regarding nonvalvular cardiovascular device-related infection [2]. In 2002, the Centers for Disease Control (CDC) published guidelines for prevention of intravascular catheter-related infections, which are now considered the best clinical practice guidelines [9]. Other recent guidelines, including those on the prevention of surgical site infection [10], hand hygiene in healthcare settings [11], and environmental infection control in healthcare facilities [12], contain recommendations relevant to the cardiac catheterization laboratory.

Throughout this document, applicable statements from these guidelines are listed separately under the heading "CDC recommendations."

Though not differentiated here, the CDC recommendations in their publications are classified as either "strongly recommended for implementation or strongly supported

TABLE I. SCAI Member Survey: Infection Control in the Cardiac Catheterization Laboratory

Members Responded (337/1768)	Number of Responses	Response Rate
1. IN WHAT COUNTRY DO YOU PRACTICE MEDICINE?		
United States	259	76.85%
2. For the catheterization laboratory, are you in a position to establish policy (e.g., director or other policymaker role)?		
Yes	240	71%
No	98	29%
3. Is there a standard written practice regarding infection control in your lab?		
Yes	201	59%
No	88	26%
DK	54	16%
4. During all invasive procedures in the lab, do you routinely wear:		
a cap or head covering?	269	80%
a facemask?	276	82%
eye protection?	274	81%
5. Are your lab table setups required to be completed by staff wearing cap, mask, gown, and gloves and practicing sterile techniques?		
Yes	250	74%
No	84	25%
DK	5	1%
6. Is air exchange rate in your cath lab satisfactory?		
Yes	207	61%
No	34	10%
DK	98	29%
7. Have you seen or heard of any serious documented infectious complications following a procedure in your lab, i.e. requiring extended admission, readmission, surgical procedure, or death?		
Yes	114	34%
No	224	66%
8. In the current era of implantable devices, do you think strict (O.R. style) sterile technique is an important issue in the catheterization/interventional lab?		
Yes	226	67%
No	45	13%
Maybe	67	20%
9. Do you think that SCAI and ACC should have a specific policy regarding infection control that is communicated via educational conferences or videotaped procedures?		
Yes	265	79%
No	19	6%
Maybe	53	16%

by well-designed experimental, clinical, or epidemiologic studies'' or ''strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies, and a strong theoretical rationale.'' Further information regarding the CDC guidelines can be found at http://www. cdc.gov/ncidod/hip.

These SCAI guidelines are presented as recommendations to assist cardiac catheterization laboratory directors and managers in establishing laboratory policy. The society recognizes the importance of local expertise from individual laboratory supervisory personnel in establishing specific policies for any individual cardiac catheterization laboratory.

SECTION I: PATIENT PREPARATION AND PROTECTION

A. Hair Removal

Consideration should be made to avoid hair removal unless it directly interferes with the procedure. If it is necessary to remove hair at the access site, use a clipper or depilatory on the day of the procedure, and not before. Shaving with a razor should be avoided because it can injure the skin and increase the risk of infection [13,14]. Literature in this area is limited to hair removal before surgical procedures. Lazenby et al. [15] reviewed 1,980 consecutive adults undergoing open heart surgery and found an increased incidence of suppurative mediastinitis manually shaving compared to electric shaving.

Clipping the day before the procedure should be avoided, because it can be associated with dermal abrasions that could be a nidus for local infection [16]. Depilatories sometimes will produce hypersensitivity reactions, so the cardiac catheterization laboratory staff should be observant for these types of complications.

CDC recommendations. Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation [10].

If hair is removed at an access site immediately before a procedure, it is preferable to use electric clippers or a depilatory cream [10].

B. Skin Cleaning

The skin at the cutdown or puncture site should be thoroughly cleaned. Immediately before the procedure, a broad-spectrum antimicrobial agent should be generously applied, in accordance with manufacturer's recommendations [17].

CDC recommendations. A 2% chlorhexidine-based preparation (e.g., Chloraprep) for skin antisepsis is preferred during central line insertion, but tincture of iodine (an iodophor) or 70% alcohol may be substituted [9].

Allow the antiseptic to remain on the insertion site (do not swab excess) and air-dry before catheter insertion when possible. Povidine iodine is most effective when allowed to remain on the skin for at least 2 min or longer if it is not yet dry [9].

For patient skin preparation in the operating room, iodophors, alcohol-containing products, and chlorhexidine gluconate (CHG) are most commonly used. CHG achieved both a greater reduction in skin microflora and had a greater residual activity after a single application when compared with providine-iodine. Further, CHG is not inactivated by blood or serum protein, whereas iodophors may be [10]. CHG is bacteriostatic and effective as long as it is present on the skin.

C. Drapes

Nonporous drapes should be used to cover the area surrounding the wound [14]. Maximum sterile barrier precautions should be utilized during catheter insertion. The sterile sheet should be large enough to cover the entire patient and any other hardware attached to the table that could come in contact with long catheter or wires. Any adhesive material attached to the skin around the wound and to the drapes should isolate the wound site from the surrounding unprepared skin.

CDC recommendations. Use surgical drapes that remain effective barriers when wet (i.e., materials that resist liquid penetration) [10].

Use aseptic technique, including the use of a cap, mask, sterile gown, sterile gloves, and a large sterile sheet, for the insertion of central venous catheters (including peripherally inserted central catheter (PICCs)) or guidewire exchange [9].

D. Antibiotics

Antimicrobial drug prophylaxis is not routinely recommended for procedures performed in the cardiac catheterization laboratory. In fact, prophylaxis is generally not indicated for "clean" surgery unless it involves implantation of certain prosthetic material [18]. Antibiotic prophylaxis should be considered for the immunocompromised patients and for any patient with probable or definite wound contamination during the procedure [19].

If an antibiotic is used prophylactically, the activity should be against common skin organisms. A cephalosporin with a moderately long serum half-life, such as cefazolin, is a common drug of choice before the catheterization procedure [18]. A single dose of parenteral antimicrobial given within 30 min of device insertion usually provides adequate tissue concentration for several hours. This is common practice for device insertions, such as in patent foramen ovale closures.

A patient with an active bacterial infection at a site remote from a surgical wound has a greater risk of wound infection than an uninfected patient. This risk may be reduced by treating the remote infection before an invasive procedure is performed [14]. While this applies to bacterial infections, the approach for local fungal infections is less well defined. In these instances, avoidance of the infected site when possible or aggressive local skin cleaning is standard practice.

CDC recommendations. Antibiotic prophylaxis is not routinely indicated for a sterile procedure, such as cardiac catheterization. In the rare circumstance when it is indicated, selection of the antibiotic agent should be based on its efficacy against most common skin pathogens [10].

In most instances, when a prophylactic antibiotic is used, it should be given 30–60 min before the procedure [10].

Whenever possible, identify and treat all infections remote to the surgical site before an elective operation; postpone elective procedures until the infection has resolved [10]. If a fluroquinolone or vancomycin is chosen, it should be given 120 minutes before the procedure [10a].

E. Catheterization Technique

Prolonged procedures and lapses in aseptic technique are important causes of wound infections [14]. Care should be taken to prevent large hematomas, which serve as a nidus for infection [14]. Although no data exist on the performance of cardiac catheterizations or coronary interventions in a febrile patient, those with ongoing infections should be appropriately treated before an elective cardiac catheterization. Fever is a relative contraindication for an elective cardiac catheterization. The risks versus benefits of performing urgent invasive procedures on a febrile patient must be weighed individually.

The choice of the access site is an issue if a second percutaneous procedure is performed shortly after the first. Local infection at the puncture site is more likely to occur after early repuncture of the ipsilateral femoral artery [20]. If a PCI procedure is performed after a 6-hr delay following a diagnostic catheterization, the operator should consider contralateral access for the PCI.

With advances in femoral and radial percutaneous access, brachial artery cutdown is now an infrequent method for artery access in patients undergoing cardiac catheterization. One study demonstrated a 10-fold increase in infectious complication with this approach [2]. If used, infection control precautions for cutdown procedures should be more rigorous than percutaneous procedures and should be similar to those used for any minor surgical procedure.

F. Sheath Removal and Vascular Closure Devices

Vascular access sheaths are routinely removed following diagnostic procedures but not infrequently left in place following femoral interventional procedures. When this is necessary, a standard wound-dressing protocol should be followed, similar to that for other indwelling vascular catheters. For in-dwelling venous catheters, the duration of the catheter placement is the most important predictor for an infection [21]. Therefore, it is prudent to remove any in-dwelling sheath or catheter as early as clinically appropriate. When clinically indicated, a catheter and rarely even a sheath may be maintained for a period of days following the

procedure. In this circumstance, appropriate wound dressings and daily wound inspections are critical.

Multiple vascular closure devices (VCDs) are available for establishing hemostasis following femoral artery access. While these devices are designed to eliminate the need for manual compression and allow for earlier ambulation postprocedure, they have not been shown to decrease vascular complications [2,6 7,22]. Vascular closure devices are used in many diagnostic catheterization laboratories and in approximately 40% of patients undergoing PCI in the National Cardiovascular Data Registry (NCDR) data registry. Occasionally, the complication with VCD is more severe than with manual compression [23]. One of the most significant of these is infection of the suture or collagen anchor leading to arteritis [24]. These complications occur in 0.5% of VCD procedures and can be limb- and life-threatening [2].

Special precautions may be warranted in patients receiving a VCD. Antibiotic coverage for common skin flora is recommended for the diabetic patient undergoing VCD placement [2].

These devices should be avoided when arterial puncture is into a preexisting synthetic vascular graft, if local or systemic infection is a possibility, or if the sheath has been in-dwelling for an extended period of time [7]. Following prolonged procedures, consideration should be given to site recleaning as well as new sterile gloves for the operator before VCD placement. The presence of a hematoma before placement of a VCD may increase the incidence of infection [22]. When sutures are involved, these should be cut so the ends retract well below the skin and a topical triple antibiotic cream applied to the puncture site. The patient should be instructed to avoid tub baths until the skin puncture site is healed and to report early any groin complications or signs of infection. A pseudoaneurysm following a closure device should be considered a possible early sign of infection and thus treatment by local injection of prothrombotic agents used with caution [22].

G. Wound Dressings

Although more applicable for prolonged use, occlusive nonpermeable plastic dressings should be avoided because they increase the infection risk two- to fourfold compared with traditional gauze dressings [25].

CDC recommendations. Use either a sterile gauze or sterile and transparent semipermeable dressing to cover the catheter site. Do not use nonpermeable (plastic) dressings [9].

If the patient is diaphoretic, or if the site is bleeding or oozing, a gauze dressing is preferable to a transparent semipermeable dressing [9].

Topical antibiotic ointments or creams promote fungal infections and antibiotic resistance. They should therefore be avoided except with dialysis catheters [9].

SECTION II: LABORATORY PERSONNEL—THE PRIMARY OPERATOR AND STAFF

A. Hand Scrub and Gloves

Hand washing is the single most important procedure for preventing nosocomial infections [11]. An operator should start the day in the laboratory with a hand scrub of at least 2 or 3 min, utilizing a sterile surgical scrub brush impregnated with detergents and a topical antiseptic agent that has a persistent chemical effect. For subsequent cases, it is best to avoid repeated scrubbing, which may irritate the skin and increase the likelihood of dermal abrasions. It is preferable to use an antiseptic solution or foam before subsequent procedures. All rings and bracelets should be removed before scrubbing. Ideally, fingernails should not extend past the fingertips and should be kept free of fingernail polish and artificial coverings.

Two types of agents are commonly used for hand washing: detergents (plain soap) and antiseptics. The primary action of plain soap and water is to remove viable noncolonizing organisms physically from the skin surface [26]. Antiseptic agents have additional important properties. No definitive clinical trial has yet conclusively demonstrated the effects of hand washing with an antiseptic agent on nosocomial infection rates.

The use of antiseptic hand scrubs is nearly universal in the operating room environment [10,11]. All agents have a bactericidal effect, killing and/or inhibiting growth of both ''normal flora'' of the skin as well as more virulent bacteria. Some antiseptics bind to the skin, resulting in persistent chemical activity that inhibits proliferation of organisms within the moist environment of rubber or plastic gloves [26]. Brushless, waterless scrubs containing alcohol are often preferred because of less hand irritation, increased efficacy, and immediate bactericidal activity.

Gloves should be applied in a sterile manner. They should be changed if a puncture occurs or blood is detected under the gloves during the procedure. As noted previously, surgical hand antisepsis using either an antimicrobial soap or an alcohol-based hand rub, with persistent activity, is recommended before donning sterile gloves.

Damage to physician gloves was evaluated in one study during cardiac catheterization [27]. No punctures were detected in 25 pairs of unused control gloves, but 19% of 200 gloves worn during procedures had small punctures. The thumb and index finger were the sites of 81% of the punctures; this was attributed to glove

trauma from manipulation of stopcocks. Therefore, consideration should be given to the use of double gloves when an operator has hand abrasions.

CDC recommendations. Observe proper hand hygiene procedures either by washing hands with conventional antiseptic-containing soap or with waterless alcohol gels or foams. Observe hand hygiene before and after palpating catheter insertion sites, as well as before and after inserting, replacing, accessing, repairing, or dressing an intravascular catheter [9].

When performing surgical hand antisepsis using an antimicrobial soap, scrub hands and forearms for the length of time recommended by the manufacturer, usually [2–5] min. Long scrub times (e.g., 10 min) are not necessary [10,11].

Scrub hands with brushes only once per day; subsequent procedures require only repeated antiseptic foam/gel hand washing [11].

When using an alcohol-based surgical hand scrub product with persistent activity, follow the manufacturer's instructions. Before applying the alcohol solution, prewash hands and forearms with a nonantimicrobial soap and dry completely. After application of the alcohol-based product as recommended, allow hands to dry thoroughly, approximately 15 to 25 seconds, before donning sterile gloves [11].

Remove debris from underneath fingernails using a nail cleaner under running water before scrubbing the hands with either a brush or antiseptic gel or foam [11].

B. Gowns and Shoe Covers

The operator should wear a nonporous gown to prevent the contamination that occurs when porous cloth gowns become wet with blood or other fluids. The operator should wear a scrub suit or other clean hospital uniforms, and not street clothes, in the cardiac catheterization laboratory. There are no scientific data to support the role of shoe covers in preventing surgical wound infections. However, they may provide protection to laboratory personnel and are commonly used to prevent tracking contaminated fluids throughout the facility by soiled footwear.

CDC recommendations. No recommendations exist on how or where to launder scrub suits, restricting the use of scrub suits to the operating suite, or for covering scrubs when out of the operating suite [10].

Change scrub suits that are visibly soiled, contaminated, and/or penetrated by blood or other potentially infectious materials [10].

Shoe covers are not required solely to prevent a surgical site infection, but are required by Occupational Safety and Health Administration (OSHA) if soiling of shoes is likely, in order to reduce contamination of other areas of the healthcare facility (i.e., room-to-room transmission) [8].

C. Caps, Masks, and Eye Protection

Although masks protect the operator's mucous membranes from contamination by a patient's body fluids, the effect of caps and masks on the incidence of infection in the cardiac catheterization laboratory is unclear. Caps and mask are standard attire in a surgical suite, but there are diverse opinions and only limited data regarding their benefit in the cardiac catheterization laboratory. A study by Laslett and Sabin [28] of 504 patients undergoing diagnostic cardiac catheterization or electrophysiology studies found no difference in infection rate, with or without caps and masks. Banai et al. [29] prospectively studied 960 patients undergoing cardiac catheterization using standard patient preparation and operator hand scrub, gloves, and gown but without a cap and mask. The four clinically significant bacteremic episodes documented after the procedure appeared to be related to intravenous lines rather than the cardiac procedure. However, given the small size of these studies and the low overall incidence of infection, these studies are likely underpowered to assess the potential association between procedure-related infections and operator use of caps and masks.

Because of the risk associated with exposure to blood-borne pathogens, the use of Universal Precautions, as applied throughout the hospital, are relevant to healthcare providers in the cardiac catheterization laboratory [8]. The operator is provided personal protection by following these precautions that include the wearing of a mask, eye protection, gloves, and nonporous gown. Therefore, it is recommended that all personnel exposed to bodily fluids in the cardiac catheterization laboratory use Universal Precautions.

Since the incidence of infections related to procedures in the cardiac catheterization laboratories is low, it is unlikely an adequately powered randomized study of caps and masks will ever be performed. However, the consequences from such infections are significant while the risk of using these precautions is nonexistent [2]. Therefore, it is the recommendation of these guidelines that the use by the operator(s) of a cap, mask, and eye protection be strongly considered, if not mandatory, for all procedures performed in the cardiac catheterization laboratory for the protection of the operator.

If an operator does not use a cap and mask routinely, they should at least be used for procedures in patients who are at increased risk for both an infection as well as for a serious complication, should one develop. Such patients include those with native valve disease or intracardiac prostheses, arterial access performed through a femoral arterial graft, prolonged catheter or procedure times, prolonged use of an in-dwelling sheath following the procedure, intra-aortic balloon pump insertion, per-

cutaneous valvular procedures, and the use of implantable devices such as stents, septal closure devices, and/or VCDs. It may not always be known at the start of the procedure if one of these higher-risk situations will occur. Accordingly, each facility should consider the best policy for their laboratory, with patient safety given the highest priority.

CDC recommendations. Use aseptic technique, including the use of a cap, mask, eye protection, sterile gown, and sterile gloves, for the insertion of catheters or for guidewire exchange. Maximum sterile barrier precaution is required during catheter insertion. The operator should ensure that assistants also use maximal barriers [9].

D. Ancillary Personnel

Technicians, nurses, and any other personnel in the catheterization laboratory should wear scrub suits, cap, mask, and gloves when they assist within the sterile field of the procedure. All should wear eye protection with proper splash protection [8]. Circulators should wear scrub suites and, as all should, observe Universal Precautions. Visitors in the laboratory should wear either a scrub suit or other appropriate available attire over their street clothes and should remain an acceptable distance from the table as to avoid potential contamination of either the patient or the equipment.

E. High-Risk Patients (for Staff Exposure)

As discussed earlier, the potential for acquired diseases from blood-borne pathogens exists for all invasive procedures. Since screening for blood-borne pathogens is not routinely performed before referral to the cardiac catheterization laboratory, it should be assumed that every patient has the potential to transmit an infectious agent. This reinforces the need to apply Universal Precautions, used throughout the hospital, in the cardiac catheterization laboratory [8]. However, some patients referred for cardiac catheterization laboratory will be known to carry HIV or the hepatitis virus. If Universal Precautions are followed, there is no reason such patients should be managed differently.

Since the hands of the operator are most likely to come in contact with blood, some operators choose to wear two pairs of gloves when it is known that a patient has a blood-borne infection. Little is known about the adequacy of available sterile gloves, but some operators claim that 2% of gloves leak even before they are used. More is known regarding the integrity of gloves during surgical procedures. In a study by Gerberding et al. [30], 17.5% of gloves developed a perforation during surgery. Wearing two pairs of gloves reduced the chances of a puncture hole in the inner glove by 60%. Though this practice has not been proven to prevent transmission of hepatitis or HIV, it seems prudent to use this technique when the operator is working with high-risk patients.

The active disposal of contaminated fluids into an open container, such as emptying a syringe or flushing a catheter, increases the risk of accidental spilling or splashing. This is prevented by discarding fluid through the manifold via an extra port that contains a one-way valve to a disposal bag. This constitutes a closed system within the manifold.

F. Skin Puncture or Laceration

Any person who suffers a puncture or laceration with a contaminated needle or blade in the catheterization laboratory should report this incident immediately to their supervisor. Each laboratory should have a protocol for the management of such events, which includes evaluation by a physician, baseline HIV, hepatitis B, and hepatitis C testing of both the patient and the person who received the puncture, along with follow-up HIV and hepatitis testing at regular intervals following the exposure. Tetanus vaccination should be updated if greater than 10 years since the last vaccination. The Centers for Disease Control has published guidelines for the management of occupational exposure to blood-borne pathogens [31]. An overview of these recommendations is provided in Table II.

G. Vaccination

Vaccination for hepatitis B virus should be strongly considered, if not mandatory, for all operators and other personnel who work in the cardiac catheterization laboratory [32].

SECTION III: LABORATORY ENVIRONMENT

A. Cleaning

The laboratory should be completely cleaned once a day and spot-cleaned between each case. The floor should be wet-mopped or wiped if gross spillage is evident. Trash should be removed between each case [10].

CDC recommendations. After the last catheterization procedure of the day or night, wet-vacuum or mop the cardiac laboratory room floors with a single mop and an EPA-registered hospital disinfectant [10].

No conclusive recommendations are available regarding the disinfecting of surfaces or equipment between cases in the absence of visible soiling [10].

B. Air Vents

The air vents should be cleaned at least monthly. The ventilation system should ideally provide at least 15 air exchanges per hour of which at least three should be fresh air [10,12].

TABLE II. Management of Occupational Exposure to HBV, HCV, and HIV

I. Definition: Direct contact with blood or body fluids including percutaneous injury, contact of mucous membranes, or skin contact, especially if abraded.

II. Procedure:

A) Clean site of exposure with soap and copious amounts of water; flush mucous membrane with large quantities of water.

B) Victim should report incident promptly, including patient/source information.

C) Provide wound care and review with victim tetanus and Hepatitis B prophylaxis information.

D) Counsel and obtain consent for HIV testing from both victim and patient/source.

E) Order the following laboratory specimen with appropriate consent obtained.

1) Victim
- Hepatitis C antibody
- Hepatitis B surface antibody
- HIV 1–2

2) Patient/Source
- ETPE Panel (Hepatitis B surface antigen and core antibody, Hepatitis C antibody, ALT, RPR, HTLV 1–2)

F) Review Hepatitis B vaccination and response status of victim and follow post exposure prophylaxis to Hepatitis B protocol.

G) If patient/source is Hepatitis C seropositive or has elevated ALT, follow-up should include:

1) Follow post exposure prophylaxis to Hepatitis B protocol.

2) Follow up for anti-HIV therapy per protocol.

3) Schedule Hepatitis C and HIV testing for 6 weeks, 3 months, 6 months.

H) Proper documentation and appropriate reference to CDC Guidelines recommended.*

*Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post-exposure Prophylaxis. Center for Disease Control and Prevention; Morbidity and Mortality Weekly Report: June 29, 2001/Vol. 50/No. RR-11, 1-52. (Ref #23).

C. Maintenance of Environment

The doors to the catheterization laboratory should be kept closed, except as necessary for passage of equipment, personnel, and the patient [12]. After a catheterization procedure has started, the number of personnel allowed to leave or enter should be kept to a minimum.

D. Fixed and Disposable Laboratory Equipment

Single-use disposable catheters are the current standard for the majority of equipment utilized in the catheterization laboratory. Standard techniques should be employed to ensure proper sterilization of equipment that is reused. Reuse of equipment should be limited to only that currently permitted by federal regulations [33]. Equipment near the catheter entry site, which has the potential for blood contamination, such as foot switches, should be covered.

Suture material should be fine and monofilament, rather than thick or braided, and a minimal amount of sutures should be used [14]. Multidose vials should be avoided because of the potential for contamination. All containers of contrast material and flush solutions that are used for one procedure should be changed for the following patient, unless an approved device that is protected against backflow is used with an aim toward contrast conservation.

E. Disposal of Waste

Blood-contaminated drapes, gowns, gloves, and sponges should be discarded in special containers and labeled as healthcare waste. Needles and blades should be placed in puncture-proof containers [8].

CONCLUSIONS

In the current cardiac catheterization laboratory environment, procedure-related infections are uncommon and probably underreported. Although multiple guidelines are available for infection control in the healthcare setting, data directly applicable to the cardiac catheterization laboratory are limited. Since the SCAI first published infection control guidelines for the catheterization laboratory in 1992, significant changes, including a marked increase in device implantation, have occurred. The society's updated guidelines provide useful recommendations to assist cardiac catheterization personnel in updating or establishing infection control policies for their own institution.

REFERENCES

1. Heupler FA, Heisler M, Keys TF, et al. Infection prevention guidelines for cardiac catheterization laboratories. Cathet Cardiovasc Diagn 1992;25:260–263.
2. Baddour LM, Bettmann MA, Bolger AF, et al. Nonvalvular cardiovascular device-related infections. Circulation 2003;108: 2015–2031.
3. Munoz P, Blanco JR, Rdoriguez-Creixems M, et al. Blood stream infections after invasive nonsurgical cardiology procedures. Arch Intern Med 2001;161:2110–2115.
4. Samore MH, Wessolossky MA, Lewis SM, et al. Frequency, risk factors, and outcome for bacteremia after percutaneous transluminal coronary angioplasty. Am J Cardiol 1997;79:873–877.
5. Ramsdale D, Aziz S, Newall N, et al. Bacteremia following complex percutaneous coronary intervention. J Invas Cardiol 2004;16:632–634.
6. Bouchart F, Dubar A, Bessou JP, et al. Pseudomonas aeruginosa coronary stent infection. Ann Thorac Surg 1997;64:1810–1813.

7. Carey D, Martin JR, Moore CA, et al. Complications of femoral artery closure devices. Catheter Cardiovasc Interv 2001;52:3–8.
8. Department of Labor, Occupational Safety and Health Administration. Occupational exposure to blood borne pathogens: final rule. Fed Reg 1991;56:64004–64182.
9. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. MMWR Recomm Rep 2002;51(RR-10):1–29.
10. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for the prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999;20:247–280.

10a. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis 2004;38:1706–1715.

11. Boyce JM, Pittet D, et al. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. MMWR Recomm Rep 2002;51(RR-16):1–45.
12. Sehulster L, Chinn RY. CDC; HICPAC. Guidelines for environmental infection control in health-care facilities. Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC). MMWR Recomm Rep 2003;52(RR-10):1–42.
13. Alexander JW, Fischer JE, Boyajian M, et al. The influence of hair-removal methods on wound infections. Arch Surg 1983;118: 347–352.
14. Center for Infectious Diseases, Centers for Disease Control, Public Health Service, U.S. Department of Health and Human Services. Guideline for prevention of surgical wound infections, 1985, revised by Garner JS. Atlanta, GA: U.S. Department of Health and Human Services.
15. Lazenby KW, Zelano JA, Isom OW, et al. Effects of shaving methods and intraoperative irrigation on suppurative mediastinitis after bypass operation. Ann Thorac Surg 1991;53:301–305.
16. Olson MM, MacCallum J, McQuarrie DG. Preoperative hair removal with clippers does not increase infection rate in clean surgical wounds. Surg Gynecol Obstet 1986;162:181–182.
17. Rutala WA. APIC guidelines for infection control practice: APIC guideline for selection and use of disinfectants. Am J Infect Control 1996;24:313–342.
18. Medical Letter on Drugs and Therapeutics. Antimicrobial prophylaxis in surgery. Med Lett 1989;12:105–108.
19. Dellinger EP, Gross PA, Barrett TL, et al. Quality standard for antimicrobial prophylaxis in surgical procedures. Clin Infect Dis 1994;18:422–427.
20. Wiener RS, Ong LS. Local infection after percutaneous transluminal coronary angioplasty: relation to early repuncture of ipsilateral femoral artery. Cathet Cardiovasc Diagn 1989:16:180–181.
21. Polanczyk CA, Rohde LE, Goldman L. Right heart catheterization and cardiac complications in patients undergoing noncardiac surgery: an observational study. JAMA 2001:286:309–314.
22. Toursarkissian B, Mejia A, Smilanich RP, Shireman PK, Sykes MT. Changing patterns of access site complications with the use of percutaneous closure devices. Vasc Surg 2001;35:203–206.
23. Samal AK, White CJ. Percutaneous management of access site complications. Catheter Cardiovasc Interv 2002;57:12–23.
24. Cooper CL, Miller A. Infectious complications related to the use of the angio-seal hemostatic puncture closure device. Catheter Cardiovasc Interv 1999;48:301–303.
25. Corona ML, Peters SG, Narr BJ, et al. Subspecialty clinics: critical-care medicine. Mayo Clin Proc 1990;65:979–986.
26. Larson E. APIC guidelines for infection control practice: guideline for use of topical antimicrobial agents. Mundelein, IL: APIC National Office.
27. Palmisano JM, Meliones JN. Damage to physicians' gloves during ''routine'' cardiac catheterization: an underappreciated occurrence. J Am Coll Cardiol 1989;14:1527–1529.
28. Laslett LJ, Sabin A. Wearing of caps and masks not necessary during cardiac catheterization. Cathet Cardiovasc Diagn 1989;17: 158–169.
29. Banai S, Selitser V, Keren A, et al. Prospective study of bacteremia after cardiac catheterization. Am J Cardiol 2003;92:1004–1007.
30. Gerberding J, Littell C, Tarkington A, et al. Risk of exposure of surgical personnel to patients' blood during surgery at San Francisco General Hospital. N Engl J Med 1990;322:1788–1793.
31. U.S. Public Health Service. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. MMWR Recomm Rep. 2001;50(RR-11):1–52.
32. Protection against viral hepatitis. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR Recomm Rep 1990;39(RR-2):1–26.
33. Feigal DW. Reprocessing of single-use devices: letter in attachment on reprocessing of single use medical devices by hospitals, from Center for Devices and Radiologic Health, U.S. Food and Drug Administration. Infect Control Hosp Epidemiol 2000;21:801–804.

#100698

COMPARISON OF CHLORAPREP® AND BETADINE® AS PREOPERATIVE SKIN PREPARATION ANTISEPTICS

Robert Garcia, B.S., M.T. (ASCP), CIC[1], Gayle K. Mulberry, M.S.[2], Ann R. Brady, A.S.[2], and John S. Hibbard, Ph.D.[3]

1. Enhanced Epidemiology, Inc., Valley Stream, NY; 2. Hill Top Research, Inc., Cincinnati, Ohio; 3. J & A Companies, L.L.C., Overland Park, Kansas

ABSTRACT

Introduction: Research has shown that bacteria from patients' skin are a primary source of surgical wound infections[1]. This trial assessed the immediate and persistent antimicrobial activity of a new topical antiseptic, ChloraPrep (2% chlorhexidine gluconate + 70% isopropyl alcohol (CHG+IPA)), compared with Betadine (10% povidone iodine (PI)).

Methods: This comparative trial randomized 55 subjects to skin preparation with CHG+IPA or PI on shaved abdominal and inguinal sites. Baseline microbial counts for inclusion were $\geq 2.5 \log_{10}$ colony forming units CFU/cm^2 on abdominal skin and $\geq 4.0 \log_{10}$ CFU /cm^2 on inguinal skin. Efficacy was assessed at 10 minutes, 24 and 48 hours and defined as a $\geq 2.0 \log_{10}$ mean reduction in CFU/cm^2 on abdominal skin and a $\geq 3.0 \log_{10}$ mean reduction on inguinal skin 10 minutes post prep.

Results: Baseline microbial counts were not statistically different across treatments ($p \geq 0.05$). On the abdomen, both antiseptics produced statistically significant ($p=0.0001$) reductions vs baseline in CFU/cm^2 of skin. Both preps met the FDA performance criteria on the abdomen. CHG+IPA demonstrated significantly greater antimicrobial activity on the abdomen compared to PI at 48 hours ($p=0.02$). On the groin, CHG+IPA produced significant reductions in CFU vs baseline (≥3logs, $p=0.0001$), but PI failed to meet the minimal 3-log reduction required by FDA for a patient preoperative skin antiseptic at 10 minutes. CHG+IPA demonstrated significantly greater antimicrobial activity on the groin compared with PI at 10 minutes ($p=0.02$) and 24 hours ($p=0.04$). At 48 hours, no differences between antiseptics were observed on the groin.

Conclusions: In this clinical trial, CHG+IPA met the FDA requirements for a patient preoperative skin prep however PI failed to satisfy FDA requirements. CHG+IPA is significantly more effective immediately and persistently than PI for preoperative skin preparation.

INTRODUCTION

- Research has shown that bacteria from patients' skin are a primary source of surgical wound infections[1].
- This clinical trial assessed the safety and immediate and persistent antimicrobial activity of a newly approved topical antiseptic, ChloraPrep (2% chlorhexidine gluconate + 70% isopropyl alcohol (CHG+IPA)), compared with Betadine (10% povidone iodine (PI)).
- This poster discusses the results of a clinical trial studying the efficacy and safety of ChloraPrep compared with Betadine (10% povidone iodine (PI) as a topical antiseptic for preoperative skin preparation.

OBJECTIVES

Determine the immediate and persistent antimicrobial efficacy and safety of ChloraPrep (2% chlorhexidine gluconate + 70% isopropyl alcohol (CHG+IPA)) compared with Betadine (10% povidone iodine (PI))

METHODS

Study Design

- This was a randomized, parallel group, open label, phase III clinical trial
- The trial included a pre-screening phase, screening phase, and testing phase
- Antimicrobial activity was measured by determining the number of colony forming units (CFU) per cm^2 of skin, using blinded procedures

Subjects

- Healthy subjects between the ages of 18 and 70

Study Procedures

Pre-Screening Phase (≥14 days prior to screening phase)

- Subjects used no topical or systemic antimicrobials, antibacterial hygiene products, or other agents known to affect normal skin microbial flora

Screening Phase

- Microbial samples were taken from right and left abdominal and inguinal designated treatment sites to exclude subjects with low microbial counts
- No bathing was allowed at least ≤24 hours before each microbial sampling day

Testing Phase

- Skin irritation was evaluated just prior to microbial sampling at baseline, at 10 minutes, at 24 hours, and at 48 hours
- Each designated treatment site was treated with 1 antiseptic and each subject randomly assigned an antiseptic application using one of the two antiseptics.
- Sampling sites were randomized within the treatment area, using a computer-generated randomization schedule
- Microbial counts were taken using cylinder sampling techniques at ~ 10 minutes, 24 hours, and 48 hours after antiseptic application
- After the 10 minute sample was taken a sterile gauze bandage was placed over the 24 and 48 hour sampling sites to prevent contamination

Antiseptic Application

- Both antiseptics were applied using back-and-forth strokes of the applicator over the treatment site for ~ 30 seconds on the abdomen and 2 minutes on the groin; antiseptics were allowed to dry for 30 seconds on the abdomen and 1 minute on the groin

Cylinder Sampling Technique

- A separate sterile cylinder (inside area of $3.80 cm^2$) was held against the site to be sampled
- Three milliliters (3.0mL) of Sterile Stripping Suspending Fluid (SSF+) with appropriate antiseptic neutralizers was instilled into cylinder and the skin area inside the cylinder was massaged in circular manner for 1 minute with a sterile policeman
- SSF+ was extracted from the cylinder with a sterile pipette and placed into sterile test tube
- Immediately after, a second 3.0-mL aliquot of SSF+ was instilled into the cylinder and the same procedure was followed for 1 minute, then collected with a pipette and pooled in the test tube with the first aliquot

CFU/cm^2 of Skin Counting

- To convert the sample volume collected into CFU/cm^2 of skin on the abdomen or groin, the following formula was used:

$$R = \log_{10}\left[\frac{F\left(\frac{\Sigma c_i}{n}\right)10^{-D}}{A}\right]$$

where:
R = average CFU count in $\log_{10}$ scale per cm^2 of skin;
F = 6 mL total volume of stripping fluid added to the sampling cylinder;
$\Sigma c_i/n$ = average of duplicate colony counts used for each sample collected;
D = dilution factor of plates counted;
A = inside area of sampling cylinder ($3.8 cm^2$)

Efficacy Assessment

- Antimicrobial efficacy was measured by determining mean number of CFU/cm^2 of skin at baseline and at ~10 minutes, 24 hours, and 48 hours after antiseptic application
- Effective antimicrobial activity was defined as ≥2.0 $\log_{10}$ decrease in the mean number of CFU/cm^2 of abdominal skin and a ≥3.0 $\log_{10}$ decrease in the mean number of CFU/cm^2 of inguinal skin 10 minutes after antiseptic application.

Assessment of Safety

- Safety was evaluated by monitoring adverse events and evaluating skin irritation before antiseptic application and at ~10 minutes, 24 hours, and 48 hours after antiseptic application
- Sampling sites were scored from 0 (none) to 3 (severe) for erythema, edema, rash, or dryness

Statistical Analyses

Efficacy Data

- Separate statistical analyses of efficacy were conducted for the abdomen and groin, at the α=0.05 level of significance
- Log_{10} CFU/cm^2 of skin microbial counts were used to assess antimicrobial activity and efficacy
- Analysis of baseline data was performed using CFU/cm^2 of skin and compared using analysis of variance technique (ANOVA)
- **Within-Treatment Analysis**
  - The $\log_{10}$ CFU/cm^2 of skin count at 10 minutes, 24 hours, and 48 hours for the 2 antiseptics was compared with their baseline $\log_{10}$ CFU/cm^2 of skin count, utilizing the Student's t-test for paired data
- **Between-Treatment Analysis**
  - Differences in reductions in mean CFU/cm^2 of skin counts between the antiseptics were evaluated at 10 minutes, 24 hours, and 48 hours using analysis of covariance techniques (ANCOVA)

Skin Irritation Data

- Erythema, edema, rash, and dryness scores assessed immediately before cylinder sampling were compared with baseline scores in the statistical analysis of irritation
- **Within-Treatment Analysis**
  - Wilcoxon's Signed Rank Test was used to evaluate changes in skin irritation from baseline at each post-treatment evaluation
- **Between-Treatment Analysis**
  - Changes from baseline were averaged across the 10-minute, 24-hour, and 48-hour evaluation times to compare the skin irritation of the antiseptics using the Kruskal-Wallis test

RESULTS

Patient Disposition and Demographics

- Demographics for the 93 subjects originally recruited into the study are listed on Table 1

Table 1. Patient Demographics

Summary of Demographics:	Subjects in the Test Phase of Study	Subjects Excluded from Study
Average age of Subject:	58	48
Number of Males:	11	2
Number of Females:	44	36
Number of Hispanics:	0	1
Number of Blacks:	2	1
Number of Caucasians:	53	36
No demographics available	0	0

Efficacy Evaluation

- **Abdominal Analysis**
  - CFU/cm² of skin counts were significantly reduced from baseline at 10 minutes, 24 hours, and 48 hours after application of both antiseptics (p=0.0001, Table 2, and Figure 1)
  - No statistically significant differences in microbial counts between the two treatments were detected at 10 minutes or 24 hours after antiseptic application
  - At 48 hours after application, ChloraPrep demonstrated a significantly greater reduction in CFU counts (Table 3, and Figure 1) compared with Betadine (p=0.0204)

Figure 1. Mean Log_{10} in CFU/cm² of Skin Counts on the Abdomen

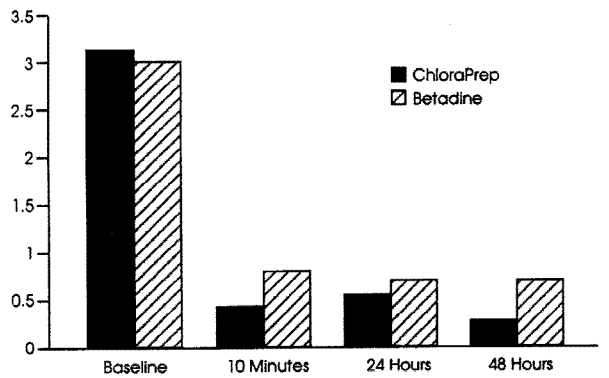

Table 2. Antiseptic Reductions in CFU Counts on the Abdomen Compared with Baseline

Drug p-value # of Skin Sites	Mean Log_{10}* Reduction from Baseline 10 Minutes	24 Hours	48 Hours
ChloraPrep	2.7881	2.6575	2.9436
p-value	0.0001†	0.0001†	0.0001†
n =	16	16	16
Betadine	2.2611	2.3607	2.3711
p-value	0.0001†	0.0001†	0.0001†
n =	19	19	19

* Log_{10} colony forming units per square centimeter of skin
† Significant reduction in CFU counts compared with baseline
n = number of sites tested

Table 3. p-value ChloraPrep vs. Betadine

p-value ChloraPrep vs. Betadine	Time After Application of Antiseptic 10 Minutes	24 Hours	48 Hours
p-value	0.1733	0.2605	0.0204*

* Significantly better antimicrombial activity by ChloraPrep than Betadine

Efficacy Evaluation

- **Inguinal Analysis**
  - CFU/cm² of skin counts were significantly reduced from baseline at 10 minutes, 24 hours, and 48 hours after application of both antiseptics (p=0.0001, Table 4, and Figure 2)
  - At 10 minutes and 24 hours after application, ChloraPrep demonstrated a significantly greater reduction in CFU/cm² of skin counts (Table 5, and Figure 2) compared with Betadine (p=0.0248 and p=0.0429 respectively). At 48 hours after application there was no significant difference between the microbial counts of the two antiseptics.

Figure 2. Mean Log_{10} in CFU/cm² of Skin Counts on the Groin

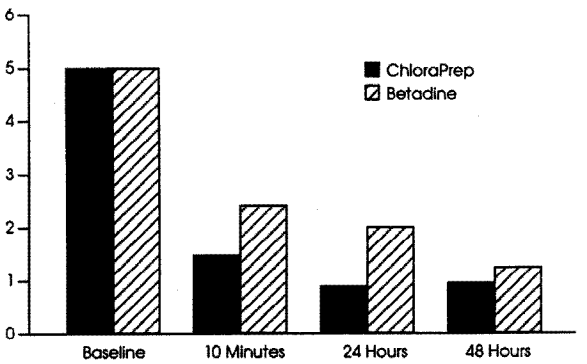

Table 4. Antiseptic Reductions in CFU Counts on the Groin Compared with Baseline

Drug p-value # of Skin Sites	Mean Log_{10}* Reduction from Baseline 10 Minutes	24 Hours	48 Hours
ChloraPrep	3.4050	4.0050	3.9410
p-value	0.0001†	0.0001†	0.0001†
n =	19	18‡	17§
Betadine	2.4445	2.9429	3.5935
p-value	0.0001†	0.0001†	0.0001†
n =	19	19	19

* Log_{10} colony forming units per square centimeter of skin
† Significant reduction in CFU counts compared with baseline
‡ Subject No. 8 gauze bandage was lost and the sampling site compromised.
§ Subjects No. 8 and 14 gauze bandages were lost and the sampling sites were compromised
n = number of sites tested

Table 5. p-value ChloraPrep vs. Betadine

p-value ChloraPrep vs. Betadine	Time After Application of Antiseptic 10 Minutes	24 Hours	48 Hours
p-value	0.0248*	0.0429*	>0.5000

* Significantly better antimicrombial activity by ChloraPrep than Betadine

Safety Evaluation

- No drug-related skin irritations or adverse reactions were reported or observed for either antiseptic during this clinical study

DISCUSSION

- ChloraPrep demonstrated better immediate and better persistent antimicrobial activity than Betadine
- ChloraPrep produced significantly more persistent antimicrobial activity than Betadine ($p=0.0204$) on the abdomen at 48 hours
- ChloraPrep produced significantly more immediate ($p=0.0248$) and persistent ($p=0.0429$) antimicrobial activity on the groin at 10 minutes and 24 hours respectively
- The mean reduction in CFU/cm^2 of skin counts on the abdomen demonstrated by each of the antiseptics exceeded FDA's proposed criteria for patient preoperative skin preparation
  - Microbial counts were reduced $\geq 2.0 \log_{10}$ CFU/cm^2 of skin at 10 minutes after antiseptic application with microbial counts maintained below baseline for at least 6 hours[2]
- The mean reduction in CFU counts on the groin demonstrated ChloraPrep exceeded FDA's proposed criteria for patient preoperative skin preparation
- The mean reduction in CFU counts on the groin demonstrated Betadine failed to meet the FDA's proposed criteria for a patient preoperative skin preparation antiseptic at 10 minutes (2.4445) and 24 hours (2.9429)
- Because bacteria from patients' skin is a primary source of surgical wound infection, ChloraPrep might reduce infection by exerting more immediate, longer, and more persistent bactericidal activity

CONCLUSIONS

- In this clinical trial, CHG+IPA met the FDA requirements for a patient preoperative skin prep however PI failed to satisfy FDA requirements for a patient preoperative skin antiseptic.
- CHG+IPA was significantly more effective immediately and persistently than PI for preoperative skin preparation.
- In this study, both antiseptics were equally safe for patient preoperative skin preparation

REFERENCES

1. Altemier WA, Culbertson WR, Hummel RP. Surgical consideration of endogenous infections sources, types, and methods of control. *Surg Clin North Am* 1968;48:227-240.
2. Tentative Final Monograph for Health-Care Antiseptic Drug Products 21 CFR Parts 333 and 369; *Federal Register*, Friday, June 17, 1994; section, 333.470 (a), (3), (iii); p. 31450

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Practice

Reduction of bloodstream infections associated with catheters in paediatric intensive care unit: stepwise approach

Adnan Bhutta, *assistant professor*[1], **Craig Gilliam**, *director of infection control*[2], **Michele Honeycutt**, *infection control practitioner*[2], **Stephen Schexnayder**, *professor*[1], **Jerril Green**, *associate professor*[1], **Michele Moss**, *professor*[1], **K J S Anand**, *professor*[1]

[1]

Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, 800 Marshall Street, Slot 512-3, Little Rock, AR 72202, USA , [2] Epidemiology and Infection Control, Arkansas Children's Hospital

Correspondence to: A Bhutta bhuttaadnant@uams.edu

Abstract

Problem Bloodstream infections associated with catheters were the most common nosocomial infections in one paediatric intensive care unit in 1994-7, with rates well above the national average.

Design Clinical data were collected prospectively to assess the rates of infection from 1994 onwards. The high rates in 1994-7 led to the stepwise introduction of interventions over a five year period. At quarterly intervals, prospective data continued to be collected during this period and an additional three year follow-up period.

Setting A 292 bed tertiary care children's hospital.

Key measures for improvement We aimed to reduce our infection rates to below the national mean rates for similar units by 2000 (a 25% reduction).

Strategies for change A stepwise introduction of interventions designed to reduce infection rates, including maximal barrier precautions, transition to antibiotic impregnated central venous catheters, annual handwashing campaigns, and changing the skin disinfectant from povidone-iodine to chlorhexidine.

Effects of change Significant decreases in rates of infection occurred over the intervention period. These were sustained over the three year follow-up. Annual rates decreased from 9.7/1000 days with a central venous catheter in 1997 to 3.0/1000 days in 2005, which translates to a relative risk reduction of 75% (95% confidence interval 35% to 126%), an absolute risk reduction of 6% (2% to 10%), and a number needed to treat of 16 (10 to 35).

Lessons learnt A stepwise introduction of interventions leading to a greater than threefold reduction in nosocomial infections can be implemented successfully. This requires a multidisciplinary team, support from hospital leadership, ongoing data collection, shared data interpretation, and introduction of evidence based interventions.

Context

Hospital acquired infections or nosocomial infections are an important problem in safe and effective health care. The Centers for Disease Control and Prevention (CDC) estimates that each year in the United States there are about 1.7 million nosocomial infections in hospitals and 99 000 associated deaths. The estimated incidence is 4.5 nosocomial infections per 100 admissions, with direct costs (at 2004 prices) ranging from $10 500 (£5300, €8000 at 2006 rates) per case (for bloodstream, urinary tract, or respiratory infections in immunocompetent patients) to $111 000 (£57 000, €85 000) per case for antibiotic resistant infections in the bloodstream in patients with transplants.[1] With these numbers, conservative estimates of the total direct costs of nosocomial infections are above $17bn. The reduction of such infections forms an important component of efforts to improve healthcare safety in the US.

This problem is not unique to one country; the British National Audit Office estimated that the incidence of nosocomial infections in Europe

ranges from 4% to 10% of all hospital admissions.[2] In the United Kingdom, they further estimated in 2000 that nosocomial infections contributed to 5000 deaths each year at an annual cost of £1bn to the NHS.[23]

Nosocomial infections are more likely to occur in patients with compromised immune systems because of their age, disease, nutritional status, and external factors such as the presence of central venous lines, bladder catheters, or endotracheal tubes. Patients in intensive care units therefore have infection rates that are three times higher than those seen in patients in other hospital locations.[4]

Children are especially vulnerable.[5] Additional factors include the involvement of multidisciplinary teams, the lack of physical barriers between bed spaces, and multiple attempts often required for placing monitoring devices, which further increase the chances of developing nosocomial infections.[6]

Bloodstream infections associated with catheters are the most commonly reported nosocomial infection in paediatric intensive care.[6] The risk of infection and the associated mortality increases significantly according to the site of the catheter (for instance, femoral or subclavian),[78] age, immune status, and paediatric risk of mortality (PRISM) score.[9] Other factors that increase the risk of infection include presence of multiple catheters (venous and arterial) and transport of patients to other parts of the hospital.[10] Mortality, increased length of stay in intensive care, and substantial additional financial costs have been reported.[11] Evidence exists for measures such as universal barrier precautions at the time of catheter insertion, chlorhexidine skin disinfection, and use of catheters impregnated with an antimicrobial, but their implementation has not been explored.[1213] Reduction of catheter infection in intensive care can lead to decreases in morbidity and mortality in children and decreased costs for the family and society.

Outline of the problem

The national nosocomial infection surveillance (NNIS) system is a national voluntary tracking system resulting from a cooperative, non-financial relationship between more than 300 hospitals and the Centers for Disease Control and Prevention for tracking hospital acquired infection (www.cdc.gov/ncidod/dhqp/nnis.html). In June 1998 they published a pooled mean rate of bloodstream infection associated with a central venous catheter of 8.0 infections per 1000 days with a catheter in the paediatric intensive care unit (median rate of 7.1 infections/1000 days).[14] In 1994-7 the rate in our 19 bed multidisciplinary unit was well above the national average. A multidisciplinary group of paediatric clinicians—including the director of infection control, critical care nurses, infectious diseases specialists, and critical care medicine physicians—formulated a strategy to decrease such infections in the unit. The hospital's medical director served as a senior leader and advocate for this project.

Key measures for improvement

Our goal was to reduce bloodstream infection associated with a catheter by 25% within 24 months in children in intensive care.

Strategy for change

After a thorough literature search and meetings with all stakeholders, the multidisciplinary team implemented a stepwise programme of evidence based measures to reduce bloodstream infection associated with a catheter.

Maximal barrier precautions for all central venous catheters, November 1998—Based on guidelines from the Centers for Disease Control and Prevention,[15] all physicians in the unit were asked to use the maximum barrier precautions during insertion of the catheter. This process included a complete surgical scrub and the use of a sterile gown, sterile gloves, and mask for the physician, masks for bedside nurses and other personnel, and skin disinfection and sterile drapes for the patient. We used a dedicated trolley with supplies for insertion or other invasive procedures that was moved to the patient's bedside and restocked by unit technicians.

Catheters impregnated with antibiotic, July 1999—As part of a preventive strategy to reduce infection, we recommended the use of catheters impregnated with antimicrobials as cost effective and clinically effective.[16] All multilumen catheters less than 25 cm long were impregnated with minocycline and rifampicin (rifampin).

Annual handwashing campaigns, March 2000—The Institute of Medicine (IOM) report showed that poor compliance with hand disinfection was associated with nosocomial infections. A performance improvement team developed a programme to increase compliance with routine handwashing. It was called "Friction Rubs Out Germs" and had a frog as a symbol and the message "I washed my hands. . . did you?" In addition, posters, hospital television video, before and after tests of knowledge, and articles in employee and medical staff newsletters emphasised the importance of hand disinfection including the use of alcohol gels and foams.

Design of physical barriers between patients' beds in new unit, occupied April 2003—Our new unit mostly had private rooms instead of open bays. The previous 19 bed unit was in about 930 m^2 with 10 hand washing and 10 alcohol foam stations. The new 26 bed unit had 22 private rooms in about 1860 m^2, with 50 handwashing stations and 49 alcohol gel stations.

Chlorhexidine skin disinfectant, May 2003—The 2002 Centers for Disease Control and Prevention guidelines recommended the use of 2% chlorhexidine for skin disinfection and formed the basis for a change in our unit. Our medical staff used 2% chlorhexidine in 70% isopropyl alcohol in all age groups and reported no adverse local skin reactions.

Data collection

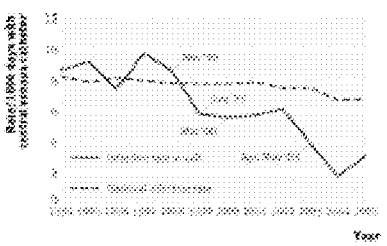
In this 292 bed paediatric facility, the infection control division has collected information on nosocomial catheter bloodstream infections since

1994. Infection control personnel make daily rounds in the intensive care unit and gather information on date of placement of the device, type of catheter placed, antibiotic versus non-antibiotic catheter, and duration of placement. They also collect information about positive results on blood cultures from the microbiology department.

We use Raad and Hanna's definitions for bloodstream infections associated with catheters.[17] We identify positive results in blood cultures by standard microbiological techniques and determined clinical relevance in consultation with the intensive care and infectious disease physicians. This information is entered on a database maintained by the programme. Quarterly reports are generated and sent to the medical and nursing leadership of the unit and the hospital.

Analysis and interpretation

The figure illustrates the effect of our ongoing efforts to decrease infection in our unit. A decrease occurred even though there was an increase in the number of catheters placed each year (242 in 1998 and 481 in 2005, a 98% increase) and an increase in the number of admissions to the unit (admissions increased by 17% and patient days increased by 21%) (table). The incidence of bloodstream infection decreased significantly over the study period ($P<0.001$) with a relative risk reduction of 75% between the start and the end of the study period (95% confidence interval 35% to 126%). The absolute risk reduction was 6% (2% to 10%) and the number needed to treat was 16 (10 to 35). In 1999 we introduced catheters impregnated with antibiotic (rifampicin and minocycline). Over seven years (1999-2005), we have examined 2126 catheters. The infection rate with impregnated catheters was 4.2/1000 days with a central venous catheter compared with 6.4/1000 days with catheters without impregnation. We did not see any increased antibiotic resistance with use of this catheter. During the first five years of use, Gram positive organisms accounted for 33% of isolates in the group with impregnated catheters and 32% in the catheters that were not impregnated. There were no differences in rates of methicillin resistant staphylococci between each group.



Trend over time (1994-2005) in bloodstream infection associated with catheters in paediatric intensive care unit compared with national mean: November 1998—introduction of maximal barrier precautions; July 1999—introduction of catheters impregnated with antibiotic; March 2000—annual handwashing campaigns; April 2003—move to new unit with private rooms; May 2003—introduction of skin disinfection with chlorhexidine

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View this table: Incidence of bloodstream infections in children in intensive care unit over study period (1998-2005)
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Effects of change

The successful stepwise implementation of various measures to decrease nosocomial bloodstream infections resulted in a steady and sustained decline in the rates of bloodstream infection associated with catheter use in our unit since 1998 (figure). Our annual handwashing campaigns increased compliance with hand disinfection before contact with patients in our unit from 47% in March 2000 to 82% in March 2005. Similarly, an observational survey by the infection control division found 98% compliance with use of maximum barrier precautions during insertion of catheters in 2005.

In 1998-2005, if our infection rate had stayed at the national mean, we would have had an additional 39 cases of bloodstream infection. As the estimated mortality attributable to each episode is 12-25%,[13] this would have been equivalent to about 5-10 deaths during this time period.

This success in the paediatric intensive care unit has been translated into use of similar strategies in other units in the same hospital. The cardiothoracic unit has seen a fall in rates of catheter associated bloodstream infection from 8.4/1000 days in 2001 to 3.6/1000 days in 2005, representing a decline of 63%.

Lessons learnt

Using a stepwise approach, we were able to successfully lowerthe rates of catheter associated bloodstream infection in a paediatric intensive care unit. Our multidisciplinary group identified the problem, created a data collection system tomeasure baseline performance and ongoing improvement, and created a data reporting system that allowed all stakeholders to understandthe extent of the problem and gauge the effects of changes in practice. We also introduced effective evidence based strategies to combat the problem and provided continued education for all staff members. The outcomes task force report from the Society of Critical Care Medicine published in January 2006 outlinesa similar stepwise approach for clinicians interested in successfully implementing a quality improvement project.[18] The Pittsburgh Regional Healthcare Initiative used a similar approach regionally in 66 intensive care units (including three paediatric units) and saw a decline in catheter associated bloodstream infection of 68% over four years.[19]

Intensive and continued educational efforts by team membersto educate unit staff together with the implementation of eachnew step, as well as renewed educational efforts when increasesin infection rates were noted in particular time periods, arean important component of our success to date. Specifically, the infection control staff report quarterly data to the nursingand medical directors of the unit. Since 2004, all new employeesin the unit are taught about this prevention project. At annualevaluation, all employees are required to perform validationof skills on aspects of catheter care such as insertion, weekly changes of dressings, and accessing lines while maintainingaseptic techniques. In 2005, our unit staff participated in the design of a web based learning module with Child HealthCorporation of America (CHCA) on prevention of catheter bloodstream infections in the intensive care unit. This programme is requiredfor registered nurses, advanced practice nurses, and resident physicians in the unit and has led to increased awareness amongphysicians, nurses, and other staff members about both nosocomial infections and the necessity to review and maintain centralvenous catheters or other devices as an integral part of dailyrounds. We believe that implementation of similar strategiesto reduce such infections in other intensive care units canlead to substantial reductions in mortality and morbidity inthis vulnerable group of patients.

Key learning points

A stepwise introduction of evidence based interventions is effective in reducing catheter associated blood stream infections

A multidisciplinary team is needed to set up a data collection system to establish baseline prevalence of such infections and ongoing surveillance

The data need to be shared with all stakeholders so that the extent of the prevalence is known and efforts to reduce it are easier to gauge

Intensive and sustained education of all staff is needed for continued success in trying to reduce these infections

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References

1. US Department of Health and Human Services. CDC's role in monitoring and preventing healthcare-associated infections: hearing before the subcommittee on oversight and investigations (29 March 2006). ()www.hhs.gov/asl/testify/t060329.html
2. Pratt RJ, Loveday HP, Pellowe CM, Harper P, Jones S, Cookson B, et al. A comparison of international practices in the management and control of hospital-acquired infections. Improving patient care by reducing the risk of hospital acquired infection: a progress report. London: National Audit Office, 2004. (HC 876, 2003-4.)
3. Bourn J. The management and control of hospital acquired infection in acute NHS trusts in England. London: National Audit Office, 2000. (HC 230, 1999-2000.)
4. Weinstein RA. Nosocomial infection update. *Emerg Infect Dis* 1998;4:416-20.[ISI][Medline]
5. Milliken J, Tait GA, Ford-Jones EL, Mindorff CM, Gold R, Mullins G. Nosocomial infections in a pediatric intensive care unit. *Crit Care Med* 1988;16:233-7.[ISI][Medline]
6. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in pediatric intensive care units in the

United States. National nosocomial infections surveillance system. *Pediatrics* 1999;103:e39.[Abstract/Free Full Text]
7. Merrer J, De Jonghe B, Golliot F, Lefrant JY, Raffy B, Barre E, et al, French catheter study group in intensive care. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 2001;286:700-7.[Abstract/Free Full Text]
8. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. Excess length of stay, extra costs, and attributable mortality. *JAMA* 1994;271:1598-601.[Abstract]
9. Singh-Naz N, Sprague BM, Patel KM, Pollack MM. Risk factors for nosocomial infection in critically ill children: a prospective cohort study. *Crit Care Med* 1996;24:875-8.[CrossRef][ISI][Medline]
10. Yogaraj JS, Elward AM, Fraser VJ. Rate, risk factors, and outcomes of nosocomial primary bloodstream infection in pediatric intensive care unit patients. *Pediatrics* 2002;110:481-5.[Abstract/Free Full Text]
11. Slonim AD, Kurtines HC, Sprague BM, Singh N. The costs associated with nosocomial bloodstream infections in the pediatric intensive care unit. *Pediatr Crit Care Med* 2001;2:170-4.[Medline]
12. Garland JS, Henrickson K, Maki DG. The 2002 hospital infection control practices advisory committee Centers for Disease Control and Prevention guideline for prevention of intravascular device-related infection. *Pediatrics* 2002;110:1009-13.[Free Full Text]
13. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. The Hospital Infection Control Practices Advisory Committee, Center for Disease Control and Prevention. *Pediatrics* 2002;110:e51.[Abstract/Free Full Text]
14. National Nosocomial Infections Surveillance (NNIS) System. Data summary from October 1986-April 1998. Atlanta, GA: Hospital Infections Program, National Centre for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, US Department of Health and Human Services, 1998. (www.cdc.gov/ncidod/dhqp/nnis_pubs.html
15. Pearson ML. Guideline for prevention of intravascular device-related infections. Hospital infection control practices advisory committee. *Infect Control Hosp Epidemiol* 1996;17:438-73.[ISI][Medline]
16. Veenstra DL, Saint S, Sullivan SD. Cost-effectiveness of antiseptic-impregnated central venous catheters for the prevention of catheter-related bloodstream infection. *JAMA* 1999;282:554-60.[Abstract/Free Full Text]
17. Raad I, Hanna H. Nosocomial infections related to use of intravascular devices inserted for long-term vascular access. In: Mayhall CG, ed. Hospital epidemiology and infection control. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 1999:165-72.
18. Curtis JR, Cook DJ, Wall RJ, Angus DC, Bion J, Kacmarek R, et al. Intensive care unit quality improvement: a "how-to" guide for the interdisciplinary team. *Crit Care Med* 2006;34:211-8.[CrossRef][ISI][Medline]
19. Centers for Disease Control. Reduction in central line-associated bloodstream infections among patients in intensive care units—Pennsylvania, April 2001-March 2005. *MMWR Morb Mortal Wkly Rep* 2005;54:1013-6.[Medline]

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Special Issue

Nosocomial Infection Update

Robert A. Weinstein
Cook County Hospital & Rush Medical College, Chicago, Illinois, USA

Historically, staphylococci, pseudomonads, and *Escherichia coli* have been the nosocomial infection troika; nosocomial pneumonia, surgical wound infections, and vascular accessrelated bacteremia have caused the most illness and death in hospitalized patients; and intensive care units have been the epicenters of antibiotic resistance. Acquired antimicrobial resistance is the major problem, and vancomycin-resistant *Staphylococcus aureus* is the pathogen of greatest concern. The shift to outpatient care is leaving the most vulnerable patients in hospitals. Aging of our population and increasingly aggressive medical and surgical interventions, including implanted foreign bodies, organ transplantations, and xenotransplantation, create a cohort of particularly susceptible persons. Renovation of aging hospitals increases risk of airborne fungal and other infections. To prevent and control these emerging nosocomial infections, we need to increase national surveillance, "risk adjust" infection rates so that interhospital comparisons are valid, develop more noninvasive infection-resistant devices, and work with health-care workers on better implementation of existing control measures such as hand washing.

As we enter the next millennium of infection control, we stand on the shoulders of giants—Jenner, Semmelweis, Nightingale, Oliver Wendell Holmes, and my own personal favorite, Thomas Crapper, the father of indoor plumbing. Modern infection control is grounded in the work of Ignaz Semmelweis, who in the 1840s demonstrated the importance of hand hygiene for controlling transmission of infection in hospitals. However, infection control efforts were spotty for almost a century. In 1976, the Joint Commission on Accreditation of Healthcare Organizations published accreditation standards for infection control, creating the impetus and need for hospitals to provide administrative and financial support for infection control programs. In 1985, the Centers for Disease Control and Prevention's (CDC's) Study on the Efficacy of Nosocomial Infection Control reported that hospitals with four key infection control components—an effective hospital epidemiologist, one infection control practitioner for every 250 beds, active surveillance mechanisms, and ongoing control efforts—reduced nosocomial infection rates by approximately one third (1).

Over the past 25 years, CDC's National Nosocomial Infections Surveillance (NNIS) system has received monthly reports of nosocomial infections from a nonrandom sample of United States hospitals; more than 270 institutions report. The nosocomial infection rate has remained remarkably stable (approximately five to six hospital-acquired infections per 100 admissions); however, because of progressively shorter inpatient stays over the last 20 years, the rate of nosocomial infections per 1,000 patient days has actually increased 36%, from 7.2 in 1975 to 9.8 in 1995 (Table 1). It is estimated that in 1995, nosocomial infections cost $4.5 billion and contributed to more than 88,000 deaths—one death every 6 minutes.

Which Nosocomial Infections Are Emerging?

Table 1. Nosocomial infections, United States (2,3)

We have witnessed a cyclical parade of pathogens in hospitals. In Semmelweis's era, group A

streptococci created most nosocomial problems. For the next 50 to 60 years, gram-positive cocci, particularly streptococci and *Staphylococcus aureus*, were the hospital pathogens of major concern. These problems culminated in the pandemic of 1940 to 1950, when *S. aureus* phage type 94/96 caused major nosocomial problems. In the 1970s, gram-negative bacilli, particularly *Pseudomonas aeruginosa* and *Enterobacteriaceae*, became synonymous with nosocomial infection. By the late 1980s and early 1990s, several different classes of antimicrobial drugs effective against gram-negative bacilli provided a brief respite. During this time, methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant enterococci (VRE) emerged, signaling the return of the "blue bugs." In 1990 to 1996, the three most common gram-positive pathogens—*S. aureus*, coagulase-negative staphylococci, and enterococci—accounted for 34% of nosocomial infections, and the four most common gram-negative pathogens—*Escherichia coli*, *P. aeruginosa*, *Enterobacter* spp., and *Klebsiella pneumoniae*—accounted for 32% (3).

Year	Admissions ($x10^6$)	Patient days[a] ($x10^6$)	Length of stay (days)	Nosocomial infection ($x10^6$)	Nosocomial infections (/1000 patient days)
1975	38	299	7.9	2.1	7.2
1995	36	190	5.3	1.9	9.8

[a]Patient days = total inpatient days

Bloodstream infections and pneumonias have increased in frequency from 1975 to 1996 (Table 2). However, tracking nosocomial infections by site has become difficult in the last few years because of shorter inpatient stays. For example, the average postoperative stay, now approximately 5 days, is usually shorter than the 5- to 7-day incubation period for *S. aureus* surgical wound infections.

Table 2. Sites of nosocomial infections (2,4)

Year	Urinary tract (%)	Surgical wound (%)	Lower respiratory tract (%)	Bloodstream (%)	Other (%)
1975	42	24	10	5	19
1990-6	34	17	13	14	21

Acquired antimicrobial resistance is the major anticipated problem in hospitals. VRE and MRSA are the major gram-positive pathogens of concern (5,6). *P. aeruginosa*, *Klebsiella*, and *Enterobacter* that harbor chromosomal or plasmid-mediated beta-lactamase enzymes are the major resistant gram-negative pathogens. The contribution of antibiotic resistance to excessive death rates in hospitals is difficult to evaluate, often depending on whether studies are population-based or case-control, but evidence is mounting that antimicrobial resistance contributes to nosocomial deaths.

While bacterial resistance is clearly the major threat, viral and fungal resistance could become important because of the small number of therapeutic options for these pathogens. Herpes viruses with acquired resistance to acyclovir and ganciclovir have emerged as problems, particularly in HIV-infected patients. Pathogens with intrinsic resistance often have lower pathogenicity and have disproportionately affected immunocompromised patients. For example, *Candida* spp. with intrinsic resistance to azole antifungal agents (e.g., *C. krusei*) and to amphotericin B (e.g., *C. lusitaniae*) have emerged as problem pathogens in oncology units.

While we are facing the era of opportunists, including fungi, viruses, and parasites in immunocompromised patients, the one we fear most is the postantibiotic era. The first nosocomial inkling is MRSA with reduced susceptibility to vancomycin (7). Beyond the postantibiotic era lies the era of xenogenic infections as organs, transplanted from nonhuman primates, bring with them a variety of potential zoonotic pathogens. Nevertheless, traditional respiratory pathogens may yet prove to be our greatest challenge; for example, a major shift in strain type (8) could result in devastating pandemic community and nosocomial influenza A outbreaks.

Who Is Affected by Emerging Nosocomial Pathogens?

Nosocomial infections typically affect patients who are immunocompromised because of age, underlying diseases, or medical or surgical treatments. Aging of our population and increasingly aggressive medical and therapeutic interventions, including implanted foreign bodies, organ transplantations, and xenotransplantations, have created a cohort of particularly vulnerable persons. As a result, the highest infection rates are in intensive care unit (ICU) patients. Nosocomial infection rates in adult and pediatric ICUs are approximately three times higher than elsewhere in hospitals. The sites of infection and the pathogens involved are directly related to treatment in ICUs. In these areas, patients with invasive vascular catheters and monitoring devices have more bloodstream infections due to coagulase-negative staphylococci. In fact, most cases of occult bacteremia in ICU patients are probably due to vascular access-related infections. Fungal urinary tract infections have also increased in ICU patients, presumably because of extensive exposure to broad-spectrum antibiotics. In the National Nosocomial Infections Surveillance system, *Candida* spp. are the main cause of nosocomial urinary infections in ICUs (9).

Why Are Nosocomial Infections Emerging Now?

Three major forces are involved in nosocomial infections. The first is antimicrobial use in hospitals and long-term care facilities. The increased concern about gram-negative bacilli infections in the 1970s to 1980s led to increased use of cephalosporin antibiotics. As gram-negative bacilli became resistant to earlier generations of cephalosporin antibiotics, newer generations were developed. Widespread use of cephalosporin antibiotics is often cited as a cause of the emergence of enterococci as nosocomial pathogens. About the same time, MRSA, perhaps also in response to extensive use of cephalosporin antibiotics, became a major nosocomial threat. Widespread empiric use of vancomycin, as a response to concerns about MRSA and for treatment of vascular catheterassociated infection by resistant coagulase-negative staphylococci, is the major initial selective pressure for VRE. Use of antimicrobial drugs in long-term care facilities and transfer of patients between these facilities and hospitals have created a large reservoir of resistant strains in nursing homes.

Second, many hospital personnel fail to follow basic infection control, such as hand washing between patient contacts. In ICUs, asepsis is often overlooked in the rush of crisis care (10).

Third, patients in hospitals are increasingly immunocompromised. The shift of surgical care to outpatient centers leaves the sickest patients in hospitals, which are becoming more like large ICUs (11). This shift has led to the greater prevalence of vascular accessassociated bloodstream infections and ventilator-associated pneumonias.

Other precipitating factors also can be anticipated in hospitals. Transplantation is a double-edged sword because of the combined effects of immunosuppression of transplant patients and of infectious diseases that come with some transplanted organs. The blood supply will continue to be a source of emerging infectious diseases. Moreover, as hospitals age, infrastructure repairs and renovations will create risks of airborne fungal diseases caused by dust and spores released during demolition and construction. Infections due to other pathogens, such as Legionella, may also result from such disruptions.

How Can We Prevent and Control Emerging Nosocomial Infections?

Infection control can be very cost-effective. Approximately one third of nosocomial infections are preventable. To meet and exceed this level of prevention, we need to pursue several strategies simultaneously (12). First, we need to continue to improve national surveillance of nosocomial infections so that we have more representative data. We must assess the sensitivity and specificity of our surveillance and of our case definitions, particularly for difficult-to-diagnose infections like ventilator-associated pneumonia. We also need to develop systems for surveillance of "nosocomial" infections that occur out of the hospital, where much health care is now given.

Second, we need to ensure that surveillance uses are valid. The Joint Commission on Accreditation of Healthcare Organization's ORYX initiative for monitoring health-care processes and outcomes will lead to core indicators and sentinel event monitoring. This initiative will be followed by increased outpatient surveillance, which ultimately may lead to systemwide real-time surveillance and reporting. Because we want to use nosocomial infection rates as

a core indicator of quality of care, we need to improve our ability to "risk adjust" infection rates so we know that our interprovider and interhospital comparisons are valid. Risk stratification will ultimately depend on organic-based computer systems that will mimic biologic events.

Third, many of our successes in controlling nosocomial infections have come from improving the design of invasive devices. This is particularly important given the marked increase in frequency of vascular access–associated bloodstream infections, particularly in ICU patients. Given the choice of changing human behavior (e.g., improving aseptic technique) or designing a better device, the device will always be more successful. Of particular importance is the development of noninvasive monitoring devices and minimally invasive surgical techniques that avoid the high risk associated with bypassing normal host defense barriers (e.g., the skin and mucous membranes).

Fourth, forestalling the postantibiotic era will require aggressive antibiotic control programs (13); these may become mandated for hospitals that receive federal reimbursements, as happened in the past with infection control programs. Risks for antibiotic-resistant strains also may be reduced in the future by controlling colonization through use of immunization or competing flora.

Fifth, antimicrobial resistance problems and the advent of xenotransplantation emphasize the importance of newer microbiologic methods. For investigation of outbreaks of multidrug-resistant pathogens, pulsed-field gel electrophoresis has become a routine epidemiologic tool (14). Molecular epidemiologic analysis also may help us better understand the factors that lead to the emergence of resistant strains. For diagnosis of syndromes caused by unusual pathogens, representational difference analysis and speciation by use of the pathogen's phylogenetic r-RNA "clock" may become routine.

Sixth, control of tuberculosis (TB) in hospitals is an excellent example of the successful collaboration of the infection control community, CDC, and regulatory agencies. But we can anticipate that the Occupational Safety and Health Administration may have many new employee health issuesbeyond TB and bloodborne pathogensto evaluate in hospitals, such as health problems related to exposure to magnetic fields, to new polymers, and to medications that contaminate the environment. Problems of mental stress due to unrelenting exposure to pagers, faxes, e-mail, holograms, and telephonic implanted communicators will require special attention.

Conclusion

Several enduring truths characterize the field of infection control. Hospitals will become more like ICUs, and more routine care will be delivered on an outpatient basis. Given the choice of improving technology or improving human behavior, technology is the better choice. All infection control measures will need to continue to pass the test of the "four Ps" (15): Are the recommendations Plausible biologically (e.g., is it likely to work)? Are they Practical (e.g., are they affordable)? Are they Politically acceptable (e.g., will the administration agree)? And, will Personnel follow them (e.g., can they and will they)?

The major advances in overall control of infectious diseases have resulted from immunization and improved hygiene, particularly hand washing. We must work with hospital personnel on better implementation of existing infection control technologies so that we will not need to rely solely on technologic advances.

Sir John Pattison (L), Medical School of University College, London, UK; Sherif Zaki, Centers for Disease Control and Prevention, Atlanta, Georgia.

Dr. Weinstein is chair, Division of Infectious Diseases, Cook County Hospital; director of Infectious Diseases Services for the Cook County Bureau of Health Services; and professor of Medicine, Rush Medical College. He also oversees the CORE Center for the Prevention, Care and Research of Infectious Disease and directs the Cook County Hospital component of the Rush/Cook County Infectious Disease Fellowship Program. His areas of research include nosocomial infections (particularly the epidemiology and control of antimicrobial resistance and infections in intensive care units) and health-care outcomes for patients with HIV/AIDS.

References

1. Haley RW, Culver DH, White J, Morgan WM, Amber TG, Mann VP, et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol 1985;121:182-205.
2. Haley RW, Culver DH, White JW, Morgan WM, Emori TG. The nationwide nosocomial infection rate: a new need for vital statistics. Am J Epidemiol 1985;121:159-67.
3. New York Times 1998 Mar 12; Sect. A12.
4. Centers for Disease Control and Prevention, Hospital Infections Program. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986-April 1996, issued May 1996: A report from the NNIS System. Am J Infect Control 1996;24:380-8.
5. Slaughter S, Hayden MK, Nathan C, Hu TC, Rice T, Van Voorhis J, et al. A comparison of the effect of universal use of gloves and gowns with that of glove use alone on acquisition of vancomycin-resistant enterococci in a medical intensive care unit. Ann Intern Med 1996;125:448-56.
6. Bonten MJM, Hayden MK, Nathan C, Van Voorhis J, Matushek M, Slaughter S, et al. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. Lancet 1996;348:1615-9.
7. Hiramatsu K, Aritaka N, Hanaki H, Kawasaki S, Hosoda Y, Hori S, et al. Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. Lancet 1997;350:1670-3.
8. Webster RG. Influenza: an emerging disease. Emerg Infect Dis 1998;4(3).
9. Fridkin SK, Welbel SF, Weinstein RA. Magnitude and prevention of nosocomial infections in the intensive care unit. Infect Dis Clin North Am 1997;11:479-96.
10. Weinstein RA. Epidemiology and control of nosocomial infections in adult intensive care units. Am J Med

1991;91:179-84.
11. Archibald L, Phillips L, Monnet D, McGowan JE, Tenover F, Gaynes R. Antimicrobial resistance in isolates from inpatients and outpatients in the United States: increasing importance of the intensive care unit. Clin Infect Dis 1997;24:211-5.
12. Scheckler WE, Brimhall D, Buck AS, Farr BM, Friedman C, Garibaldi RA, et al. Requirements for infrastructure and essential activities of infection control and epidemiology in hospitals: a consensus panel report. Infect Control Hosp Epidemiol 1998;19:114-24.
13. Goldmann DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. A challenge to hospital leadership. JAMA 1996;275:234-40.
14. Tenover FC, Arbeit RD, Goering RV. How to select and interpret molecular strain typing methods for epidemiological studies of bacterial infections: a review for healthcare epidemiologists. Infect Control Hosp Epidemiol 1997;18:426-39.
15. Weinstein RA. SHEA consensus panel report: a smooth takeoff. Infect Control Hosp Epidemiol 1998;19:91-3.

Address for correspondence: Robert A. Weinstein, Cook County Hospital, Division of Infectious Diseases, 129 Durand, 1835 W. Harrison St., Chicago, IL 60612, USA; fax: 312-572-3523; e-mail: rweinste@rush.edu.

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Skin Antisepsis

Past, Present, and Future

Cynthia T. Crosby, BS Alicia K. Mares, BSN, CRNI

Introduction

In the United States approximately 5 to 10 billion dollars are spent annually on the treatment of nosocomial infections.[35] These hospital-acquired infections increase patient morbidity, lengthen hospital stays, require additional medical interventions along with their associated costs, and possibly increase mortality rates. The risk of acquiring a nosocomial infection is greatly increased if the patient has a serious underlying disease, and with each invasive procedure performed on that patient. Interestingly, the primary source of nosocomial infections is from poor skin antisepsis of both the patient and the healthcare worker.[20,21]

A catheter-related bloodstream infection (CRBI) is one type of nosocomial infection that is becoming a serious problem. Within the United States alone there are 400,000 catheter-related infections annually, accounting for 40,000 to 80,000 deaths per year, at an additional cost of $3,000 to $28,000 per episode.[28] CRBI can be predominately linked to the patient's skin at the catheter exit site and/or the catheter hub.

Evidence suggests that the most prevalent source of CRBI is from the resident microorganisms on the patient's skin, comprised primarily of coagulase-negative *Staphylococcus* species (CoNS).[14,18,21]

A surgical site infection is another type of nosocomial infection primarily caused by CoNS. Of the almost 30 million surgical procedures performed annually in the United States, approximately 750,000 will result in an infection of some kind and typically cost an additional $7,500 per patient for treatment.[21]

Another area of concern regarding skin antisepsis is when drawing blood for cultures, where, again, the primary contaminant is CoNS. Contamination of blood-cultures is associated with a 50% increase in hospital charges, and for each false-positive blood culture, antibiotic use and its associated costs increase by 39%.[31,32,34] With increased antibiotic use, the threat of resistance is prevalent; methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and vancomycin-intermediate *Staphylococcus aureus* (VISA) have become common themes at infection control conferences around the world.

In the instance of CRBI, surgical site infections, and contaminated blood-cultures, the primary source of the infective agents is the resident skin microorganisms of the patient or the attending healthcare workers. Therefore, compliance with simple hand washing regimens could greatly reduce nosocomial infections. Proper skin cleansing and protection processes are essential to pre- and post-care regarding invasive medical procedures.

Background

Topical skin antisepsis is vital for the control of infection. The ideal antimicrobial agent should have the following properties:

- a broad spectrum of activity;
- rapid bactericidal activity;
- persistence or residual properties on the skin;
- maintain its activity in the presence of organic matter;
- be non-irritating or have low allergic and/or toxic responses; and
- no or minimal systemic absorption.

The activity of an antimicrobial solution can be affected by a number of factors, including the pathogenic organisms' concentration and composition,

and the composition of the antimicrobial agent. The larger the microorganism's concentration, the longer it takes to inhibit or kill the individual microorganisms. It takes even longer to achieve an exponential decrease in the numbers of pathogenic entities.

The structure of the microorganisms' population also can determine the effectiveness of an antimicrobial agent. For instance, endospores of *Mycobacterium* species are thick-walled, demonstrate a high degree of resistance to chemical agents, and have the capacity to survive repeated applications of one or more different antimicrobial agents.

Alternately, the concentration of an antimicrobial agent can influence its efficacy against skin-colonizing pathogens. The general rule has been that the more concentrated the antimicrobial agent, the more effective it will be, although the association between concentration and mortality of the pathogen does not increase in a linear fashion. Most often, increases beyond a certain concentration have little effect or value to the efficacy of the antimicrobial, and, in some instances, using a more dilute concentration is more effective. For example, alcohol can be just as effective at a 60% concentration level as it is at a 90% concentration level. With alcohol, the dilution with water appears to aid in the denaturing of proteins.[1]

Finally, the amount of time that the organism is exposed to the antimicrobial agent is a very important factor in the effectiveness of that agent. Generally the rule is that longer exposure times result in better efficacy. However, this rule requires refinement since the length of exposure should be suitable for the particular antimicrobial agent to kill or inhibit its target pathogen. This concept is probably the number one aspect about the use of antimicrobial agents that is misunderstood among clinicians. Take, for example, a standard skin preparation before the insertion of a vascular access device. It involves the application of alcohol followed by povidone iodine (PVP-I). Because PVP-I is an aqueous solution, it can take two to three minutes to dry. The clinician sometimes cannot wait this long and will wipe off the PVP-I solution with a sterile gauze or alcohol pad before it has dried. As a result, the antimicrobial effect of the PVP-I does not have adequate exposure time to kill or inhibit the microorganism, and any residual property that might be left on the skin is no longer available.

Beyond the scope of chemical agents, the environment of skin around the procedural site also can influence the efficacy of an antimicrobial agent. Most antimicrobial agents are neutralized in the presence of organic matter, and in fact organic matter can provide a safe haven for microorganisms to proliferate.

The Era of Discovery

Since the beginning of medical history, illness has been associated with a lack of personal hygiene, while wellness has been associated with cleanliness. Prudent use of body washings, typically incorporating herbs and oils native to the region and era, were common. The earliest records of minerals and herbs being used in a medicinal application are those of the ancient Hindu and Mediterranean societies.[2] The first pharmacopoeias were introduced in the 16th and 17th centuries, while during the early 19th century, knowledge of potent chemical structures, such as morphine, quinine and cocaine, brought scientists into the laboratory in the attempt to synthesize these chemical agents.

By the middle of the 19th century, observational studies noted a correlation between pathogen movement and the condition of the host. The noted American jurist Oliver Wendell Holmes observed the contagious property of puerperal fever, and in Vienna, Semmelweis observed that infections could be transmitted via infected hands and proposed the use of a chlorine rinse during hand washing. By instituting this simple procedure, the death rate in Vienna's obstetric clinics was reduced considerably.

In the latter part of the 19th century, Louis Pasteur introduced the Germ Theory, wherein he stated that clothing, utensils, and other objects could transmit microorganisms. Finally, in the 1860s, Joseph Lister's studies of the use of carbolic acid in surgery resulted in acceptance in the medical community that microorganisms indeed did cause infection and disease.[3]

Antiseptics commonly used during the period, boiled water, phenols, alcohol and iodine, are still used today however in different applications. Heating water to the point of boiling was not only an effective method to kill surface microbes, but also was readily available and cost-effective. Although most medical instruments are no longer sterilized in boiling water, some are still placed in an autoclave and sterile saline and sterile water continue to be used to clean the skin of hospitalized neonates.

Phenols have been used for both instrument disinfection and skin antisepsis for many years. Phenols such as Lysol™ continue to be used in hospitals and clinical laboratories today for general surface disinfection.

Tincture of iodine was used commonly as a skin antiseptic during the Civil War, with continued use in both World Wars I and II. Isopropyl alcohol or ethanol has a long history as a sk antiseptic. Ethanol, in the form o whiskey, was not only a great anesthetic agent but also a great agent to clean wounds and the surface of the skin.

Antimicrobial Agents of Today

Alcohol

Alcohol has been and is still used extensively in skin preparations. Alcohol exerts its antimicrobial effect by denaturing the cell proteins and dissolving the cell lipids. This is commonly referred to as "defatting." Alcohol demonstrates excellent bactericidal effect on both gram-positive and gram-negative bacteria, including *Tubercle bacillus* (tuberculosis). It has good fungicidal and virucidal activity, even showing an effect against the human immunodeficiency virus (HIV).[4]

The two alcohols most commonly used for skin antisepsis are isopropy alcohol and ethanol. The concentratio of the alcohol is the most important

asset when evaluating its antimicrobial effect. Alcohol between 70% and 90% (v/v) is the most effective. The lower the alcohol percentage (concentration), the less irritating it is to the skin. Major disadvantages of alcohol are the lack of residual antimicrobial property once the alcohol evaporates, irritation and drying of the skin, and its volatile or flammable nature.

Waterless hand wash solutions containing alcohol are now being combined with skin emollients to help decrease its drying and cracking effects on the skin.[3] Cracked and bleeding skin provide an excellent environment for the growth of skin microflora.

Iodine and Iodophors

Tincture of iodine and iodophors are safe antimicrobial agents effective against gram-positive and gram-negative bacteria, fungi, and viruses. However, they have minimal effect upon bacterial spores. Cell wall penetration and oxidation, with the substitution of available free iodine is how these agents exhibit their bactericidal activities. Percutaneous absorption of iodine has been noted in neonates, with hypothyroidism induction in the newborn.[7, 19, 25, 28, 35]

Tincture of iodine solutions contain 1% to 2% iodine, potassium iodine in 47% alcohol. A 2% tincture of iodine provides approximately 20,000 ppm of available iodine. Free iodine is associated with skin irritation and because of this the practice of wiping off the iodine once the procedure is complete was instituted. This practice removes the iodine and therefore no residual property is left on the skin. Allergenic or toxic effects have also been noted in sensitive individuals.

Iodophors are solutions of iodine, and anionic and nonionic complexes that contain a low amount of free iodine, ranging from 0.8 to 1.2 percent.[17] Povidone-iodine (*e.g.*, Betadine™) is composed of iodine, polyvinylpyrrolidone (PVP), and a detergent. Povidone-iodine (PVP-I) solutions range between 7.5% and 10%, which provide 0.75% to 1% free iodine for skin antisepsis. PVP-I solutions are less irritating to the skin because the PVP complex allows only small amounts of free iodine to be available on the skin surface at any given time. Iodophors must be allowed to have contact with the skin for 2-minutes or more in order for the release of free iodine to occur. Once in place, iodophors exhibit a residual effect for approximately two hours. However if iodine comes into contact with organic matter, such as blood, it is neutralized and is no longer effective. It should be noted that PVP-I solutions have been associated with microbial contamination.[9] It also has been demonstrated that multi-use povidone-iodine bottles can become contaminated with normal use in the hospital setting.[2]

New skin antiseptics combining alcohol with either povidone iodine or chlorhexidine have recently become available in the United States. Unlike tincture of iodine these products provide a greater concentration of alcohol, 60% to 90%, with an antimicrobial agent that provides residual or persistent activity on the skin surface.

Chlorhexidine

Chlorhexidine is a cationic biguanide. Its antimicrobial action is in the disruption of the cell membrane, which results in precipitation of the cell contents. Chlorhexidine is a broad spectrum antiseptic effective against gram-positive and gram-negative bacteria. It is a fair fungicidal agent and is effective against most viruses.[10] Chlorhexidine has a strong binding property to skin, contributing to 6-hours of residual activity, and is not neutralized in the presence of organic material on the skin surface.

Chlorhexidine currently is available for surgical site, wound, and hand antisepsis. In a prospective, randomized comparative trial, chlorhexidine was shown to provide superior skin antisepsis in the prevention of local or cutaneous infection prior to insertion of an intravascular device.[15] Because chlorhexidine is a large chemical compound, it has little systemic absorption and low toxic effects. However sensitization to chlorhexidine/silver sulfadiazine-coated central catheters has been noted in certain ethnic populations.[4]

Outside the U.S., chlorhexidine has been used extensively for skin antisepsis and is considered the gold standard by many infection control clinicians. Recently the Food and Drug Administration (FDA) has approved a solution containing 2% chlorhexidine and 70% isopropyl alcohol for use as a preoperative skin preparation solution. In parallel, the FDA currently is reviewing a 1% chlorhexidine and polymer formulation in alcohol for IV site preparation and maintenance. It will be important to see

Definitions:

Antiseptic: a chemical agent that destroys or inhibits microorganisms on skin or tissue and has an effect of limiting or optimally preventing infection.

Disinfectant: a chemical agent that destroys microorganisms, but it does not necessarily kill all microorganisms, but does reduce them to a non-lethal level. Associated with inanimate objects.

Preservatives: a low percentage or ppm of a chemical compound to prevent microbial spoilage of preparations.

Sterilization: the total removal or destruction of all living microorganisms, sterilization is usually associated with gas, heat, or irradiation methods.

Bactericidal: Kills microorganisms.

Bacteriostatic: Temporarily prevents microorganisms from multiplication, disrupts minor chemical reactions and slows metabolism resulting in increased time between cell divisions.

the effects these combination products exhibit on the incidence of nosocomial infections; particularly if there is a reduction in surgical site infections and catheter-related bloodstream infections. It seems ironic that after 40 years in use, the U.S. is just now receiving the benefits of chlorhexidine.

Miscellaneous Antimicrobial Agents

Para-chlor-meta-xylenol (PCMX) and triclosan have made an appearance in the antiseptic market in the past ten years. The modes and mechanisms of PCMX and triclosan are still being studied. Comparative, prospective and randomized studies are few for these two compounds.

PCMX is a broad-spectrum antimicrobial agent that has good activity against gram-positive organisms, but demonstrates a lesser antimicrobial activity against gram-negative bacteria, especially *Pseudomonas* species. It has fair antimicrobial activity against some fungi and viruses. In several studies, PCMX has been shown to be less effective than PVP-I or chlorhexidine in reducing skin flora.[22, 30]

In contrast triclosan, a diphenyl ether, causes disruption of the microbial cell wall. Triclosan is a broad-spectrum antimicrobial agent that works well against gram-positive and gram-negative bacteria, but is a poor fungicidal agent. Its antimicrobial activity against viruses is unknown. It has an excellent residual property on the skin surface and is not affected by the presence of organic matter. Even though it is absorbed through intact skin, it has shown little toxic effect. Additional safety and efficacy data are needed.

Triclosan is found in most antibacterial solutions sold in the consumer market today. It also is contained in some plastics and kitchenware. The percentage of triclosan is very low, 0.03%, for most products in the market. The mode of action of triclosan is still being studied and the possibility of a secondary mode of action is, that it inhibits bacterial fatty acid synthesis[16, 33] which could lead to the possibility of resistance. *Staphylococcus aureus* strains resistant to triclosan have started to appear in healthcare facilities, yet every day the U.S. population is increasingly exposed to triclosan through consumer and over the counter products.

Chlorine is a very powerful oxidizing agent. It is a broad-spectrum antimicrobial agent that is bactericidal, fungicidal, and virucidal, but its efficacy is affected by the presence of organic matter. Chlorine is used extensively for the disinfection of water supplies and a 10% sodium hypochloride solution (such as household bleach) has been used for surface cleaning.

Chlorine-based solutions have been used for many years to clean dialysis equipment. Although clinical studies for the disinfection of dialysis equipment are available, very little has been written about its use as a skin antiseptic agent. Pharmaceutical grade sodium hypochloride for skin antisepsis is now available in the U.S.; these products are imported from Italy. The main features of these products are low chlorine concentration (1.1%) and a high concentration of sodium chloride (18%).

Modes and Mechanisms of Antimicrobial Agents*

Agent	Site of Action	Efficacy	Notes
Alcohol	Cell wall, denatures proteins and cell lipids	Excellent against gram-positive and gram-negative bacteria. Good fungicial and virucidal activity.	No residual property, drying to skin, and solution is flammable
Tincture of Iodine/Iodophors (Betadine™)	Cell wall, oxidation with substitution of iodine	Excellent against gram-positive bacteria. Good activity against gram-negative bacteria, fungi and viruses.	Skin irritation, absorption with possible toxic effects, especially in the neonate
Chlorhexidine	Cell wall	Excellent against gram-positive bacteria. Good activity against Gram-negative bacteria, fungi and viruses.	Neurotoxicity, avoid contact with eyes, ears and mucous membranes.
PCMX (para-chloro-meta-xylenol)	Cell wall	Good activity against gram-positive bacteria, fair activity against gram-negative bacteria, fungi and viruses.	More data needed, especially in the clinical setting.
Triclosan	Cell wall Secondary mode: inhibition of fatty acid synthesis	Good activity against gram-positive and gram-negative bacteria, exception *Pseudomonas* spp. Poor activity for fungi.	More data needed; possibility of resistance.

*Larson E. Guideline for use of topical antimicrobial agents. Amer J Infect Control 1988; 16(6): 253-266.

Neonatal Considerations

In the neonatal population, sterile water and normal saline are used, especially for premature infants, since their underdeveloped stratum corneum is highly permeable to chemical compounds. Iodine has been noted as being highly absorbed and linked to hypothyroidism in the very young infant.[17, 19, 25, 28, 29] Chlorhexidine has been seen to be effective and only absorbed at minimal levels in the very young infant.[8, 12, 15] In the infant younger than 27 weeks gestational age, antimicrobial choices are few.

Considerations for Antimicrobial Application

The Intravenous Nursing Society Standards of Practice state that antiseptic solutions should be applied with friction, working outward from the insertion site in a circular pattern (Figure 1). This is usually repeated three times with a swab stick saturated with an antimicrobial solution. Following this circular pattern three times in the same direction may not allow penetration of the antiseptic solutions into the cracks and fissures of the epidermal layer of the skin. It would seem more appropriate to apply each swab stick with mechanical friction in the following manner. Use the first swab stick in a horizontal plane, cleansing the skin from side to side. Apply the second swab stick on a vertical plane, up and down. The final swab stick would then be applied in a circular pattern moving outward from the procedural site (Figure 2). The American Association of Blood Banks recommends a procedure similar to this for donor site preparation.

The Antimicrobial Future

Products that combine polymers with two or more antimicrobial agents have entered the healthcare market and are under evaluation in the U.S. today. These agents provide a protective barrier or liquid drape that enhances the antimicrobial properties for skin antisepsis, and might help address compliance issues with cleaning and preparing the skin for medical procedures.

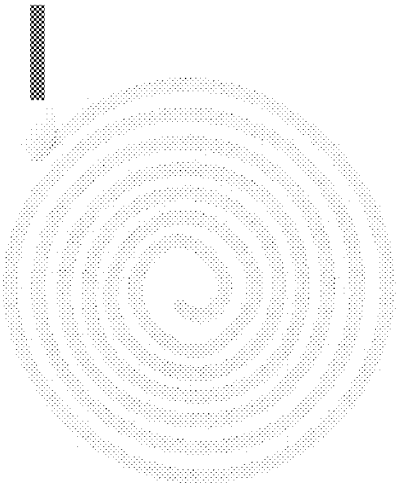


Figure 1

Application in concentric circles, repeated three times.

Octenidine, a bispyridine compound that exhibits a broad-spectrum antimicrobial activity, has been introduced in Europe and is gaining recognition as the future "gold standard" for skin antisepsis. Further testing of octenidine in the clinical setting is needed.

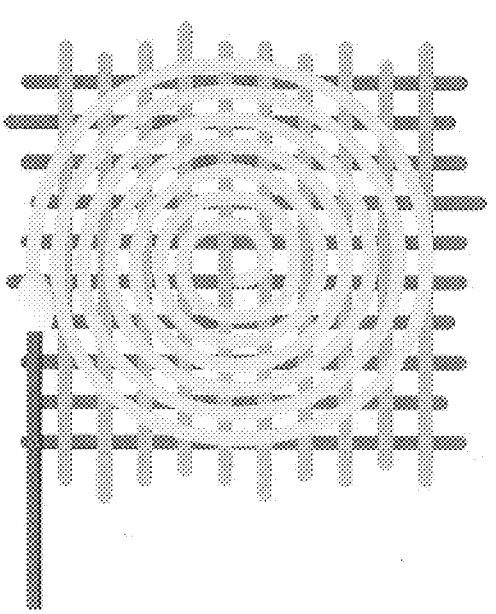
Natural cationic peptides occur in most living organisms. These peptides are small molecules that have a positive charge that kill or inhibit the growth of bacteria, and fungi. Cationic antimicrobial peptides physically attack the cell membrane. The peptides' main function is to offer an effective non-specific immune response that protects against opportunistic microorganisms. Studies have demonstrated a novel cationic antimicrobial peptide to be safe and effective in eliminating IV catheter colonization.[24] Phase III clinical trials are being conducted in the U.S. currently.

Finally, the oil from the tea tree (*Melaleuca alternifolia*) is being investigated in Australia as a topical antimicrobial agent. In 1990, tea tree oil sparked interest after a clinical study for the treatment of acne was published.[5, 6, 27] Since that trial, the susceptibility data on isolates from infections has been accumulated for potential areas of treatment with the agent. Tea tree oil activity is at the cell membrane, but other sites of action may exist. Have we made a full circle in the development of antimicrobial agents from the ancient Hindu and Mediterranean practices to present?

The future is bright, especially in the preventative properties that antimicrobial solutions can provide in the prevention of disease and infection due to skin pathogens. "Cost and quality. Quality and cost. No matter how you slice it, virtually every purchase decision in a health care setting must weigh these two fundamental factors."[13] Preventative measures seem to be the highest quality in medical treatment and the most cost efficient. ❤

Figure 2

Application with horizontal movement, followed by vertical movement, followed with the third application in concentric circles.



Cynthia is a microbiologist who has worked extensively with antimicrobial agents and their clinical applications. Her expertise includes the laboratory and hospital settings in addition to research and development with industry.

Alicia is currently a clinical resource specialist for BD Medical Systems, Sandy, Utah. She has extensive experience in infusion therapy including acute care, home infusion, and product development.

1. Altemeier WA. Surgical Antisepsis. Block SS. Ed. Disinfection, sterilization, preservation. 3rd ed. Philadelphia: Lea and Febiger, 1987.
2. Bumbach DJ, Stain DJ, Murray O, Thys DM, Sordillo EM. Povidone iodine and skin disinfection before initiation of epidural anesthesia. *Anesthesiology* 1998; 88(3):668-672.
3. Boyce JM. Using alcohol for hand antisepsis: dispelling old myths. *Infect Control Hosp Epidemiol* 2000; 21(7): 438-441.
4. Burlington, FDA Public Notice: Hypersensitivity to chlorhexidine/silver sulfadiazine-coated catheters, 1998.
5. Carson CF, Riley TV, Cookson BD. Efficacy and safety of tea tree oil as a topical antimicrobial agent. *J Hosp Infect* 1998;40(3):175-178.
6. Carson CF, Riley TV. Antimicrobial activity of the major components of the essential oil of Melaleuca alternifolia. *J Appl Bacteriol* 1995;78(3): 264-269.
7. Choonara I. Percutaneous drug absorption and administration. *Arch Dis Child* 1994; 71(2): F73-F74.
8. Cowen J, Ellis S, McAinsh J. Absorption of chlorhexidine from intact skin of newborn infants. *Arch Dis Child* 1979; 54: 379-383.
9. Craven, et al. MMWR. Contamination of Povidone Iodine solution with Pseudomonas aeruginosa. *N Engl J Med* 1981.
10. Denton G. Chlorhexidine. Block SS. Ed. Disinfection, sterilization, preservation 4th ed. Philadelphia: Lea and Febiger, 1991.
11. Encyclopaedia Britannica: Pharmaceutical Industry: History. [Online] http://www.britannica.com.
12. Garland JS, Buck RK, Maloney P, et al. Comparison of 10% povidone-iodine and 0.5% chlorhexidine gluconate for the prevention of peripheral intravenous catheter colonization in neonates: A prospective trial. *Pediatr Infect Dis J* 1995; 14: 510-516.
13. Garcia R. Getting down to the business of infection control. *Mater Manag Health Care* 1999; 8(8): 22, 24, 26.
14. Garrett Do, Jochimsen E, Murfitt K, et al. The emergence of decreased susceptibility to vancomycin is Staphylococcus epidermidis. *Infect Control Hosp Epidemiol* 1999; 20: 167-170.
15. Gongwer LE, Hubbank K, Lenkiewicz RS, et al. The effects of daily bathing of neonatal rhesus monkeys with an antimicrobial skin cleanser containing chlorhexidine gluconate. *Toxicol Appl Pharmacol* 1980; 52:255-261.
16. Heath RJ, et al. Mechanism of triclosan inhibition of bacterial fatty acid synthesis. *J Biol Chem* 1999; 274(16): 11110-11114.
17. Larsen E. Guideline for use of topical antimicrobial agents. *Amer J Infect Control* 1988; 16(6): 253-266.
18. Linden PK. Clinical implications of nosocomial gram positive bacteremia and superimposed antimicrobial resistance. *Am J Med* 1998; (5A): 24S-33S.
19. Linder N, Davidovitch N, Reichman B, Kuint J, Lubin D, Meyerovitch J, Sela BA, Dolfin Z, Sack J. Topical iodine-containing antiseptics and subclinical hypothyroidism in preterm infants. *J Pediatr* 1997;131(3): 434-439.
20. Maki DG. Skin as a source of nosocomial infection Direction for future research. *Infection Control* 1986; 7(2): 113-117.
21. Maki DG. Infections caused by intravascular devices used for infusion therapy: pathogenesis, prevention and management. *Infection Assoc with Med Dev* 1994; (2): 155-213.
22. Maki DG, McCormick R. 1984. Abstract. Reducing skin flora with antimicrobials. Interscience Conference on Antimicrobial Agents and Chemotherapy ICAAC.
23. Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *The Lancet* 1991; 338: 339-343.
24. Micrologix Biotech Inc. Micrologix successfully completes phase I and phase II clinical trials for the prevention c bloodstream infections [Online] http://www.mbiotech.com, April 1999:27.
25. Parravicini E, Fontana C, Paterlini GL, Tagliabue P, Rovelli F, Leung K, Stark R. Iodine, thyroid function, and very low birth weight infants. *Pediatrics* 1996; 98(4):730-734.
26. Raad I, Darouiche, RO. Catheter-related septicemia: risk reduction. *Infect Med* 1996;13(9):807-812, 815-819, 823.
27. Raman A, Weir U, Bloomfield SF. Antimicrobial effects of tea-tree oil and its major components on Staphylococcus aureus, Staph. epidermidis and Propionibacterium acnes. *Lett Appl Microbiol* 1995;21(4): 242-245.
28. Rutter N. Percutaneous drug absorption in the newborn: Hazards and uses. *Clin Perinatol* 1987; 14:911-930.
29. Siegfried E, Shah P. Povidone-iodine may increase cerebral palsy risk. *Pediatric News* 1997; 31(11):11.
30. Sheehan AZ. J Food Protec 1982.
31. Souvenir D, Anderson DE jr, Palpant S, Mroch H, Askin S, Anderson j, Claridge J, Eiland J, Malone C, Garrison MW, Watson P, Campbell DM. Blood cultures positive for coagulase-negative staphylococci: Antisepsis, pseudobacteremia, and therapy patients. *J Clin Microbiol* 1998;36(7):1923-1926.
32. Strand CL, Wajsbort RR, Sturmann K. Effect of iodophor vs iodine tincture skin preparation on blood culture contamination rate. *JAMA* 1993;169(8):1004-1006.
33. Suller MT, Russell AD. Triclosan and antibiotic resistancer in Staphylococcus aureus. *J Antimicrob Chemother* 2000; 46:11-18.
34. Washington JA. An international multicenter study of blood culture practices. The International Collaborative Blood Culture Study Group. *Eur J Clin Microbiol Infect Dis* 1992;11(12):1115-1128.
35. Wenzel RP. The economics of nosocomial infection. *J Hosp Infect* 1995; 31:79-81.

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Evidence-Based Practice in the Management of Vascular Access Devices for Home Parenteral Nutrition Therapy

Marcia Ryder, PhD, MS, RN

From Research and Consulting, Healthcare-acquired Infections/Vascular Access, San Mateo, California

Correspondence: Marcia A. Ryder, RN, Research and Consulting, Healthcare-acquired Infections/Vascular Access, 1504 Forge Road, San Mateo, CA 94402. Electronic mail may be sent to ryder1234@aol.com .

ABSTRACT

Catheter-related bloodstream infection and catheter occlusion are potential significant complications of parenteral nutrition therapy. The increased incidence and associated morbidity, mortality, increased costs, and quality-of-life issues experienced with these adverse events necessitate specialized management of vascular access devices. The host coagulation response to biomaterials and the associated development of biofilm on vascular devices are complex phenomena. Multiple interventions are required to prevent access of bacteria to both intraluminal and extraluminal catheter surfaces, and the occurrence of catheter occlusion. The discovery of the biofilm form of microbial life and the associated recalcitrance of biofilm bacteria to antimicrobials has provided insight into the failure of current prevention, diagnostic, and treatment protocols. Critical interventions are presented correlating current evidence with new discoveries in pathogenesis.

The revolution in health-care delivery systems over the last 2 decades has shifted the care of patients from the acute care setting to alternate sites. Provision of healthcare in the home has become the fastest-growing segment of the healthcare system to the extent that nearly as many patients are receiving care in the home as in the hospital setting.[1]

Nearly eight million people in the United States received medical care at home in 1996,[2] of which 774,113 (10%) were estimated to have at least 1 indwelling medical device.[3] The use of a medical device is the greatest predictor (exogenous) of healthcare-associated infection.[3] Complications related to vascular access devices (VADs) have reportedly been the primary cause of morbidity, mortality, and rehospitalization related to parenteral nutrition therapy in hospitalized patients,[4,5] home patients—including adults[6–8] and pediatrics[9,10]—in the United States and abroad.[11–13] Unfortunately, the transfer of care to alternate sites was not accompanied by the development of national surveillance systems to monitor outcomes and adverse events or with the establishment of formal infection

control programs for standardization in the prevention, diagnosis, and treatment of complications.[3,14]

The safe administration of parenteral nutrition (PN) requires the use of a central venous catheter (CVC) due to the hypertonic and acidic properties of the solution. CVCs most appropriate for PN therapy in the home include peripherally inserted central catheters (PICC), tunneled catheters, and implanted ports[15,16] (see Ryder Appendix). However, the use of these devices is not without serious risk. Thrombotic catheter occlusion and catheter-related infections are the most frequently reported catheter complications for all types of CVCs in all healthcare settings. In an analysis of data from the Strategic Health Care Programs National Database (April 1999 to September 2000) that included 50,470 patients receiving home infusion care (2.83 million catheter-days), the rate of CVC complication was 1.5 per 1000 catheter-days.[17] The most common events (per 1000 catheter-days) were catheter dysfunction (0.83; nonthrombotic 0.6, thrombotic 0.23), cathetersite infections (0.26), and bloodstream infections (0.19). In the face of the increasing shift of care for the more acutely ill and immunocompromised patients to the nonhospital setting, an increase in the rate of these complications might be expected.

Prevention of complications remains the cornerstone of quality patient care and improved outcomes. Harbarth et al[18] conducted a systematic review of the literature published in the last decade to generate a crude estimate of the proportion of potentially preventable nosocomial infections under current healthcare conditions. The evaluation of 30 reports suggests that at least 20%, ranging from 10% to 70%, of all nosocomial infections are preventable. The most important reduction effect was discovered for catheter-related bloodstream infection (CRBSI). Little is known about the proportion of preventable infections in the homecare setting.

With continued concern for the increased morbidity, mortality, and risk of device-related complications and the lack of standardization of care in alternate sites, it is prudent to identify key evidence-based strategies applicable to home PN patients for the care and management of VADs. The purpose of this paper is to review the evidence for implementation of critical preventative strategies linked to the pathogenesis of the most common VAD complications, catheter-related infections and thrombotic catheter occlusion.

CATHETER-RELATED INFECTIONS

The estimated 20% prevention rate for nosocomial infections raises the question of why 80% are not preventable. Recent discoveries related to microbial survival strategies and antimicrobial resistance provide insight into the pathogenesis of CRBSIs. Understanding pathogenesis gives clear direction to prevention.

Pathogenesis of Catheter-Related Infections

IV catheters inserted into the bloodstream are subject to the hydrodynamics of 2 flow systems. The external surface of the catheter interfaces with the circulating blood, whereas the internal surface interacts with a variety of infusates, including crystalloid solutions, drug admixtures, blood and blood products, and nutritive solutions. The rate of blood flow is dependent on the diameter of the catheterized vessel and the patient's physiologic status. The rate of flow within the catheter is highly variable, depending on the infusion therapy, or there may be no flow when the catheter is "locked." Both Silastic and polyurethane are negatively charged, and hydrophobic biomaterials that promote adherence of various contacting particles in solutions and host products form a "conditioning film" on the catheter surface.

Under any circumstance, the external and internal catheter luminal surfaces are not mirror images. Microorganisms in contact with either surface interact with the biomaterial under very different conditions. The pathogenesis of infection at each surface must be considered independently in order to develop effective measures for prevention. Catheter-related infections occur as the result of a complex series of events: (a) microbial contamination of the internal or external surface of the catheter or add-on devices, (b) microbial adherence, (c) biofilm development, and (d) dispersal and dissemination of biofilm bacteria into the bloodstream.[19]

The patient's skin is the primary source of contamination of the external catheter surface. During insertion, bacteria are impacted on the tip and external catheter surface as the catheter transcends the epidermis. Thus, the catheter arrives in the bloodstream with a specific quantity of adherent bacteria. Elliott et al[20] verified this phenomenon in a study of 30 cardiac surgical patients requiring central venous catheterization. After insertion, the skin at the insertion site and all devices used during the procedure were cultured. The tip of each catheter was cultured *in situ* within 90 minutes of the insertion during surgery. Sixty-seven percent of cultures from the insertion site were positive, as well as 50% of guidewires, 4% of skin dilators, 36% of insertion needles, and 17% of the catheter tips. Within 3 days, 11% of catheters had >15 colony forming units (cfu) on the external surface despite rigorous skin antisepsis and aseptic technique. These results are further substantiated in 2 subsequent studies using pulsed gel electrophoresis techniques to match organisms attached to the tip of the catheter with organisms at the insertion site.[21,22]

Arrival of the catheter into the bloodstream triggers a well-defined host response.[23] Plasma proteins instantly adhere to the catheter surface upon contact with the blood. Attachment of arriving platelets, neutrophils, and fibrin(ogen) forms a "conditioning layer" on the catheter surface over the next few hours. Thrombus may then form to a variable extent over the fibrin sheath. After approximately 1 week, migratory fibroblasts and smooth muscle cells from the injured vessel wall cover the fibrin sheath/pericatheter thrombus. By 2 weeks, a layer of migratory endothelial cells that may then be protective against microbial attachment encases the host-derived sheath. Planktonic bacteria "free floating" in the bloodstream from distant sources may attach to the developing conditioning layer or pericatheter thrombus and further colonize the catheter.[24–26] The

preattached bacteria immediately develop a biofilm for survival in a new hostile environment.

Concurrently, contamination and colonization of the skin tract or subcutaneous tunnel may continue to occur during the inflammatory phase of wound healing within the first few days of catheterization. Microorganisms from the skin surface at the insertion site are passively transported within the edematous skin tract by capillary action.[27] The arriving microorganisms attach to the catheter surface or surrounding traumatized tissue and form colonizing biofilm. The progression from colonization to infection depends on the bacterial count, the species present, the virulence of the organisms, and the host immune response.[28]

Microorganisms gain entrance to the internal lumen of the catheter at any entry point, anywhere along the fluid path where the system is manipulated (ie, IV solution connection sites, administration tubing junctions, access portals, and needleless connectors). The source of contamination is primarily the hands of medical personnel and the patient's own skin or body fluids in contact with the access sites. Bacteria flowing through any of the administration devices that come in direct contact with the inner lumen attach to surface and form colonizing biofilms. The same process of protein attachment, fibrin deposition, and clotting occurs within the lumen when used for blood sampling and blood product administration or when blood is allowed to remain within the lumen. The host conditioned surface then provides attachment sites for arriving bacteria.[25,28]

Biofilm: Microbial Life on Surfaces

The initial event in the formation of biofilm is the attachment of microbes to the surface of the biomaterial or conditioned surface. Within 10–20 minutes of direct contact, phenotypic changes within the microbial cell wall initiate the production of species-dependent adhesins and accumulation proteins.[29,30] Self-produced exopolymer saccharides embed the proliferating cells into cell clusters or microcolonies.

Although each biofilm is unique in structure, most biofilms develop as multilayered cell clusters with a complex architecture of towers and flow channels for the delivery of nutrients and removal of waste. This structure sustains an environment heterogeneous to oxygen level, nutrient availability, and metabolic state, depending on the location of the cell within the biofilm. The parent cells adherent to the biomaterial surface are the most deprived of nutrient availability and are the most metabolically altered into a slow-growing or nongrowing, dormant lifestyle. Development of the biofilm evolves according to the local microenvironment conditions and is often incorporated structurally within host conditioning layers or tissue matrices. The rate of growth is influenced by flow rate, nutrient composition of the liquid (blood or infusate), and temperature.[31] The bloodstream provides ideal conditions to support biofilm growth on indwelling devices. Depending on the location and number of attached or "sessile" bacteria, the biofilm forms in patchy sections or develops in a contiguous layer completely covering the surface.

Biofilms harbor large numbers of organisms within a small scale, and pathogen cell densities can reach as many as 10^7 cells/cm^2 on a surface.[32] Increasing cellular density

within the biofilm triggers an elaborate cell-to-cell communication that regulates biofilm structure and progeny cell dispersal.[33] Dissemination of biofilm cells is species dependent but typically occurs by the shedding of single daughter cells or detachment of clumps of biofilm cells by hydrodynamic shear forces or by cell-cell signaling that directs the production of substances that lyse the biofilm matrix.[34] Cells dispersed as single planktonic cells are readily killed by normal host defense mechanisms, and the biofilm remains nonpathogenic. However, when the dissemination becomes extensive or if the host becomes immunosuppressed, colonization develops into overt infection.[30] Dispersal in clumps, particularly *Staphylococcus aureus*, containing hundreds of resistant cells may result in metastatic infections.[35]

Biofilms mature at variable rates dependent on the microbial species. Staphylococcus biofilms mature within 7 days, whereas *Pseudomonas* biofilms mature later, around 10–12 days.[36,37] Extraluminal catheter-related infections are typically evidenced within the first week of catheterization.[38] This correlates well with heavy initial colonization of the external catheter surface that was most likely inserted through poorly disinfected skin. Infection from the internal lumen typically occurs after 1 week as the number of manipulations increase; however, more recently the internal lumen has been shown to be the primary source of bloodstream infection as early as 3 and 6 days in short-term catheters.[39] The mean time to infection in long-term catheters is >10 days and implicates the internal lumen as the major site of CRBSI.[40]

It has been estimated that as many as 65% of bacterial infections treated by physicians in the developed world are related to biofilms.[34] Clinical implications for prevention, diagnosis, and treatment of vascular catheter-related infections can be derived from understanding the pathogenesis of biofilm infections. The following characteristics of biofilm infections should be considered in the management of CVCs[25,29,35,41]:

- virtually any organism in contact with a biomaterial can form a biofilm;
- microbial attachment to surfaces results in extensive phenotypic changes profoundly different from unattached cells;
- bacteria growing in biofilm may be in a dormant but viable state and initially may fail to grow in culture;
- biofilm infections are inherently resistant to all antimicrobial agents (by 10–1000 times) and to the host's immune system;
- aging biofilms become increasingly more difficult to treat;
- in general, exposure of biofilm to prolonged and elevated concentrations of antibiotic agents kills approximately 90% of biofilm cells; the persisting cells survive and regenerate the biofilm after cessation of antibiotic therapy.

Evidence-Based Prevention Strategies

The Centers for Disease Control and Prevention's (CDC) *Guidelines for the Prevention of Intravascular Catheter-Related Infections* offers 113 recommendations for implementation in all healthcare settings.[15] This extensive set of guidelines represents the complexity of effort required for the safe use of these devices. Harbarth et al[18] found that the most effective approach to the reduction of nosocomial infections includes the

implementation of a multimodal quality improvement program applying standardized policies and, if necessary, mandatory practice changes. Considering the pathogenesis of catheter-related infections, interventions should be designed to prevent microbial contact with the external catheter surface and microbial entry to the internal surfaces of the entire delivery system. Given that the major sources of microorganisms are the patient's own skin and the hands of medical personnel, a multimodal intervention package must be implemented to prevent microbial access from these sources.

Extraluminal contamination: skin antisepsis. Contamination of the external lumen during insertion and throughout the duration of use is most effectively minimized by systematic skin antisepsis and the use of an antimicrobial dressing (Table I). Preoperative skin preparation is probably the most important intervention for the prevention of CRBSI. Protocol development for effective skin antisepsis requires an understanding of the anatomy, physiology, and microbiology of the skin at the chosen site of insertion.

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TABLE I *Evidence-based recommendations for the prevention of contamination of the external lumen of central venous catheters*

The basic structure of the skin from outer- to innermost layer includes the superficial horny cell layer of the stratum corneum (1–2 mm thick), the viable or stratified cell layer of epidermis (50–100 mm thick), the dermis (1–2 mm thick), and the hypodermis (1–2 mm thick).[42] The stratum corneum is composed of approximately 15 layers of corneocytes that provide the barrier function of the skin. The corneocytes are remnants of terminally differentiated keratinocytes generated by the stratified epidermis positioned directly under the stratum corneum. The stratified epidermis is composed of 10–20 layers of keratinized epithelial cells. The stratum corneum receives a new basal layer of cells to replace the outermost surface layer of dead cells (squames) shed from the skin surface each day. The stratum corneum is replaced in total approximately every 2 weeks.[43] Healthy skin disseminates approximately 10^7 squames daily, 10% of which contain viable bacteria.

The microbiology of the skin varies widely, depending on body location and nutrient and water availability. Normal colony count of the skin at the subclavian and jugular insertion sites is approximately 1000–10,000 cfu/cm^2 compared with approximately 10 cfu per cm^2 at the antecubital space.[44] The transient skin flora arrives from the environment and may include bacteria, fungi, and virus. The resident flora is found mainly in the stratum corneum, 80% of which are located within the first 5 layers.[45] The remaining 20% inhabit

the deeper reservoirs of sebaceous glands and hair follicles sustained within biofilms that provide added protection against antiseptic agents.[29,46,47] The dominant species of resident flora is the coagulase negative staphylococci (CNS; mostly *Staphylococcus epidermidis*). *S epidermidis* grows in prolific biofilms between the squamous cells of the outer 3–10 layers of the stratified epithelium and colonize the hair follicles and sebaceous glands quite successfully.[32]

Topical application of antimicrobial agents eliminates CNS on the skin surface but does not sterilize the underlying stratum corneum, sebaceous glands, or hair follicles.[48] The bacterial concentration of the skin is most effectively reduced by the combination of physical removal, along with antimicrobial activity by antiseptic exposure.[49] The CDC guidelines[15] and the *2004 AORN (Association of Operating Room Nurses) Standards, Recommended Practices, and Guidelines*[50] recommend a 2-step process for preoperative skin preparation and continued catheter insertion site care. The 2 steps include skin cleansing, followed by application of an antiseptic. The CDC guidelines recommend specific antiseptics for use on clean skin but do not address methods for cleansing the skin. The AORN guidelines provide specific recommended practice techniques for both skin cleansing and surgical site preparation. Recommendations for skin cleansing include (a) patient showering before arrival at the practice setting, (b) washing the surgical site before arrival in the practice setting, and (c) washing the surgical site immediately before applying the antiseptic agent.[50]

Data presented by Seal and Paul-Cheadle[51] further support the utility of a systems approach to surgical-site preparation. Use of a combination of antiseptic shower(s) or bath(s), followed by antiseptic surgical site preparation with alcohol-based antiseptics resulted in a positive impact on the incidence of surgical-site infections.

Substantial evidence indicates that chlorhexidine gluconate (CHG) solutions are the superior agents for use in vascular catheter insertion care for the reduction of CRBSIs. The CDC guidelines recommend 2% CHG as the preferred antiseptic for skin preparation and designate its use as a performance indicator for reducing CRBSI. The economic benefits of CHG use for vascular catheter site care have been compared with povidone iodine use in a decision analysis model.[52] The model estimates that the use of CHG compared with povidone iodine results in a 1.6% decrease in the incidence of CRBSI, a 0.23% decrease in the incidence of death, and a cost savings of $113 per catheter used.

CHG in combination with alcohol increases the potential activity of the antiseptics. The alcohol provides rapid reduction in bacterial counts but has minimal persistence. The CHG remains active for at least 6 hours and is minimally affected by the presence of organic material.[53,54] Repeated use of CHG increases effectiveness over time due to the binding and retention of active antiseptic to the surface epithelial cell walls.[55] A preoperative 4% CHG skin scrub (Hibiclens scrub sponge, Regent Medical Ltd, Irlam, UK) followed by the application of a 2% CHG/70% alcohol antiseptic (ChloraPrep, Medi-Flex Inc., Kansas City, KS) is suggested for maximum physical and chemical reduction of transient and resident flora before passage of the catheter through the skin.

Within 18 hours of antiseptic application, resident bacteria surface from the deeper reservoirs and recolonize the skin surface, regardless of the type of sterile dressing applied over the insertion site.[45,48,53] Repeated skin antisepsis may be important within the first 24–48 hours of insertion to remove repopulating bacteria from the insertion site avoiding migration into the skin tract by capillary action. Postinsertion site care is accomplished by using the same 2-step process. Skin cleansing with gentle mechanical friction accomplishes removal of desquamed epithelial cells, repopulating bacteria, inactive antiseptic, oils, sweat, and any drainage if present. The antiseptic is then applied to clean skin. A multidirectional, back-and-forth cleansing using alcohol saturated swab sticks, followed by circular application of a 2% CHG/70% alcohol combination, is suggested.[56]

Extraluminal contamination: antimicrobial dressing. Considerable debate over the role of gauze and tape dressings *vs* transparent polyurethane film dressings in the prevention of catheter-related infections has been observed in the literature. Gillies et al[57] recently completed a Cochran database systematic review to identify by meta-analysis any differences between gauze and tape dressings and transparent polyurethane film dressings in the incidence of CVC-related local infection or CRBSI, catheter security, dressing condition, tolerance to the material, and ease of application in hospitalized patients. There was no evidence of any difference in the incidence of infectious complications between any of the dressing types compared in the review. Traditional sterile gauze and tape dressings and transparent polyurethane film dressings provide protection for the catheter site from trauma and transient bacteria and prevent the accumulation of moisture; however, neither have any antimicrobial properties. This illustrates the critical importance of effective skin antisepsis as the major intervention in the prevention of catheter site infection, tunnel and port pocket infection, and CRBSI from the extraluminal source.

The use of a CHG-impregnated polyurethane foam disc applied around the catheter and in direct contact with the skin surface at the insertion site has demonstrated the ability to maintain a sterile skin surface at the insertion site over the lifetime of the catheter.[58] In a randomized clinical trial, 50 patients undergoing abdominal surgery had a CVC placed for PN and received either a transparent polyurethane film dressing (Bioclusive, Johnson & Johnson, Inc, New Brunswick, NJ) or a CHG-impregnated disc (Biopatch, Johnson & Johnson) covered with a transparent film dressing. Two skin cultures were taken once a week during the dressing change, 1 from under the CHG disc and 1 from a distant site under the transparent dressing. Contamination was detected under the transparent dressing in 14 of 60 cases (23.3%), whereas no bacterial contamination was observed under the CHG disc ($p < .0001$). In the control group (transparent dressing alone), bacterial contamination was detected in 7 of 64 cases (10.9%) at the insertion site and in 17 of 64 cases (26.6%) at the distant site under the dressing ($p < .0001$). The difference in contamination at the insertion site between the CHG disc and control was significant in favor of the CHG disc ($p < .01$). There was no difference in contamination under the dressing at the distant site between the 2 groups.

In a second, randomized, blinded, controlled, multicenter trial by Maki et al,[59] use of a CHG-impregnated foam disc (Biopatch) was compared with a control transparent

polyurethane film dressing in 589 hospitalized patients receiving short- and medium-term CVCs and arterial catheters.[59,60] All CRBSIs were confirmed by concordance between microorganisms isolated from peripheral blood and the catheter tip, hub, or infusate demonstrated by DNA subtyping. The CHG dressing significantly reduced the risk of local catheter-related infection (CHG disc, 28.14%; and control, 45.24%; $p < .001$) and CRBSI (CHG disc, 2.37%; and control, 6.12%; $p < .05$). Not surprisingly, the greatest benefit was the prevention of local infection and the extraluminal source of CRBSI.

The cost benefit and impact on CRBSI mortality has also been assessed. A cost-benefit sensitivity analysis estimates potential US net benefits from CHG dressing use to range from $275 million to approximately $1.97 billion, and a preventable mortality between 329 and 3906 deaths annually.[60]

The combination of the 2-step protocol of cleansing and antiseptic site preparation for both preoperative and insertion site preparation using 2% CHG and 70% alcohol combinations along with application of the CHG-impregnated disc appears to be very powerful and cost-effective for the prevention of catheter-related infections in short-term transcutaneous catheters. This combination may be beneficial for prevention of tunnel infections in cuffed catheters, particularly within the first 2 weeks until adhesion of the cuff to the subcutaneous tissue is complete.

Intraluminal contamination: hand hygiene. Entry of microorganisms through contaminated access sites of the infusion system is the major source of intraluminal contamination and the major source of CRBSI in long-term catheters. Interventions should be focused on prevention of touch contamination, access-site disinfection, and use of prophylactic flush solutions (Table II).

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TABLE II *Evidence-based recommendations for the prevention of contamination of the internal lumen of central venous catheters*

As early as 1 week after admission, hospitalized patients become colonized with antimicrobial-resistant pathogens that may be transferred into the home on hospital discharge.[61] Fundamental to developing infection-control policies for the delivery of medical care in the home is the need to recognize that people live in an environment where all types of human activities are ongoing and that pathogens are continually introduced into the home on people, food and water, pets, insects, and by air

transmission.[62] Hand hygiene is intended to decrease contamination of the hands with transient organisms from the local environment.

The term *hand hygiene* includes handwashing, antiseptic hand wash, antiseptic hand rub, or surgical hand antisepsis. In both the CDC *Guidelines for the Prevention of Intravascular Device-Related Infections*[15] and the CDC *Guideline for Hand Hygiene in Health-Care Settings*,[42] decontamination of hands is recommended before and after providing care procedures for intravascular devices. An antiseptic hand rub or antiseptic hand wash is recommended for hand decontamination.

Hand hygiene is the simplest, most effective measure for preventing healthcare-acquired infections.[53,54] However, it is well known that compliance with hand hygiene by medical and nurse clinicians has historically been dismal.[42,54] Hand hygiene protocols for home patients should be incorporated into the provider's infection control program and should include education and compliance monitoring of the nursing staff, education and compliance monitoring of the patient/caregiver, provision of appropriate hand hygiene products, and routine observation and feedback of technique to patients and caregivers.[62,63]

Intraluminal contamination: access-site disinfection. Access-site disinfection is probably the most important step in prevention of CRBSI in long-term catheters. The CDC guidelines strongly recommend cleaning access ports with 70% alcohol or an iodophor before accessing the system; however, no recommendation regarding the duration or method for cleaning is provided (Table II). Three studies were cited in support of the Category IA recommendation. The study by Salzmanetal[64] compared the efficacy of CHG (1% with and without 70% alcohol), ethanol (70% and 97%), and normal saline in eradicating microorganisms in an *in vitro* model of catheter hub contamination. They found that 70% ethanol was more effective than 1% CHG and concluded that ethanol is likely to be the safest treatment.

In the second *in vitro* study by Luebke et al,[65] the septum of 2 devices, one a conventional latex injection port and the other a split-septum injection system (Interlink, Baxter Healthcare Corp, Deerfield, IL), was inoculated with an *Enterococcus faecium* suspension of 10^4–10^5 cfu/mL. Each system was swabbed with a 70% alcohol-saturated pad using either a single-motion wipe or a 5-second wipe followed by a 1-minute drying period before puncture for flushing. The control group had no cleansing before puncture and flushing. The devices were accessed by either a needle (injection port) or blunt cannula (Interlink).

When 1 single-motion wipe was performed, the recovery fluid from the needleless device was positive in 6%, and 4% were positive in the conventional system. In the 5-second wipe/1-minute drying group, the recovery fluid was positive in 4% of needleless devices, whereas none of the conventional system cultures were positive. When no disinfection was performed, the transfer of organisms into the fluid path of the split septum was positive in 31%–80% of the needleless devices and 72%–90% of the conventional injection ports. The authors concluded that the needleless system performed like the

conventional system, but reinforced the need for an appropriate disinfection procedure before accessing either system.

The third cited study documented the potential spread of iatrogenic infection through contaminated multidose vials but did not examine the effect of antiseptics for disinfection before entry into the vial.[66] Casey et al,[67] in a more recent randomized, prospective, controlled trial, compared the microbial contamination rate of standard injection caps and a needleless positive-pressure valve. Seventy-seven patients undergoing cardiac surgery and requiring a CVC were randomly allocated to receive either needleless connectors (BD PosiFlow, BD Medical, Sandy, UT) or standard injection caps attached to stopcock entry points at the catheter hub. The microbial contamination rate of the external compression seals of 274 needleless connectors and 306 standard caps was assessed to compare the efficacy of 3 disinfectants: 70% isopropyl alcohol, 0.5% CHG gluconate in 70% isopropyl alcohol, and 10% povidone iodine. Each device was cleaned before and after each manipulation, allowing the disinfectant to dry for 2 minutes on each occasion. Each device was exchanged after 72 hours.

Forty-one percent of the needleless valves were externally contaminated at exchange. Contamination of the external compression seals was significantly lower when disinfected with CHG ($p < .0001$) and povidone iodine ($p < .0001$). There was no statistically significant difference in contamination rates between the CHG and povidone iodine group ($p = .4$). Seven percent of the needleless-valve stopcock entry points were internally contaminated, with no statistical difference between any of the disinfectants.

In the standard-cap group, 18% of the septa were externally contaminated, with no significant difference between the rate and extent of microbial contamination after swabbing with each of the disinfectants. Eighteen percent of the stopcock entry points were contaminated. Disinfection of the entry ports with either CHG or povidone iodine resulted in a reduced rate of internal contamination compared with alcohol. Overall, the use of 0.5% CHG gluconate in 70% isopropyl alcohol before and after each manipulation resulted in the lowest contamination rates.

These results are comparable to the results in a trial by Maki et al,[68] who compared the use of 2% aqueous CHG, 10% povidone iodine, and 70% alcohol for preinsertion skin antisepsis and access-site disinfection. The use of 2% CHG was associated with the lowest rates of localized infection and bacteremia.

Intraluminal contamination: prophylactic flush solution. The third critical intervention for prevention of intraluminal contamination is the instillation of an anti-infective locking solution when the catheter is not in use. The current standard includes normal saline or heparinized saline for maintaining catheter patency. Neither of these solutions inhibit microbial growth. To the contrary, heparin has been shown to support microbial growth in solution and in biofilm.[69–72] Preliminary findings by Hostetler et al have raised concern that heparin used in intravascular catheters may play a role in triggering a series of events that result in the production of a life-threatening toxic shock–like reaction with fungal (*Candida*) infections.[73]

In at least 3 studies, prophylactic antibiotic catheter locking has demonstrated efficacy in the prevention of CRBSI[74–76]; however, with the rapid emergence of Gram-positive, Gram-negative, and fungal antibiotic resistant strains, frontline antibiotics such as vancomycin, quinilones, ß lactams and aminoglycosides should be reserved for treatment of systemic infections.[40,77] Thus, the strong recommendation of the CDC is to not routinely use antibiotic lock solutions to prevent CRBSI.[15] The efficacy of a combination solution of minocycline (Wyeth-Ayerst, Pearl River, NY) and disodium EDTA (Endrate; Abbott Laboratories, Chicago, IL) (M-EDTA) as a broad-spectrum antimicrobial/antibiofilm and antithrombotic agent has been thoroughly studied *in vitro*.[69–71] Raad et al[70] investigated the prophylactic use of minocycline (3 mg/mL) and disodium EDTA (30 mg/mL) in 14 children with cancer for whom the solution was used to lock their ports. They found that M-EDTA significantly decreased the risk of CRBSI in comparison to the control group of 48 children using heparin ($p = .05$). These results are promising; however, IV minocycline has recently been discontinued by the manufacturer and is no longer available.

Tetrasodium EDTA (tEDTA) has been investigated as an antimicrobial agent in both *in vitro* and *ex vivo* studies. Ryder et al[78] compared ciprofloxacin 10, 100, 1000, and 5000 x MIC to tEDTA 40 mg/mL for the eradication of coagulase negative staphylococcus and *Pseudomonas aeruginosa* (*PA*) biofilm bacteria grown on glass fiber membranes. The mean log reduction (MLR) of *CNS* after 6 hours of exposure to ciprofloxacin was 7% at 10 x MIC, 15% at 100 x MIC, 26% at 1000 x MIC, and 35% for 5000 x MIC. The MLR of *PA* at 6 hours was 58% at 10 x MIC, 74% at 100 x MIC, 68% at 1000 x MIC, and 82% for 5000 x MIC. The MLR of the tEDTA at 6 hours was 100%, a statistically significant reduction against all other tested concentrations of ciprofloxacin ($p \leq .001$), except for *CNS* at 100 x MIC at 6 hours ($p = .06$).

Kite et al[79] investigated the effect of tEDTA in an *ex vivo* study of 20 clinically infected hemodialysis catheters. The explanted catheters were screened by a culture of through-catheter flush technique. Bacteria identified in the biofilms were Gram-positive, Gram-negative, and mixed species. The initial biofilm cell count levels averaged above 10^5 cfu/1 cm of intraluminal catheter surface. tEDTA 40 mg was instilled into equal catheter sections and remained "locked" for 24 hours. tEDTA was effective at complete eradication of the total viable count in almost all cases. tEDTA appears to be a very promising agent for the prophylaxis and treatment of vascular catheters, but randomized clinical trials are needed.

THROMBOTIC CATHETER OCCLUSIONS

TOP
ABSTRACT
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Pathogenesis of Intraluminal Thrombotic Catheter Occlusions

Catheter occlusion may be partial or complete and is typically evidenced by inability to infuse or aspirate, sluggish flow, or frequent pump alarms. Thrombotic catheter occlusion occurs as a result of clotted blood within the lumen or from the buildup of fibrin on the intraluminal surface over time. Plasma proteins and fibrin(ogen) are deposited during aspiration or administration of blood or blood products. Clotting of whole blood within the lumen is usually a consequence of an inadequate volume of flush solution, inadequate flushing technique, or retrograde blood flow on disconnect from needless connectors. Clotting directly at and slightly within the tip of the catheter may result from convex blood flow and fluid displacement that occurs while the catheter is locked, regardless of flushing method or needleless connector design.[80]

The correlation between thrombosis and infection has been well described.[81] Some microbial species quickly attach directly to polymer surfaces, whereas others more readily adhere to a fibrin/platelet matrix. The biofilm/fibrin matrix formation may become thick enough to cause partial or complete occlusion. Sherertz et al[82] investigated the sensitivity of various culture methods in the diagnosis of triple-lumen catheter infections. A strong correlation was identified between failed blood aspiration and the titer of microorganisms cultured from each lumen (r = .85). The inability to aspirate blood for culture was experienced in 51% of aspiration attempts, a likely indicator of partial or complete occlusion. The frequency of failed blood aspiration was 91% in catheters with significantly positive lumen cultures (100 cfu) compared to 58% when the cultures were negative (<100 cfu; p = .001).

Evidence-Based Prevention Strategies

Strategies for prevention of thrombotic occlusion should be focused on methods to maintain patency by keeping blood out of the catheter (Table III). The prevention of thrombotic catheter occlusion is centered primarily on 2 interventions: catheter flushing and the use of antireflux needleless connectors and valves (Table III).

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TABLE III *Evidence-based recommendations for the prevention of thrombotic catheter occlusion*

Intraluminal thrombotic occlusion: prophylactic flush solutions. There are 3 components important to the flushing protocol for maintaining patency of vascular catheters: the flush solution, the volume of solution, and the flushing technique. The use of normal saline and heparin has been studied extensively over the last 2 decades. Two meta-analyses published in the early 1990s set the current standard specifically for peripheral IV catheters. The results of the analysis by Peterson and Kirchhoff[83] found no significant difference in duration of patency between IV catheters flushed with saline solution and those flushed with a heparinized solution. Goode et al[84] concluded that saline is as effective as heparin in maintaining patency, preventing phlebitis, and increasing duration of use in peripheral IV locks. Saline has been used successfully in maintaining patency of CVCs as well.[85]

Despite these findings, the rate of catheter occlusion,[15] the incidence of intraluminal clots,[86–88] the risk of heparin-induced thrombocytopenia,[89] and the lack of antimicrobial activity of saline and heparin continue to be of great concern. EDTA has been explored as a potential agent for protection against catheter infection. EDTA is a calcium and iron chelator with very effective anticoagulation activity. Along with infection rates, Chatzinikolaou et al also compared occlusion rates of implanted vascular ports in the pediatric cancer patients using either a heparin lock or M-EDTA.[90] Two thrombotic episodes occurred in 48 patients in the heparin group, whereas no thrombotic events occurred in the M-EDTA group of 14 patients. tEDTA also appears to be a promising agent with dual application for both antimicrobial and anticoagulant capability.[79]

The volume of flush solution is an important factor not only to prevent intraluminal clotting but also catheter tip occlusion, a phenomenon that occurs as a result of laminar flow and the flow distribution as predicted by the Hagen-Poiseuille law when the catheter is locked.[91] The *IV Nursing Society's Standards of Practice* recommend that the volume of flush solution be equal to at least twice the volume capacity of the catheter.[91] The findings of Polaschegg and Shah[92] support this standard. In an *in vitro* study using dye and saline dilution, the investigators demonstrated that approximately 14% of the injected flush solution spills from the catheter when the exact priming volume is injected, resulting in a mean concentration of approximately 90% of the locking solution's concentration remaining in the fluid at the tip of the catheter. They concluded that the injection volume must exceed 120% of the catheter lumen to achieve the full strength of the locking solution at the tip.

Intraluminal thrombotic occlusion: antireflux needleless connectors. Needleless connectors are important devices in the reduction of needlestick injuries in healthcare workers. However, the net benefit of these devices has been called into question as a result of several reports of associated increased infection risk.[93,94] Early device designs also reportedly increased the incidence of catheter occlusion, particularly in the smaller-lumen catheters where a longer length of catheter is filled by a reflux displacement volume of blood on disconnection of the syringe.[95]

Currently, at least 5 needleless connectors redesigned with an end positive-pressure mechanism and 2 devices incorporating a neutral displacement valve exist in the

marketplace; however, evidence-based literature involving each of these devices is limited. Four randomized or prospective controlled trials investigating 3 antireflux devices—2 testing a neutral valve and 2 a positive-end-pressure valve—report a reduced incidence of catheter occlusion with the use of these devices.[96–99] Reduced occlusion rates were also reported in 3 clinical studies evaluating use of 2 positive-end-pressure needleless connectors.[95,100,101]

Currently, at least 2 marketed devices have not been validated in well-designed clinical trials or descriptive clinical investigations regarding infection risk or efficacy in the reduction of occlusion rates. Clinicians should be cautious when using these devices without implementation of strict protocols and close monitoring of clinical outcomes. Access-site disinfection and timely changes of the devices has been stressed as a safety measure in the prevention of needleless device-associated CRBSI.[67,94,102–106] The use of well-designed antireflux devices is an effective strategy for the prevention of CRBSI when appropriately disinfected before use and replaced at recommended intervals.

In summary, the prevention of catheter-related infections and thrombotic intraluminal occlusion requires strict adherence to evidence-based protocols. The development of effective protocols for the prevention, diagnosis, and treatment of CRI requires an understanding of the pathogenic mechanisms of microbial access to both the external and internal catheter lumen and the subsequent development of biofilm. A multimodal intervention strategy is required to address the multiple potential sources of microbial access to the catheter and delivery system. Recommended strategies critical in the prevention of extraluminal contamination include skin antisepsis and antimicrobial dressings. Hand hygiene, access-site disinfection, and antimicrobial flush solutions address prevention of intraluminal contamination. Although some of these are based on strong evidence, others are based on best practice theory and clinical evaluation.

Interventions to reduce the incidence of thrombotic catheter occlusions improve outcomes related to infection, delayed therapy, cost of treatment, and loss of access. Although not well studied, needleless devices designed to eliminate the presence of blood within the catheter while not increasing the risk of infection should be used with active outcome monitoring and quality-improvement controls. The use of normal saline as a flush solution may be a prudent choice in the face of the current concerns with heparin use. Continued investigation regarding the efficacy of new and promising flush solutions is urgently needed.

REFERENCES

TOP
ABSTRACT
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REFERENCES

1. Jarvis WR. Infection control and changing health-care delivery systems. *Emerg Infect Dis.*2001; 7:170 –173.[Medline]

2. Pearson ML, Banerjee SN. Home care in the United States: a national perspective [abstract]. *Infect Control Hosp Epidemiol.*2000; 21:114 –115.

3. Manangan LP, Pearson ML, Tokars JI, Miller E, Jarvis WR. Feasibility of national surveillance of health-care-associated infections in home-care settings. *Emerg Infect Dis.*2002; 8:233 –236.[Medline]

4. Ryan JA, Abel RM, Abbott WM, et al. Catheter complications in total parenteral nutrition: a prospective study of 200 consecutive patients.*N Engl J Med.* 1974;290:757 –761.[Medline]

5. Wolfe BM, Ryder MA, Nishikawa RA, Halstead CH, Schmidt BF. Complications of parenteral nutrition. *Am J Surg.*1986; 152:93 –99.[Medline]

6. Steiger E. *North American Home Parenteral and Enteral Nutrition Patient Registry: Annual Report: 1992.* Albany, NY: Oley Foundation; 1994.

7. Richards DM, Deeks JJ, Sheldon TA, Shaffer JL. Home parenteral nutrition: a systematic review. *Health Technol Assess.*1997; 1:i –iii, 1–59.[Medline]

8. Scolappio JS, Fleming SR, Kelly DJ, et al. Survival of home parenteral nutrition-treated patients: 20 years of experience at the Mayo Clinic. *Mayo Clinic Proc.*1999; 74:217 –222.[Medline]

9. Moukarzel AA, Haddad I, Ament ME, et al. 230 Patient years of experience with home long-term parenteral nutrition in childhood: natural history and life of central venous catheters. *J Pediatr Surg.*1994; 29:1323 –1327.[Medline]

10. Knafelz D, Gambarara M, Diamanti A, et al. Complications of home parenteral nutrition in a large pediatric series. *Transplant Proc.* 2003;35:3050 – 3051.[Medline]

11. Reimund JM, Arondel Y, Finck G, Zimmerman F, Duclos B, Baumann R. Catheter-related infection in patients on home parenteral nutrition: results of a prospective survey. *Clin Nutr.*2002; 21:33 –38.[Medline]

12. Bozzetti F, Mariani L, Bertinet DB, et al. Central venous catheter complications in 447 patients on home parenteral nutrition: an analysis of over 100,000 catheter days. *Clin Nutr.*2002; 21:475 –485.[Medline]

13. Planas M, Castella M, Leon M, et al. Parenteral nutrition at home: NADYA register for the year 2000. *Nutr Hosp.*2003; 18:29 –33.[Medline]

14. Rhinehart E. Infection control in home care. *Emerg Infect Dis.* 2001;7:208 – 211.[Medline]

15. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. *Infect Control Hosp Epidemiol.* 2002;23:759 –769.[Medline]

16. Ryder MA. Peripheral access options. *Surg Oncol Clin North Am.* 1995;4:395 – 427.[Medline]

17. Moureau N, Poole S, Murdock MA, Gray SM, Semba CP. Central venous catheters in home infusion care: outcomes analysis in 50,470 patients.*J Vasc Interv Radiol.*2002; 13:1009 –1016.[Abstract/Free Full Text]

18. Harbarth S, Sax H, Gastmeier P. The preventable portion of nosocomial infections: an overview of the published reports. *J Hosp Infect.* 2003;54:258 – 266.[Medline]

19. Habash M, Reid G. Microbial biofilms: their development and significance for medical device-related infections. *J Clin Pharmacol.* 1999;39:887 –889.[Abstract]

20. Elliott TS, Moss HA, Tebbs SE, et al. Novel approach to investigate a source of microbial contamination of central venous catheters. *Eur J Clin Microbiol Infect Dis.*1997; 16:210 –213.[Medline]

21. Livesley MA, Tebbs SE, Moss Ha, Farouqi MH, Lambert PA, Elliott TS. Use of pulsed electrophoresis to determine the source of microbial contamination of central venous catheters. *Eur J Clin Microbiol Infect Dis.* 1998;17:108 – 112.[Medline]

22. Jeske C, Raedler C, von Goedecke A, et al. Early identification of bacteria leading to central venous catheter contamination. *Anesth Analg.* 2003;97:940 – 943.[Abstract/Free Full Text]

23. Ryder M. The role of biofilm in vascular catheter-related infections. *New Dev Vasc Dis.* 2001;2:15–25. Available at: http://www.medpub.com. Accessed on March 2, 2005.

24. Herwaldt LA, Hollis RJ, Boyken LD, Pfaller MA. Molecular epidemiology of coagulase negative staphylococci isolated from immunocompromised patients. *Infect Control Hosp Epidemiol.*1992; 13:86 –92.[Medline]

25. Costa SF, Miceli MH, Anaissie EJ. Mucosa or skin as source of coagulase-negative staphylococcal bacteremia? *Lancet Infect Dis.* 2004;4:278 – 286.[Medline]

26. Cooper GL, Schiller AL, Hopkins CC. Possible role of capillary action in pathogenesis of experimental catheter-associated dermal tunnel infections. *J Clin Microbiol.*1988; 26:8 –12.[Abstract/Free Full Text]

27. Edwards R, Harding KG. Bacteria and wound healing. *Curr Opin Infect Dis.* 2004;17:91 –96.[Medline]

28. Mueller-Premru M, Gubina M, Kaufman ME, Primozic J, Cookson BD. Use of semiquantitative and quantitative culture methods and typing for studying the epidemiology of central venous catheter-related infections in neonates on parenteral nutrition. *J Med Microbiol.*1999; 48:451 –460.[Abstract]

29. Williams I, Paul F, Lloyd D, et al. Flow cytometry and other techniques show that *Staphylococcus aureus* undergoes significant physiological changes in the early stages of surface-attached culture.*Microbiology.* 1999;145(pt 6): 1325–1333.[Abstract]

30. Costerton W, Veeh R, Shirtliff M, Pasmore M, Post C, Ehrlich G. The application of biofilm science to the study and control of chronic bacterial infections. *J Clin Invest.*2003; 112:1466 –1477.[Abstract/Free Full Text]

31. Donlan RM. Biofilms and device-associated infections. *Emerg Infect Dis.* 2001;7:277 –281.[Medline]

32. Hall-Stoodley L, Stoodley P. Biofilm formation and dispersal and the transmission of human pathogens. *Trends Micrbiol.*2005; 13:7 –10.

33. Hall-Stoodley L, Stoodley P. Developmental regulation of microbial biofilms. *Curr Opin Biotechnol.*2002; 13:228 –233.[Medline]

34. Hall-Stoodley L, Costerton JW, Stoodley P. Bacterial biofilms: from the natural environment to infectious diseases. *Nat Rev Microbiol.* 2004;2:95 –108.[Medline]

35. Fux CA, Wilson S, Stoodley P. Detachment characteristics and oxacillin resistance of *Staphylococcus aureus* biofilm emboli in an *in vitro* catheter infection model. *J Bacteriol.*2004; 186:4486 –4491.[Abstract/Free Full Text]

36. Khoury AE, Lam K, Ellis B, Costerton JW. Prevention and control of bacterial infections associated with medical devices. *ASAIO J.*1992; 38:M174 – M178.[Medline]

37. Sauer K, Camper AK, Ehrlich GD, Costerton JW, Davies JD. *Pseudomonas aeruginosa* displays multiple phenotypes during development as a biofilm. *J Bacteriol.*2002; 184:1140 –1154.[Abstract/Free Full Text]

38. Darouiche RO, Raad II, Heard SO. A comparison of two antimicrobial-impregnated central venous catheters: Catheter Study Group.*N Engl J Med.* 1999;340:1 –8.[Abstract/Free Full Text]

39. Safdar N, Maki DG. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. *Intensive Care Med.* 2004;30:62 –67.[Medline]

40. De Cicco M, Campisf C, Matovic M. Central venous catheter-related bloodstream infections: pathogenesis factors, new perspectives in prevention and early diagnosis. *J Vasc Access.*2003; 4:83 –91.

41. Roberts ME, Stewart PS. Modelling protection from antimicrobial agents in biofilms through the formation of persister cells.*Microbiology.* 2005;151:75 – 80.[Abstract/Free Full Text]

42. Boyce JM, Pittett D. Guideline for hand hygiene in health-care settings: recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA/Hand Hygiene Task Force.*Am J Infect Control.*2002; 30:S1 –S46.[Medline]

43. Larson E. Hygiene of the skin: when is clean too clean?*Emerg Infect Dis.* 2001;7:225 –230.[Medline]

44. Maki DG, Ringer M. Evaluation of dressing regimes for prevention of infection with peripheral intravenous catheters: gauze, a transparent polyurethane dressing, and an iodophor-transparent dressing.*JAMA.* 1987;258:2396 –2403.[Abstract]

45. Brown E, Wenzel RP, Hendley JO. Exploration of the microbial anatomy of normal human skin by using plasmid profiles of coagulase-negative staphylococci: search for the reservoir of resident skin flora. *J Infect Dis.* 1989;160:644 –650.[Medline]

46. Baquero F, Patron C, Canton R, Martinez Ferrer M. Laboratory and *in-vitro* testing of skin antiseptics: a prediction for *in-vivo* activity? *J Hosp Infect.*1991; 18(suppl B):5 –11.[Medline]

47. Messager S, Hann AC, Goddard PA, Dettmar PW, Maillard JY. Use of the "*ex vivo*" test to study long-term bacterial survival on human skin and their sensitivity to antisepsis. *J Appl Microbiol.* 2004;97:1149 –1160.[Medline]

48. Hendley JO, Ashe KM. Effect of topical antimicrobial treatment on aerobic bacteria in the stratum corneum of human skin. *Antimicrob Agents Chemother.* 1991;35:627 –631.[Abstract/Free Full Text]

49. Messager S, Goddard PA, Dettmar PW, Maillard JY. Comparison of two *in vivo* and two *ex vivo* tests to assess the antibacterial activity of several antiseptics. *J Hosp Infect.*2004; 58:115 –121.[Medline]

50. AORN Recommended Practices Committee. *2004 Standards, Recommended Practices and Guidelines.* Denver, CO: AORN.

51. Seal LA, Paul-Cheadle D. A systems approach to preoperative surgical patient skin preparation. *Am J Infect Control.*2004; 32:57 –68.[Medline]

52. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Sullivan SD, Saint S. Vascular catheter site care: the clinical and economic benefits of chlorhexidine gluconate compared with povidone iodine. *Clin Infect Dis.* 2003;37:764 –771.[Medline]

53. Rotter ML. 150 Years of hand disinfection: Semmelweis' heritage.*Hygiene Med.* 1997;22:332 –339.

54. Pittet D. Improving adherence to hand hygiene practice: a multidisciplinary approach. *Emerg Infect Dis.*2001; 7:234 –240.[Medline]

55. Aly R, Bayles C, Maibach H. Restriction of bacterial growth under commercial catheter dressings. *Am J Infect Control.*1988; 16:95 –100.[Medline]

56. Crosby CT, Mares AK. Skin antisepsis: past, present, and future.*JVAD* . 2001;spring:26 –31.

57. Gillies D, O'Riordan E, Carr D, Frost J, Gunning R, O'Brien I. Central venous catheter dressings: a systematic review. *J Adv Nurs.* 2003;44:623 –632.[Medline]

58. Hanazaki K, Shingu K, Adachi W, Miyazaki T, Amano J. Chlorhexidine dressing for reduction in microbial colonization of the skin with central venous catheters: a prospective randomized controlled trial. *J Hosp Infect.* 1999;42:165 – 167.[Medline]

59. Maki DG, Mermel LA, Kluger D, et al. *The Efficacy of a Chlorhexidine-Impregnated Sponge for the Prevention of Intravascular-Related Infection: A Prospective, Randomized, Controlled, Multicenter Study.* Washington, DC: American Society for Microbiology;2000 .

60. Crawford AG, Fuhr JP, Rao B. Cost-benefit analysis of chlorhexidine gluconate dressing in the prevention of catheter-related bloodstream infections. *Infect Control Hosp Epidemiol.*2004; 25:668 –674.[Medline]

61. Terpstra S, Noordhoek GT, Voesten HG, Hendriks B, Degener JE. Rapid emergence of resistant coagulase-negative staphylococci on the skin after antibiotic prophylaxis. *J Hosp Infect.* 1999; 43:195 –202.[Medline]

62. Bloomfield SF, Scott EA. Developing an effective policy for home hygiene: a risk-based approach. *Int J Environ Health Res.* 2003; 13(suppl 1):S57 – S66.[Medline]

63. Boyer CL, Wade DC. The impact of compliance on quality outcomes in the home infusion population. *J Intraven Nurs.* 1998; 21(5 suppl):S161 –S165.[Medline]

64. Salzman MB, Isenberg HD, Rubin LG. Use of disinfectants to reduce microbial contamination of hubs of vascular catheters. *J Clin Microbiol.* 1993;31:475 – 479.[Abstract/Free Full Text]

65. Luebke MA, Arduino MJ, Duda, DL, et al. Comparison of the microbial barrier properties of a needleless and a conventional needle-based intravenous access system. *Am J Infect Control.* 1998; 26:437 –441.[Medline]

66. Plott RT, Wagner RF, Tyring SK. Iatrogenic contamination of multidose vials in simulated use: a reassessment of current patient injection technique. *Arch Dermatol.* 1990; 126:1441 –1444.[Abstract]

67. Casey AL, Worthington T, Lambert PA, Quinn D, Faroqui MH, Elliott TS. A randomized, prospective clinical trial to assess the potential infection risk associated with the PosiFlow needleless connector. *J Hosp Infect.* 2003;54:288 – 293.[Medline]

68. Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet.* 1991; 338:339 –343.[Medline]

69. Root JL, McIntyre OR, Jacobs NJ, Daghlian CP. Inhibitory effect of disodium EDTA upon the growth of *Staphylococcus epidermidis in vitro*: relation to infection prophylaxis of Hickman catheters. *Antimicrob Agents Chemother.* 1988;32:1627 –1631.[Abstract/Free Full Text]

70. Raad I, Hachem R, Tcholakian RK, et al. Efficacy of minocycline and EDTA lock solution in preventing catheter-related bacteremia, septic phlebitis, and endocarditis in rabbits. *Antimicrob Agents Chemother.* 2002;46:327 – 332.[Abstract/Free Full Text]

71. Raad I, Chatzinikolaou I, Chaiban G, et al. *In vitro* and *ex vivo* activities of minocycline and EDTA against microorganisms embedded in biofilm on catheter surfaces. *Antimicrob Agents Chemother.* 2003;47:3580 – 3585.[Abstract/Free Full Text]

72. Shah CB, Mittelman MW, Costerton JW, et al. Antimicrobial activity of a novel catheter lock solution. *Antimicrob Agents Chemother.*2002; 46:1674 – 1679.[Abstract/Free Full Text]

73. Stephenson J. Can common medical practice transform *Candida* infections from benign to deadly? *JAMA.*2001; 286:2531 –2532.[Free Full Text]

74. Henrickson KJ, Axtell RA, Hoover SM, et al. Prevention of central venous catheter-related infections and thrombotic events in immunocompromised children by use of vancomycin/ciprofloxacin/heparin flush solution: a randomized, multicenter, double-blind trial. *J Clin Oncol.*2000; 18:1269 – 1278.[Abstract/Free Full Text]

75. Carratala J, Niubo J, Fernandez-Sevilla A, et al. Randomized, double-blind trial of an antibiotic-lock technique for the prevention of gram-positive central venous catheter-related infection in neutropenic patients with cancer. *Antimicrob Agents Chemother.*1999; 43:2200 –2204.[Abstract/Free Full Text]

76. Schwartz C, Henrickson KJ, Roghmann K, Powell K. Prevention of bacteremia attributed to luminal colonization of tunneled central venous catheters with vancomycin-susceptible organisms. *J Clin Oncol.*1990; 8:1591 –1597.[Abstract]

77. Grohskopf LA, Maki DG, Sohn AH, Sinkowitz-Cochran RL, Jarvis WR, Goldmann DA. Reality check: should we use vancomycin for the prophylaxis of intravascular catheter-associated infections? *Infect Control Hosp Epidemiol.* 2001;22:176 –179.[Medline]

78. Ryder M, Nishikawa R, Liu YL, et al. Tetra sodium EDTA: a novel antimicrobial agent superior to ciprofloxacin in eradicating biofilm bacteria: implications for catheter-related bloodstream infections [abstract].*JPEN J Parenter Enteral Nutr.*2005; 29:S18 .

79. Kite P, Eastwood K, Sugden S, Percival SL. Use of *in vivo* generated biofilms from hemodialysis catheters to test the efficacy of a novel antimicrobial catheter lock for biofilm eradication *in vitro*.*J Clin Microbiol.* 2004;42:3073 – 3076.[Abstract/Free Full Text]

80. Friedrich P, Reininger AJ. Occlusive thrombus formation on indwelling catheters: *in vitro* investigation and computational analysis. *Thromb Hemost.*1995; 73:66 – 72.[Medline]

81. Mohammad SF. Enhanced risk of infection with device-associated thrombi. *ASAIO J.* 2000;46:S63 –S68.[Medline]

82. Sherertz RJ, Heard SO, Raad II. Diagnosis of triple-lumen catheter infection: comparison of roll plate, sonication, and flushing methodologies.*J Clin Microbiol.* 1997;35:641 –646.[Abstract]

83. Peterson FY, Kirchhoff KT. Analysis of the research about heparinized versus nonheparinized intravascular lines. *Heart Lung.* 1991;20:631 –642.[Medline]

84. Goode CJ, Titler M, Rakel, et al. A meta-analysis of effects of heparin flush and saline flush: quality and cost implications. *Nurs Res.* 1991;40:324 –330.[Medline]

85. Smith S, Dawson S, Hennessey R. Maintenance of the patency of indwelling central venous catheters: is heparin necessary? *Am J Pediatr Hematol Oncol.* 1991;13:141 –143.[Medline]

86. Anderson AJ, Krasnow SH, Boyer MW, et al. Hickman catheter clots: a common occurrence despite daily heparin flushing. *Cancer Treat Rep.* 1987;71:651 – 653.[Medline]

87. Biagi E, Arrigo C, DellíOrto MG, et al. Mechanical and infective central catheter-related complications: a prospective non-randomized study using Hickman and Groshong catheters in children with hematological malignancies. *Support Care Cancer.*1997; 5:228 –233.[Medline]

88. Cosca PA, Smith S, Chatfield S, et al. Reinfusion of discard from venous access devices. *Oncol Nurs Forum.*1998; 25:1073 –1076.[Medline]

89. Rosenthal K. Type II heparin-induced thrombocytopenia: toward developing a strategy to determine the role of routine vascular access device heparinization. *JAVA.*2004; 9:221 –225.

90. Chatzinikolaou I, Zipf TF, Hanna H, et al. Minocycline-ethylenediamine-tetraacetate lock solution for the prevention of implantable port infections in children with cancer. *Clin Infect Dis.* 2003;36:116 –119.[Medline]

91. Intravenous Nursing Society. Infusion nursing standards of practice. *J Infusion Nurs.*2000; 23(6 suppl):S53 –S54.

92. Polaschegg H-D, Shah C. Overspill of catheter locking solution: safety and efficacy aspects. *ASAIO J.*2003; 49:713 –715.[Medline]

93. Donlan RM, Murga R, Bell M, et al. Protocol for detection of biofilms on needleless connectors attached to central venous catheters.*J Clin Microbiol.* 2001;39:750 –753.[Abstract/Free Full Text]

94. Lenhart C. Preventing central venous access device occlusions with saline only flush by use of an adapter. *JVAD.*2001; summer:34 –35.

95. Hanchett M, Kung L-Y. Do needleless intravenous systems increase the risk of infection? *J Intraven Nurs.* 1999; 22:117 –121.[Medline]

96. Jacobs BR, Schilling S, Doellman D, Hutchinson N, Rickey M, Nelson S. Central venous catheter occlusion: a prospective, controlled trial examining the impact of a positive-pressure valve device. *JPEN J Parenter Enteral Nutr.* 2004;28:113 – 118.[Abstract]

97. Buehrle D. A prospective randomized comparison of three needleless IV systems used in conjunction with peripherally inserted central catheters.*JAVA.* 2004;9:35 – 38.

98. Hoffer EK, Bloch RD, Borsa JJ, Peripherally inserted central catheters with distal versus proximal valves: prospective randomized trial.*J Vasc Interv Radiol.*2001; 12:1173 –1177.[Abstract/Free Full Text]

99. Hoffer EK, Borsa J, Santulli P, Bloch R, Fontaine AB. Prospective randomized comparison of valved versus nonvalved peripherally inserted central vein catheters. *AJR Am J Roentgenol.*1999; 173:1393 –1398.[Abstract]

100. Rummel M, Donnelly P, Fortenbaugh C. Clinical evaluation of a positive pressure device to prevent central venous catheter occlusion: results of a pilot study. *Clin J Oncol Nurs.*2001; 5:261 –265.[Medline]

101. Berger L. The effects of positive pressure devices on catheter occlusions. *JVAD.* 2000;5:31 –33.

102. Yebenes JC, Vidaur L, Serra-Prat M, et al. Prevention of catheter-related bloodstream infection in critically ill patients using a disinfectable, needle-free connector: a randomized controlled trial. *Am J Infect Control.* 2004;32:291 – 295.[Medline]

103. Do AN, Ray BJ, Banerjee SN, et al. Bloodstream infection associated with needleless device use and the importance of infection-control practices in the home healthcare setting. *J Clin Infect Dis.*1999; 179:442 –448.

104. Cookson ST, Ihrig M, O'Mara EM, et al. Increased bloodstream infection rates in surgical patients associated with variation from recommended use and care following implementation of a needleless device.*Infect Control Hosp Epidemiol.*1998; 19:23 –27.[Medline]

105. McDonald LC, Banerjee SN, Jarvis WR. Line-associated bloodstream infections in pediatric intensive-care-unit patients associated with a needleless device and intermittent intravenous therapy. *Infect Control Hosp Epidemiol.* 1998;19:772 –777.[Medline]

106. Arduino MJ, Bland LA, Danzig LE, McAllister SK, Aguero SM. Microbiologic evaluation of needleless and needle-access devices. *Am J Infect Control.* 1997;26:377 –380.

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The Effectiveness of Chloraprep™ in the Reduction of Blood Culture Contamination Rates in the Emergency Department

Dwayne Tepus, RN, BSN; Sandra R. Cox, RN, BSN; Susan Hazelett, RN, MS
Summa Health System Hospitals, 525 East Market Street, Akron, OH 44309

Purpose: Contamination of blood cultures by coagulase-negative Staphylococci on the skin has been associated with increased length of stay, in addition to increased hospital, laboratory, and pharmacy charges. Poor skin preparation is usually the cause of contamination. A newer product made of 2% chlorhexadine and 70% isopropanol (Chloraprep™) requires a 15-second drying time, compared to two minutes for the widely used povodine-iodine solutions, making it an attractive candidate for improved clinical effectiveness. The purpose of this study was to compare blood culture contamination rates in samples obtained in the emergency department (ED) for one year using a tincture of iodine skin preparation technique to the contamination rate for one year using the Chloraprep™ skin preparation technique. Previous studies have shown that both techniques are efficacious, however studies of the effectiveness of one technique compared to the other in an ED setting are lacking.

Design: This was an observational study.

Setting: The setting was a 963-bed community teaching hospital's emergency department in the Northeastern United States.

Sample: All blood cultures drawn in the emergency department one year prior to and one year following the implementation of the Chloraprep™ skin preparation technique.

Method: This study used a pre-/post-implementation design. All blood cultures obtained via a peripheral vein or femoral vein were included in the comparison. Data regarding blood culture contamination rates are routinely tracked by this institution's clinical laboratory. All staff (RNs and LPNs) who previously obtained blood cultures using the tincture of iodine preparation were inserviced individually on use of the Chloraprep™ skin preparation product by the principal investigator. Chi-square analysis was used to compare the pre- and post-implementation proportion of contaminated blood cultures.

Results: In the year prior to implementation of the Chloraprep™ technique, 251 of 7,158 blood cultures (3.5%) were contaminated, compared to 169 of 7,606 (2.2%) in the year after implementation. This difference was statistically significant ($p < .0001$). Contamination rates did not differ substantially between individual nurses using either technique. Skin preparation costs using Chloraprep™ increased $.48 per sample ($.20 for the tincture of iodine and $.68 for Chloraprep™, excluding nursing time).

Recommendations: Although there are numerous skin preparation techniques for blood culture collection with proven efficacy, in busy clinical settings proper site preparation may be difficult. Although this was not a randomized trial, our results show a statistically significant improvement in contamination rates using the Chloraprep™ technique. Two studies in the 1990s showed that the extra costs associated with contaminated blood cultures were in excess of $4,000 per patient. Thus, the increased costs associated with the Chloraprep™ technique (7,606 x $.48 = $3,650) are easily absorbed by the savings associated with the lower contamination rate (approximately 100 fewer contaminated samples x $4,000 = $400,000). Based on these findings, we recommend the use of the Chloraprep™ technique in the ED setting.

THREE YEARS EXPERIENCE IN IMPLEMENTING HICPAC RECOMMENDATIONS FOR THE REDUCTION OF CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTIONS

Garcia R.*, Jendresky L., Landesman S., Maher A., Nicolas F.
Brookdale University Medical Center (BUMC), Brooklyn, NY.

MODIFIED ABSTRACT

Three Years Experience in Implementing HICPAC Recommendations for the Reduction of Central Venous Catheter-Related Bloodstream Infections. Garcia R.*, Jendresky L., Landesman S., Maher A., Nicolas F. Brookdale University Medical Center (BUMC), Brooklyn, NY.

BACKGROUND: An estimated 250,000 Central Venous Catheter (CVC)-Related Bloodstream infections (CR-BSI) occur each year in the United States resulting in extensive mortality, excess length of stay, and cost increases.

OBJECTIVES: To determine the effectiveness of implementing various scientifically supported interventions in reducing the incidence of CR-BSI.

METHODS: Infection Control Professionals (ICPs) conducted surveillance for CR-BSI between Jan 1999-Dec 2002 using definitions published by the Centers for Disease Control and Prevention (CDC). Interventions included the following: Establishment of an education and awareness program, conversion of silver-chlorhexidine (CHG) to silver-platinum catheters, use of a barrier kit containing sterile gloves, gown and mask, and using a 2% CHG-70% alcohol skin prep.

RESULTS: Rate of CR-BSI during Jan-Dec 1999 was 15.0 cases/1000 catheter days (CD) (pre-intervention period; period of use of silver-CHG catheters). Focused education for nurses and physicians during 2000 resulted in a 57.3% reduction in the rate to 6.4 (rates rose in the later 7 months although below 1999 mean rate levels). In Jan '01, conversion to silver-platinum catheters (Jan '01-Sep '01) resulted in a 48.4% reduction from prior mean to 3.3. A slight increase in the rate to 4.2 was observed after requiring the use of maximal sterile barriers (Oct '01-Dec '01). A further decrease to 1.6 (equal to a rate reduction of 61.9% from prior mean) was attained by the use of a 2% CHG-70% isopropyl alcohol skin prep (Jan '02-Mar '03). Overall, the rate of CR-BSI was reduced by 89.3%.

CONCLUSION: Four key interventions resulted in the overall avoidance of 237 CR-BSI cases over 39 months. These interventions are addressed in the 2002 HICPAC guideline on prevention of CR-BSI. Using cited cost per infection figures of $34,508 to $56,000, the annual savings is estimated to range between $2,519,084 to $4,088,000.

BACKGROUND

It is estimated that >150 million intravascular devices are purchased by healthcare facilities each year for the administration of IV fluids, medications, blood products, and parenteral nutrition[1]. One particular device, the central venous catheter (CVC), has become increasingly common (>5 million used per year) due to its flexibility in allowing simultaneous fluid and medication administrations as well as hemodynamic monitoring of critically ill patients. Such devices account for 15 million CVC days in ICUs each year[2]. Despite the extensive medical benefits provided, the use of CVCs is associated with a significant number of BSIs. It is estimated that 75% of all catheter-related bloodstream infections that occur in hospitals are associated with the use of CVCs[3,4]. When non-ICU patients are included, the total number of CR-BSI occurring per year in U.S. hospitals may exceed 250,000[5]. Up to 35% of patients who develop CR-BSI, expire as a result of developing such infections[6].

The need to reduce the occurrence of CR-BSI has become a major issue in both the quality improvement and patient safety arenas. The federal agency responsible for coordinating efforts in research and promotion of patient safety, the Agency for Healthcare Research and Quality (AHRQ) has developed evidence-based safety practices that are applicable to a wide range of healthcare facilities[7]. Working from the premise that a patient safety practice is "*...a type of practice or structure whose application reduces the probability of adverse events resulting from exposure to the health care system across a range of diseases and procedures*", AHRQ reviewed 73 patient safety practices and rated

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BACKGROUND

them based on their potential impact on reducing negative outcomes and strength of scientific evidence. Using maximal sterile barriers and antimicrobial-coated catheters were found to have the greatest strength of evidence at a low cost and complexity of implementation. Although the use of chlorhexidine as a skin antiseptic was rated lower, the cost for implementation was also concluded to be low.

The findings by the AHRQ were subsequently used by the National Quality Forum to create the first set of national voluntary standards for measuring the quality of care provided to patients (the NQF is a non-profit public benefit group created in 1999 as a response to the need to establish a national strategy for healthcare quality measurement and reporting and is supported by more than 170 organizations who represent all sectors of the healthcare industry, including consumers, employers, insurers, healthcare providers, and policy groups). Infections associated with the use of CVCs are included among the first 31 recommended measures to be monitored[7].

OBJECTIVES

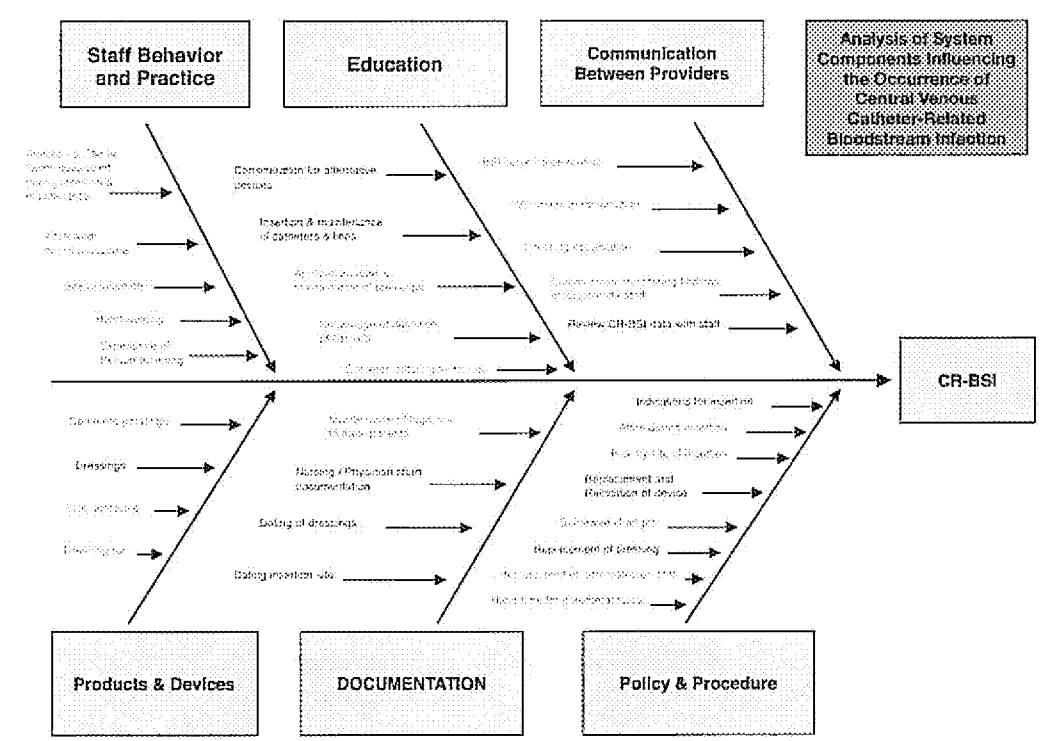
To determine the effectiveness of implementing various scientifically supported interventions in reducing the incidence of CR-BSI. Interventions to be taken were based on information in the medical literature and as contained in the guidelines on the prevention of CR-BSI as published by the CDC[8,9].

METHODS

Nosocomial house-wide bacteremia data which implicated CVCs as the likely source of an increasing number of nosocomial infection cases became the impetus for re-assigning infection control resources to conducting focused surveillance for CR-BSI starting in January 1999. One ICP was assigned to conduct daily surveillance of all adult patients with a CVC insertion in both ICU and non-ICU settings. Data collected included patient name, medical record number, location, date of insertion, date of removal, physician inserting device, blood and central line tip culture results, and information regarding the condition of the site dressing. Patients with CVCs were identified by interviewing nursing and physician staff, by the review of an established documentation form kept on all nursing stations, and by direct observation. Central line tips were collected in an aseptic manner on all patients suspected of a CR-BSI and cultured using the recommended semi-quantitative method. Definition of a CR-BSI was that as published by the CDC[9].

Infection Control organized a series of meetings with key representatives from medicine and surgery, nursing staff from both medical and critical care units, anesthesiology, the emergency room, materials management, and performance improvement. Information needed to identify factors influencing the occurrence of CR-BSI

FIGURE ONE



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METHODS

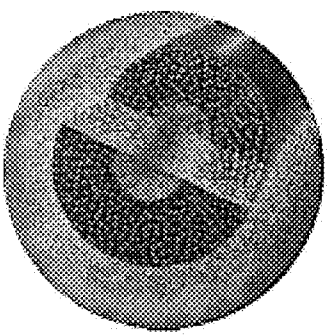
were gathered through this working group, through assessment sessions conducted by ICPs (consisting of interviews of nurses, medical and surgical attendings and residents, and anesthesiology personnel), and via observations conducted during catheter insertion and maintenance procedures. This process, along with other information derived from literature sources, resulted in the development of a VAP fishbone diagram which highlighted the healthcare groups, practices, and devices which impact the outcome of CR-BSI (Fig. 1).

The process was also beneficial in identifying various needs: the need for staff to understand the nature and severity of the problem; a uniform education program for nurses and physicians; a certification process for first-year resident physicians; selection of insertion site to reduce infection risk; standards for aseptic practice during catheter insertion and replacement; standardization of sterile attire and compliance with its use; standardization of skin antisepsis. A master plan was developed by the Infection Control Department (ICD) and subsequently approved by the Infection Committee Control (ICC) and Performance Improvement. At the core of the plan were four key strategies:

Education. Targeted medical residents (92% captured), surgical residents (98%), anesthesiologists (100%), and all nurses involved in the maintenance of the insertion site (89%). Topics covered included the morbidity, mortality, and costs associated with the occurrence of CR-BSI; hospital rates vs. national benchmarks; indications for use of a CVC; risk of infection by insertion site; procedure and timing of handwashing; proper sterile attire to be used during catheter insertion; aseptic techniques during initial catheter insertion and replacement (conducted by an experienced surgical attending); the nature and mechanism of infection prevention when using antimicrobial catheters; proper placement and maintenance of dressings including the recommended regimen for the application of skin antiseptic; review of the revised process for physician certification (first-year residents are required to successfully complete five insertions under supervision prior to solo attempts). Physician education also was conducted during new resident orientation sessions and monthly for residents covering critical care areas. (Implementation: January 2000)

Replacement of Silver-Chlorhexidine CVCs to Catheters Composed of Silver-Platinum Material (Vantex®, Edwards Lifesciences LLC, Irvine, CA). During 1997-1999, all patients requiring CVC access used a silver-chlorhexidine catheter. Significantly high rates observed during 1999 with these catheters resulted in the recommendation of the working group and the ICC to seek alternative antimicrobial devices. A novel antimicrobial catheter combining polyurethane with silver, carbon and platinum was considered (Fig 2). Studies published in the literature appeared to indicate effectiveness in reducing infection (see Discussion section). Cost of the insertion kit with a silver-platinum catheter was approximately 20% less expensive than comparable kits using silver-chlorhexidine catheters. Based on the clinical and financial information, a decision was made to convert to silver-platinum catheters for all adult patients requiring CVC devices. All CVCs during the four years were triple-lumen models. (Implementation: January 2001)

FIGURE TWO



Universal Line Insertion Kits (Tri-State Hospital Supply Corporation, Howell, MI). Observation sessions conducted by ICPs at BUMC revealed that physicians did not uniformly adhere to a policy of wearing of maximal sterile attire during insertion. Physicians were observed either not wearing any gown, did not wear a sterile gown (due to unavailability on specific units), did not wear a mask, and used various items as patient drapes which were inadequate in size and configuration (obtained from the catheter kit or from other supply). A select group of senior medical and surgical residents were gathered in order to solicit information on an ideal kit for use when inserting not only CVCs, but peripherally inserted central catheters (PICCs), arterial, and swan-ganz lines. It was decided that a custom kit to

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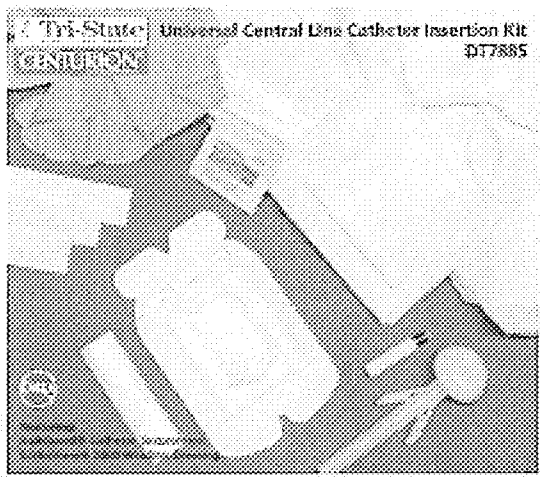
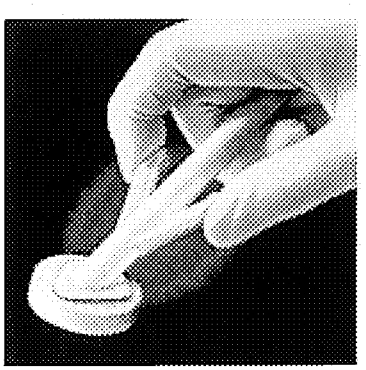
include a 36" x 60" sterile drape, sterile gown (folded in a manner to avoid contamination when donning), a mask, sterile gloves, and enclosed wound dressing kit (Sorbaview® transparent dressing, tape strips, 70% isopropyl alcohol-2% chlorhexidine antiseptic applicator, gauze, small drape) would be needed (Fig. 3). Central Supply ensured distribution to all patient care units, including the operating and emergency departments. The vendor conducted Inservice on the use of the kit and the practice of using maximal sterile barriers was incorporated in all subsequent educational sessions. (Implementation: September 2001)

FIGURE THREE



Use of 2% Chlorhexidine as the Standard Skin Antiseptic (ChloraPrep®, Medi-Flex, Inc., Overland Park, KS). Skin organisms, particularly Staphylococcusaureus and coagulase-negative Staphylococci, have been known for many years as the predominant pathogens causing both wound infections and those related to the use of intravascular catheters[10-13]. Maki and colleagues reported in 1988 that colonization of the skin at the insertion site was the predominant source for both local site infection and bacteremia[14]. Addressing the issue of adequately degerming the skin prior to catheter insertion becomes a central issue in projects aimed at reducing adverse events such as CR-BSI. Prior to January 2001, the hospital used a 10% tincture of iodine solution as its base antiseptic product. Careful examination of the literature indicated that in trials conducted to compare the efficacy of 2% chlorhexidine (CHG) to 10% povidone iodine (PI), 2% CHG exhibited a much greater ability to reduce colonization and bacteremia. In a large study involving 668 patients with central and arterial lines, Maki and researchers showed that BSI occurred seven-times as much as when using a 2% CHG skin prep[15]. CHG has also been shown to have greater antimicrobial residual effect than literature indicated that in trials conducted to compare the efficacy of 2% chlorhexidine (CHG) to 10% povidone iodine (PI), 2% CHG exhibited a much greater ability to reduce colonization and bacteremia. In a large study involving 668 patients with central and arterial lines, Maki and researchers showed that BSI occurred seven-times as much as when using a 2% CHG skin prep[15]. CHG has also been shown to have greater antimicrobial residual effect than 10% PI, a characteristic of great importance since the period between CVC dressing changes may be as long as 4-5 days[16]. Based on this information, and the approval by the FDA of ChloraPrep® as a skin antiseptic (Fig. 4), the Infection Control and the Products Evaluation & Standardization Committees approved the product for use. Bottles, swabs, and other applicators containing povidone-iodine were removed from all patient units and kits and replaced with 2% chlorhexidine. Educational sessions on the use and application of the product were conducted for the majority of staff. (Implementation: January 2002)

FIGURE FOUR



RESULTS

A total of 3,079 patients with 31,445 catheter days (average duration of catheterization equaled 10.2) were included in this study. CR-BSI rates by month for the four-year study period are shown in Figure 5. The period of January-December 1999 is considered in this study to be the pre-intervention period. Silver-chlorhexidine CVCs had been used in the institution for all adult patients since 1997 and was the only major intervention used during the pre-intervention period. During 1999, the mean rate of CR-BSI was 15.0 cases per 1000 catheter days (CD). Focused education for nurses and physicians during 2000 resulted in a 57.3% reduction in the mean rate to 6.4. However, educational efforts alone did not result in a sustained low rate; the occurrence of CR-BSI rates rose in the later 7 months of 2000, although still below 1999 mean rate levels. Conversion to silver-platinum central line catheters (Jan '01-Sep '01) resulted in a 48.4% reduction from the 2000 mean rate to 3.3 BSIs per 1000 CD. An increase in the rate to 4.2 BSIs per 1000 CD was observed after instituting new kits containing barriers (Oct '01-Dec '01). The mean rate for the 15-month period in which 2% chlorhexidine was used for prepping skin prior to catheter insertion was calculated to be 1.6 cases per 1000 CD, an approximate 62% reduction from the prior mean of 4.2. The four interventions resulted in an overall CR-BSI rate reduction of 89.3%. The overall effect of each of the four interventions is summarized in Table 1.

During the 39 month period of intervention, there were an estimated 237 cases of CR-BSI avoided (Table 2). This figure was derived by calculating the difference in cases between the expected number of BSIs (approximately 8 per month if no interventions had been taken) and the actual number of BSIs identified. Surveillance data collected in 2003 indicates that the number of CR-BSI cases occurring per month has been reduced to 0.3 or one case per quarter.

When the CDs were categorized as to location, it was determined that for the 51-month period, 52.7% of all the CDs occurred in non-ICU patient units (16,579 days) and 47.3% (14,875 days) were attributed to the adult ICUs. Rates for each type of unit are shown in Figure 6.

FIGURE FIVE

CVC-RELAYED BLOODSTREAM INFECTIONS, 1999-2003
BROOKDALE UNIVERSITY MEDICAL CENTER

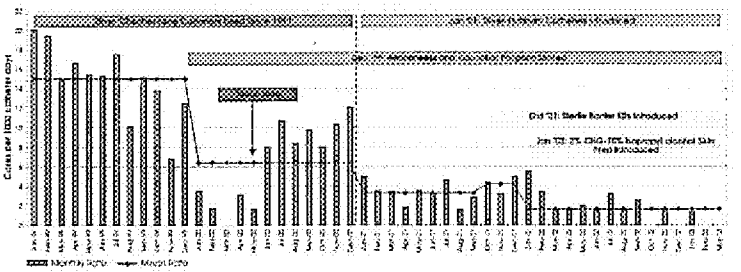


FIGURE SIX

CR-BSI RATES IN ADULT ICU AND NON-ICU PATIENT UNITS

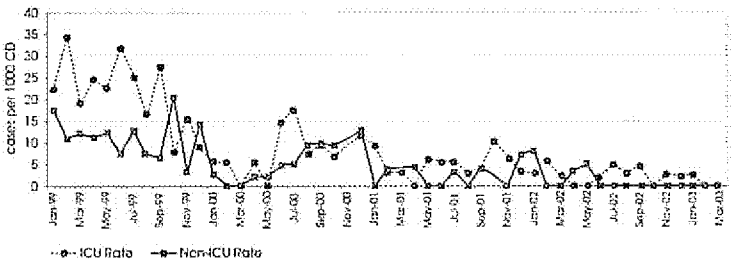


TABLE ONE

Intervention	Period	Months Between Interventions	Expected # of BSIs	Actual # of BSIs	# BSIs Avoided
(Baseline)	Jan 99-Dec 99	12	—	97	—
Education	Jan 00-Dec 00	12	97	47	50
Silver-platinum catheters	Jan 01-Sep 01	9	72	6	66
Maximal sterile barriers	Oct 01-Dec 01	3	24	6	18
2% chlorhexidine skin antiseptic	Jan 02-Mar 03	15	120	17	103
Totals:					237

 # BSIs Avoided = Expected # BSI - Actual # BSI

TABLE TWO

Intervention	Period	Months Between Interventions	# Patients	# CD	# BSI	Mean Rate	Percent Change from Prior Mean	Percent Change from Baseline
(Baseline or pre-intervention period)	Jan 99-Dec 99	12	642	6,457	97	15.0	—	—
Education	Jan 00-Dec 00	12	668	7,305	47	6.4	-57.3	-57.3
Silver-platinum catheters	Jan 01-Sep 01	9	628	5,438	6	3.3	-48.4	-78.0
Maximal sterile barriers	Oct 01-Dec 01	3	197	1,915	8	4.2	21.4	-72.0
2% chlorhexidine skin antiseptic	Jan 02-Mar 03	15	944	10,330	17	1.6	-61.9	-89.3
Totals:			3,079	31,445				

CD = catheter days, BSI = bloodstream infection

DISCUSSION

This study demonstrates that the implementation of well-supported interventions can have dramatic effects by reducing the rates of CR-BSI. The interventions used in this study as the foundation of a master plan to improve adverse infection outcomes related to CVC use have been addressed in two guidelines published by the CDC. Both guidelines were applicable due to the timeframes in which the study was conducted. The CDC statements relating to the four interventions used in this study are summarized in Table 3.

TABLE THREE

	CDC 1996 Guideline	CDC 2002 Guideline
Education	Conduct ongoing education and training of health care workers regarding indications for the use of and procedures for the insertion and maintenance of intravascular devices and appropriate infection control measures to prevent intravascular device-related infections. *Category IA*	Educate healthcare workers regarding the indication for intravascular catheter use, proper procedures for the insertion and maintenance of intravascular catheters, and appropriate infection-control measures to prevent intravascular catheter-related infections. *Category IA*
Antimicrobial Catheters	In adults, consider use of a silver-impregnated collagen cuff or an antimicrobial- or antiseptic-impregnated central venous catheter if, after full adherence to other catheter infection control measures (e.g., maximal barrier precautions), there is still an unacceptably high rate of infection. *Category II*	Use an antimicrobial or antiseptic-impregnated CVC in adults whose catheter is expected to remain in place >5 days if, after implementing a comprehensive strategy to reduce rates of CR-BSI, the CR-BSI rate remains above the goal set by the individual institution based on benchmark rates and local factors. *Category IB*
Maximal Sterile Barriers	Use sterile technique, including a sterile gown and gloves, a mask, and a large sterile drape (i.e., maximal sterile barrier precautions), for the insertion of central venous and arterial catheters. Use these precautions even if the catheter is inserted in the operating room. *Category IB*	Use aseptic technique including the use of a cap, mask, sterile gown, sterile gloves, and a large sterile sheet, for the insertion of CVCs (including PICCS) or guidewire exchange. *Category IA*
Skin Antiseptic	Cleanse the skin with an appropriate antiseptic, including 70% alcohol, 10% povidone-iodine, or 2% tincture of iodine, before catheter insertion *Category IA*	Disinfect clean skin with an appropriate antiseptic before catheter insertion and during dressing changes. Although a 2% chlorhexidine-based preparation is preferred, tincture of iodine, an iodophor, or 70% alcohol can be used. *Category IA*

Category IA. Strongly recommended for all hospitals and strongly supported by well-designed experimental or epidemiologic studies.

Category IB. Strongly recommended for all hospitals and viewed as effective by experts in the field and a consensus of Hospital Infection Control Practices Advisory Committee (HICPAC), based on strong rationale and suggestive evidence, even though definitive scientific studies may not have been done.

Category II. Suggested for implementation in many hospitals. Recommendations may be supported by suggestive clinical or epidemiologic studies, a strong theoretical rationale, or definitive studies applicable to some, but not all, hospitals.

No recommendation; unresolved issue. Practices for which insufficient evidence or consensus regarding efficacy exist.

Successful outcomes involving education as a sole means of reducing CR-BSI has been reported[17-22]. Coopersmith and colleagues at the Barnes-Jewish Hospital in St. Louis developed a self-study module aimed primarily at nurses[17]. Pre- and post-tests were required of the participants in the ICU. Surveillance indicated a 66% decrease in the rate of infection with a corresponding avoidance of 48 cases of CR-BSI. Efforts at educating medical students involved in the care of CVCs have resulted in a 28% decrease in the bacteremia rate[18]. Education projects aimed at all healthcare workers involved in the process of insertion and care of CVCs has yielded even greater results, in one case an overall reduction of 67%[19]. The results of the education portion of this project, which was directed to all healthcare workers involved in the process, resulted in a comparable rate reduction of approximately 57%.

Silver-platinum catheters are designed to create an oligodynamic iontophoresis effect, a process whereby silver ions are released in a reaction created when the catheter contacts a fluid that is electrolytic, in this case blood[23]. The bactericidal effect of silver, in this product an action occurring from both the inner and outer surfaces of the catheter, against bacteria and fungi has been well researched[24]. There is evidence that suggests that the use of the silver-platinum CVC used in this study is effective in reducing both the proliferation of bacteria that occurs during colonization and of subsequent BSI. Studies conducted on silver-platinum CVCs in vitro reported reductions in gram-positive, gram-negative and yeast microorganisms of >3 logs[25]. The results of a large clinical trial indicated marked reductions in the rates of CR-BSI when using silver-platinum catheters vs. catheters made of polyurethane alone[26]. Pooled analysis of three small, randomized trials also suggests a beneficial effect when using these catheters (RR, 0.41)[27-29].

A meta-analysis involving 13 randomized, controlled studies has reported a mean rate of 3.1 BSIs per 1000 device days when using non-cuffed, antiseptic-coated CVCs[30]. The results of this study compare favorably with this reported figure; a mean rate of 3.3 BSIs per 1000 catheter days was achieved after the introduction of silver-platinum catheters. These findings, coupled with broad physician support regarding the technical aspects of insertion using this catheter and the kit components, plus the lower purchase cost of the device compared with the prior product, it appears to have been a reasonable and beneficial decision to convert to silver-platinum catheters.

Although the rate of infection increased after the introduction of a new barrier kit, there are several reasons as to why this may have occurred. First, the period of time (3 months) to conduct a valid assessment of this product probably was too short. Second, the transition between "old" and "new" product may have caused shortages of any available barriers. Third, the availability of the new kit did not guarantee its use. This was addressed at later sessions. Regardless of the results, the literature clearly indicates that the use of sterile barriers reduces both colonization at the insertion site and the occurrence of CR-BSI[31].

CHG has been used successfully as a topical antiseptic for decades in Europe and Canada. A review of several principal characteristics of CHG indicates that this antiseptic provides a significant

continued next page

DISCUSSION

advantage over other agents such as 10% povidone-iodine in providing optimal skin antisepsis: (1) a broad antimicrobial spectrum with good activity against gram-positives and somewhat less activity against gram-negatives[33]; (2) an intermediate level in its speed of antimicrobial effect, with good reductions in the levels of organisms after 15 seconds of contact[33]; (3) a prolonged bactericidal effect that may last for up to 6 days after application; its persistent effect may be the best among all antiseptics available[32]; and (4) unlike povidone-iodine, CHG has continued activity in the presence of blood and other organic matter[34,35]. The addition of 70% isopropyl alcohol to the formulation of the product used in this trial adds an agent with the greatest speed of action[36]. A meta-analysis of trials comparing the efficacy of chlorhexidine with povidone-iodine solution in preventing BSI in patients using either CVCs, peripheral venous, peripheral arterial, pulmonary arterial, peripherally inserted central venous, or hemodialysis catheters has been published[37]. Using extensive statistical analysis to select those studies that were randomized and controlled, were blinded, and which did not include publication bias, the authors included 8 studies for final review. Assessment for risk indicated a reduction in CR-BSI of 51% in those patients using CVCs and an overall reduction of 57% when the patients were prepped with a chlorhexidine alcohol solution. In the study at BUMC, the reduction from the prior mean rate was 62% after the introduction of a 70% isopropyl alcohol-2% chlorhexidine antiseptic. Chalyakunapruk and colleagues also concluded that the absolute difference in cost between chlorhexidine and povidone-iodine is small (approximately $0.92 vs. $0.41 respectively for a quantity sufficient to prep a CVC insertion site) and would thus be likely to be cost-effective. Additional work by these authors reports a reduction in healthcare cost of $113 per catheter used ($224 for PI vs. $111 for CHG)[38].

It should be noted that three of four recommendations used in this study evolved to a category IA ranking in the 2002 CDC guideline. This highest of all categories indicates that the recommendation is strongly supported by scientific studies and should be in practice by all hospitals. Therefore, the selection of these interventions by BUMC for implementation appears to have been well justified.

Few studies have reported on CVC use outside of ICUs. Using point prevalence data on 2,265 patients gathered from six hospitals participating in the National Nosocomial Infection Surveillance System, the CDC discovered that 70% of all patients with CVCs were located outside of ICUs[39]. Our study indicates that intervention programs need to target practices performed in medical settings outside of ICUs.

COST SAVINGS

It is estimated that 73 (237/39 months x 12) cases of BSI were avoided per year during the 39-month period of intervention. Reported figures on attributable cost per infection are estimated at $34,508 to $56,000[40,41]. The cost savings per year in this study are therefore calculated to range from $2,519,084 to $4,088,000.

CONCLUSION

Patient safety not only has evolved to include the occurrence of nosocomial infection, but also errors of omission[42]. Interventional epidemiology advocates extensive assessment of processes in order to clarify "real world" practice, focus evidence-based interventions and implement those interventions with a heightened attention to detail. The study results reported here, with an overall reduction in the rate of nearly 90%, demonstrates the need to combine focused education with the use of novel technology in order to achieve maximum outcomes.

The authors gratefully acknowledge the critical contribution of the nursing, physician and materials management staff at BUMC in the success of this project.

REFERENCES

1. Maki DG, Mermel LA. Infections due to infusion therapy. In: Bennett JV, Brachman PS, eds. *Hospital Infections*. Philadelphia: Lippincott-Raven, 1998:689-724.

2. Mermel LA, Farr BM, Sherertz RJ, Raad II, O'Grady N, Harris JS, Craven DE. Guidelines for the Management of Intravascular Catheter-Related Infections. *CID* 2001;32:1249-72.

3. Pittet D, Tarara D, Wenzel R. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. *JAMA* 1994;271:1598-601.

4. Rello J, Ochagavia A, Sabanes E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Am J Respir Crit Care Med* 2000;162:1027-30.

5. Kluger D, Maki DG. The relative risk of intravenous device-related bloodstream infections with different types of intravenous devices in adults: a meta-analysis of 206 published studies (abstract). *Infect Control Hosp Epidemiol* 2000;21:95-6.

6. Making Health Care Safer: A Critical Analysis of Patient safety Practices. Agency for Healthcare Research and Quality, U.S. Department of health and Human Services. Evidence Report/Technology Assessment, No. 43, July 2001. (available at www.ahrq.gov)

7. National Quality Forum Endorses new Hospital Care National Performance Measures and a Comprehensive Framework for Hospital Care Performance Evaluation. The National Quality Forum. January 30, 2003. **(available at www.????)**

8. Guideline for the Prevention of Intravascular Device-Related Infections. Hospital Infection Control Practices Advisory Committee, Centers for Disease Control, Atlanta, GA, 1996.

9. Guidelines for the Prevention of Intravascular Catheter Related Infections. Centers for Disease Control, Atlanta, GA, 2002.

10. Schaberg DR, Culver DH, Gaynes RP. Major trends in the microbial etiology of nosocomial infection. *Am J Med* 1991;91(suppl 3B):72S-75S.

11. Armstrong CW, Mayhall G, Miller KB, et al. Prospective study of catheter replacement and other risk factors for infection of hyperalimentation catheters. *J Infect Dis* 1986;154:808-816.

12. Richet P, Hubert B, Nitemberg G, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. *J Clin Microbiol* 1990;28:2520-2525.

13. Bjornson HS, Colley R, Bower RH, et al. Association between microorganism growth at the catheter site and colonization of the catheter in patients receiving total parenteral nutrition. *Surgery* 1982;92:720-772.

14. Maki DG, Cobb L, Garman JK, et al. An attachable silver-impregnated cuff for prevention of infection with central venous catheters. A prospective randomized multi-center trial. *Am J Med* 1988;85:307-314

15. Maki DG, Ringer M, Alvarado CJ. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidene for the prevention of infection associated with central venous and arterial catheters. *Lancet* 1991;338:339-43.

16. Garcia R, Mulberry GK, Brady AR, Hibbard JS. Comparison of ChloraPrep™ and Betadine™ as preoperative skin preparation antiseptics. (abstract) Association for Infection Control and Epidemiology, 29th Annual Educational Conference and International Meeting, Nashville, TN, June 2002.

17. Coopersmith CM, Rebmann TL, Zack JE, et al. Effect of an education program on decreasing catheter-related bloodstream infections in the surgical intensive care unit.

18. Shertz RJ, Ely EW, Westbrook DM, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med* 2000;132:641-48.

19. Eggimann P, Harbarth S, Constantin MN, et al. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. *Lancet* 2000;355:1864-68.

20. Brennan PJ, Hoegg C, et al. Performance improvement in a medical intensive care unit (MICU) resulting from device based surveillance (DBS) from central venous catheter related bloodstream infections (CVC-BSI) (abstract). *Infect Control Hosp Epidemiol* 1997;18(5pt 2):20.

21. Armstrong P, Alferi N, Clowser M, et al. Central line-associated (CLA) surveillance and continuing quality improvement in an intensive acre unit (ICU) (abstract). *J Hosp Infect* 1998;40(Suppl A):8.1.8.

22. Vander Hyde K, Vanderelzen K, Chenoweth C. A "passive" education program aimed at improving knowledge about infections and reducing central venous catheter-related bloodstream infection rates. (abstract) Association for Infection Control and Epidemiology, 29th Annual Educational Conference and International Meeting, Nashville, TN, June 2002.

23. The Science of Oligon. Edwards Lifesciences LLC, 2000.

24. Russell AD, Hugo WB. Antimicrobial activity and action of silver. *Prog Med Chem* 1994;31:351-70.

25. Vantex Central Venous Catheter with Oligon Material. Evaluation of Antimicrobial Effectiveness. Edwards Lifesciences LLC, 2000.

26. Bong JJ, Kite P, Wilcox MH, et al. Reduction of the incidence of catheter-related sepsis (CRS) in high-risk patients by silver iontophretic central venous catheters (CVCs) (abstract 1918). In: 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA. *American Society for Microbiology*; 1999:649.

27. Parkhouse DAFH, Hocking GR, Shaikh LS. Advanced catheter related infection and line sepsis following the use of Vantex central venous catheters in the critically ill (abstract 54). *Crit Care Med* 2000;28(12 Suppl):A48.

28. Bong JJ, Kite P, Wilcox MH, McMahon MJ. Efficacy of silver iontrophetic central venous catheters in preventing catheter-related bloodstream infection amongst high-risk patients: a randomized controlled trial (abstract K-1425). In: Program and abstracts of the 41st Interscience Conference on Antimicrobial Agents and Chemotherapy (Chicago). Washington DC: American Society for Microbiology, 2001:425.

29. Ibanez-Nolla JJ, Corral ML, Nolla M, et al. A randomized study using Oligon Vantex central venous catheters (CVC) to reduce bacterial colonization (abstract K-1428). In: Program and abstracts of the 41st Interscience Conference on Antimicrobial Agents and Chemotherapy (Chicago). Washington DC: American Society for Microbiology, 2001:426.

30. Maki DG. A meta-analysis of the risk of intravascular device-related bloodstream infection based on 223 published prospective studies. (abstract) *4th CDC Decennial*. Atlanta, GA.

31. Raad II, Hohn DC, Gilbreath BJ, Suleiman N, et al. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *ICHE* 1994;15:231-8.

32. Guideline for Hand Hygiene in Health-Care Settings. Recommendations of the healthcare Infection Control Practices Advisory Committee and the HICPAC/SHES/APIC/IDSA Hand Hygiene Task Force. Centers for Disease Control and Prevention. *MMWR* 2002;51 (RR-16):1-48.

33. Maki DG, Zilz MA, Alvarado CJ. Evaluation of the antimicrobial efficacy of four agents for handwashing. *Curr Chemother Infect Dis* 1979;11:1089-90.

34. Larson E, Bobo L. Effective hand degerming in the presence of blood. *J Emerg Med* 1992;10:7-11.

35. Lowbury EJL, Lilly HA. The effect of blood on the disinfection of surgeons hands. *Br J Surg* 1974;61:19-21.

36. Groschel DHM, Pruett TL. Surgical antisepsis. In: Block SS, ed. Disinfection, sterilization and preservation. 4th ed. Philadelphia: Lea & Febiger, 1991:642-54.

37. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med* 2002;136:792-801.

38. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Sullivan SD, Saint S. The clinical and economic benefits of chlorhexidine compared to povidone-iodine for vascular catheter site care. (abstract #50808) 25th Annual meeting of the Society of General Internal Medicine, Atlanta, GA, May 2-4, 2002.

39. Prevalence of central line use in and outside the intensive care unit: results of a survey among hospitals in CDC's Prevention Epicenter Program. (abstract) Society for Healthcare Epidemiology of America, 12th Annual Meeting, Arlington, VA, April 2002.

40. Rello J, Ochagavia A, Sabanes E, et al. Evaluation of outcome of intravenous catheter-related infections in critically ill patients. *Respir Crit Care Med* 2000;162:1027-30.

41. Dimick JB, Pelz RK, Consunji R, et al. Increased resource use associated with catheter-related bloodstream infection in the surgical intensive care unit. *Arch Surg* 2001;136:229-34.

42. O'Grady NP, Gerberding JL, Weinstein RA, Masur H. Patient safety and the science of prevention: the time for implementing the Guidelines for the prevention of intravascular catheter-related bloodstream infections is now. *Crit Care Med* 2003;31:291-92.

John S. Hibbard, PhD
Gayle K. Mulberry, MS
Ann R. Brady, AS

A Clinical Study Comparing the Skin Antisepsis and Safety of ChloraPrep, 70% Isopropyl Alcohol, and 2% Aqueous Chlorhexidine

Abstract

ChloraPrep (2% chlorhexidine gluconate + 70% isopropyl alcohol [CHG + IPA] in a 3.0-mL applicator) is a recently approved antiseptic for preoperative skin preparation. This controlled open-label trial assessed the immediate and persistent antimicrobial efficacy and safety of CHG + IPA compared with 70% IPA or a 2% CHG aqueous solution alone. Each antiseptic significantly reduced abdominal and inguinal microbial counts from baseline at 10 minutes, 6 hours, and 24 hours (P = .0001). CHG + IPA provided significantly more persistent antimicrobial activity on abdominal sites than IPA (P = .003) or CHG (P = .028) at 24 hours. No skin irritations were reported for any of the three antiseptics.

The incidence of nosocomial infections more than doubled between the mid-1980s and mid-1990s.[1] A primary cause of nosocomial infections is the use of intravascular devices.[2] Catheter-related septicemias are the most serious complication associated with catheter insertion[2] and the majority of septicemias begin with colonization of the device-insertion tract by bacteria from patients' own skin flora.[3] Surgical-site infections also are a major complication contributing to the growing number of reported nosocomial infections. Of the 18 million surgical procedures performed in the United States each year, 2.7% (approximately 486,000) are complicated by a

John S. Hibbard is a consultant at J & A Companies, LLC, Overland Park, Kan.
Gayle K. Mulberry is Technical Director, Hill Top Research, Inc., Cincinnati, Ohio.
Ann R. Brady is Study Manager, Hill Top Research, Inc., Cincinnati, Ohio.
Address correspondence to: John Hibbard, Medilex Hospital Products, Inc., 8717 West 110th Street, Suite 750, Overland Park, KS 66210.

nosocomial infection.[4] Surgical-site infections cause considerable mortality and morbidity, extend hospital stays, and increase the cost of hospitalization.[4] As with catheter-related infections, bacteria from patients' own skin is responsible for a significant number of surgical wound infections.[5,6] Bacterial colonization caused by microflora present on patients' skin is also a common cause of contamination of blood cultures.

The well-documented and primary role of bacteria from patients' own skin in the development of bacterial colonization of catheters and septicemias, the increase of surgical-site infections, and the contamination of blood cultures reinforces the importance of thorough skin preparation with an effective topical antiseptic. Chlorhexidine gluconate (CHG) is a topical antiseptic that has been used for more than 30 years; most often it is incorporated in a detergent solution and used for hand-washing. CHG has been shown to be highly and broadly bactericidal with low levels of toxicity and strong skin-binding properties.[5,7] CHG is primarily bactericidal against gram-positive and gram-negative microorganisms, and its activity extends to yeasts, including *Candida albicans*.[5,7] The bactericidal activity of CHG differs from that observed with povidone-iodine or 70% isopropyl alcohol (IPA). CHG has demonstrated an immediate bactericidal effect as well as a cumulative effect that persists for hours and even days after it is applied[4,7,8] and, unlike iodophors, the germicidal activity of CHG has shown statistically significant efficacy in reducing bacterial counts in the presence of blood and other protein-rich biomaterials.[7,9]

The Food and Drug Administration (FDA) has recently approved the first 2% formulation of CHG in 70% isopropyl alcohol called ChloraPrep (Medi-Flex Hospital Products, Inc., Overland Park, Kan) for use as a topical antiseptic for preoperative skin preparation. The formulation is contained in a one-step 3.0-mL applicator. This article describes the results of a clinical trial comparing the immediate and persistent antimicrobial efficacy and safety of ChloraPrep (CHG + IPA) with 70% IPA alone and 2% aqueous CHG alone.

METHODS

Subjects

Healthy subjects between the ages of 18 and 70 years, free from dermatoses, inflammation, or injuries to the abdominal or inguinal (groin) area were eligible to participate in the study. Subjects were included if microbial counts on sampling sites were ≥ 2.2 $\log_{10}$ colony-forming units (CFU) per square centimeter (cm^2) of abdominal skin and ≥ 4.0 $\log_{10}$ CFU/cm^2 of inguinal skin. All subjects gave written informed consent before entering the trial.

Study Design

This randomized, parallel-group, active-control, open-label, clinical trial included prescreening, screening, and testing phases. An open-label design was chosen because the sampling time, site, location, and drug applied was unknown to technicians handling the plates, counting CFUs, and recording data. During the prescreening period ($\geq$14 days before screening), subjects used no topical or systemic antimicrobials, antibacterial hygiene products, or other agents known to affect normal skin flora. Instead, subjects were given nonbactericidal personal hygiene kits to use throughout the duration of the study. Before screening, treatment areas were shaved (if necessary) and microbial samples were taken from right and left abdominal and inguinal treatment sites to ascertain eligibility based on microbial counts.

No bathing was allowed within 24 hours before the microbial testing day. On the testing day, skin irritation was rated just before sampling at baseline, and again before sampling at 10 minutes, 6 hours, and 24 hours after study drug application. Antiseptic application skin areas were first sampled for baseline microbial counts. Then each subject was randomly assigned to receive application of one or two of the three test antiseptics, which were administered using identical 3-mL one-step applicators. The first randomly assigned antiseptic was applied to sampling areas on the left abdomen and left groin; the second was applied to sampling areas on the right abdomen and right groin. Sampling sites were randomized within the sampling area using a computer-generated schedule. Antiseptics were applied using back-and-forth strokes of the applicator for approximately 30 seconds on the abdomen and 2 minutes on the groin. The antiseptics were allowed to dry for 30 seconds on the abdomen and 1 minute on the groin. Aqueous CHG was blotted dry using a sterile towel 30 seconds after application on the abdomen and 1 minute after application on the groin. A gauze and fenestration bandage (Tegaderm, 3M Company, St. Paul, Minn) were placed over the treated area to prevent microbial contamination.

Microbial counts were taken using a cylinder-sampling technique. A sterile cylinder (inside area 3.80 cm^2) was held firmly to the sampling site. Three milliliters of sterile stripping suspending fluid (SSF+) with appropriate antiseptic neutralizers was instilled into the cylinder and the skin area inside the cylinder was massaged with a sterile glass rod with a Teflon tip in a circular manner for 1 minute. The SSF+ was collected using a sterile pipette and placed in a sterile test tube. Immediately after, a second 3.0-mL aliquot of SSF+ was instilled into the cylin-

der and the previous procedure was followed. The solution was collected with a pipette, and then pooled in the test tube with the first aliquot.

The number of CFUs/cm^2 of skin was determined as follows: 1.0-mL aliquots of SSF+ fluid were drawn from the test tube and 10-fold serial dilutions were prepared in Butterfield's phosphate buffer with neutralizer. Duplicate pour plates were prepared from each dilution using tryptic soy agar. Plates were incubated for approximately 72 hours at 30° ± 2°C and duplicate pour plates from each dilution were examined for CFUs. Plates containing between 25 and 250 CFUs were used to determine the number of CFU/cm^2 of skin. The numbers of CFUs on the duplicate plates were averaged to determine mean CFU counts for each sample. The volume of sample collected was converted into CFU/cm^2 of skin on the abdomen or groin using the following formula:

$$R = \text{Log}_{10} \frac{F\,(\Sigma c_i/n)10^{-D}}{A}$$

Where:

R = average CFU count in $\log_{10}$ scale per cm^2 of skin;

F = 6 mL of stripping fluid added to the sampling cylinder;

$\Sigma c_i \div n$ = average of duplicate colony counts used for each sample collected;

D = dilution factor of the plate counted;

A = the area inside the sampling cylinder (3.8 cm^2).

Efficacy Assessment

Antimicrobial efficacy was measured by determining the change in the mean number of CFUs/cm^2 of skin from baseline to 10 minutes after antiseptic application (immediate activity) and at 6 and 24 hours (persistent activity) after application. Effective antimicrobial activity was defined as a $\geq$2.0 $\log_{10}$ decrease in the mean number of CFUs/cm^2 of abdominal skin or a $\geq$3.0 $\log_{10}$ decrease in the mean number of CFUs/cm^2 of inguinal skin 10 minutes after application of the antiseptics. Additionally, the mean number of CFUs/cm^2 of skin must have remained below the baseline count for 6 hours after antiseptic application. Efficacy of each antiseptic was assessed within treatment (compared with baseline) and between treatments (compared with the other two antiseptics).

Safety Assessment

Safety was assessed by monitoring adverse events and by evaluating skin irritation, (erythema, edema, rash, or dryness) before and at 10 minutes, 6 hours, and 24 hours after, antiseptic application. Presence and severity of skin irritation were rated from 0 (none) to 3 (severe and extensive).

Statistical Analyses

Separate statistical analyses of efficacy were conducted for the abdomen and the groin, at the $\alpha = 0.05$ level of significance. R values (ie, the average CFU count in $\log_{10}$ scale per cm^2 of skin,) were used for efficacy assessments. Baseline CFU/cm^2 skin were compared using analysis of variance. Within-treatment analyses were made using the Student's t test for paired data. Summary statistics consisted of mean $\log_{10}$ CFU (± 95% confidence interval) and mean $\log_{10}$ CFU differences (± 95% confidence interval) expressed as geometric mean $\log_{10}$ reductions. Between-treatment analyses were performed using an analysis of covariance model with a baseline $\log_{10}$ CFU count as the covariate.

Skin irritation scores for erythema, edema, rash, and dryness were compared in within-treatment analyses using the Wilcoxon signed rank test to evaluate changes in skin irritation from baseline to each posttreatment evaluation, and a Kruskal-Wallis test was used for between-treatment comparisons.

• RESULTS

Patient Disposition and Demographics

A total of 190 healthy subjects were recruited into the prescreening phase of the study. Screening samples were collected from 153 subjects. One hundred thirteen subjects met inclusion criteria for qualifying CFU counts on the abdomen and groin. Of these 113, 106 subjects were treated with one or two of the three antiseptics and 85 subjects completed the study. Of the 21 subjects who discontinued, the majority were excluded for low microbial counts at baseline sampling on the test day. All protocol-compliant subjects who met inclusion criteria for CFU counts were included in efficacy analyses. Table 1 shows subjects' demographic characteristics. There were no statistical differences among the CHG + IPA, IPA, and aqueous CHG treatments for baseline $\log_{10}$ CFU counts on abdominal (3.060, 2.919, and 2.943 $\log_{10}$ CFUs/cm^2, respectively; $P > .05$) or inguinal (5.039, 4.961, and 4.953 $\log_{10}$ CFUs/cm^2, respectively; $P > .05$) sites.

Efficacy

The numbers of samples from abdominal sites were 42, 42, and 43 for CHG + IPA, IPA, and CHG, respectively. Within-treatment analyses of abdominal antiseptic

TABLE 1

Study Demographics

Variable	Number
Subjects in the test phase of study	106
Age (mean years)	56
Gender	
Males	32
Female	74
Race	
White	96
Black	9
Asian	1

treatment showed CFU counts were significantly reduced from baseline at 10 minutes, 6 hours, and 24 hours after application of each of the three antiseptics ($P = .0001$). Table 2 shows decreases in CFUs/cm^2 and Figure 1 shows actual mean CFUs/cm^2 of abdominal skin at baseline and at the three sampling times. Between-treatment analyses indicated no statistically significant differences in microbial count reductions among the three treatments at 10 minutes or 6 hours after antiseptic application. Twenty-four hours after application, CHG + IPA was associated with significantly lower CFU counts (Table 3) than IPA ($P = .0031$) and aqueous CHG ($P = .0280$).

The numbers of samples from inguinal sites were 26, 28, and 20 for CHG + IPA, IPA, and CHG, respectively. Within-treatment analyses of antimicrobial effects on inguinal sites showed significant reductions in CFUs/cm^2 from baseline with all three antiseptics at all sampling times ($P = .0001$; Table 4). Between-treatment analyses indicated no significant differences in microbial count reductions among the three antiseptics at any sampling time. Figure 2 shows actual mean CFU/cm^2 of skin on inguinal skin at baseline and at the three sampling times.

TABLE 2

Reductions in Colony-Forming Units Counts on the Abdomen Compared With Baseline

Drug *P* No. of Skin Sites	Mean R* Reduction From Baseline		
	10 Minutes	6 Hours	24 Hours
CHG + IPA	2.52	2.37	2.69
P	.0001†	.0001†	.0001†
n = 42	42	42	42
IPA	2.54	2.23	1.79
P	.0001†	.0001†	.0001†
n = 42	42	42	42
CHG	2.30	2.40	2.12
P	.0001†	.0001†	.0001†
n = 43	43	43	43

CHG, chlorhexidine gluconate; IPA, isopropyl alcohol.
*Log_{10} colony-forming units per square centimeter of skin.
†Significant reduction in colony-forming units counts compared

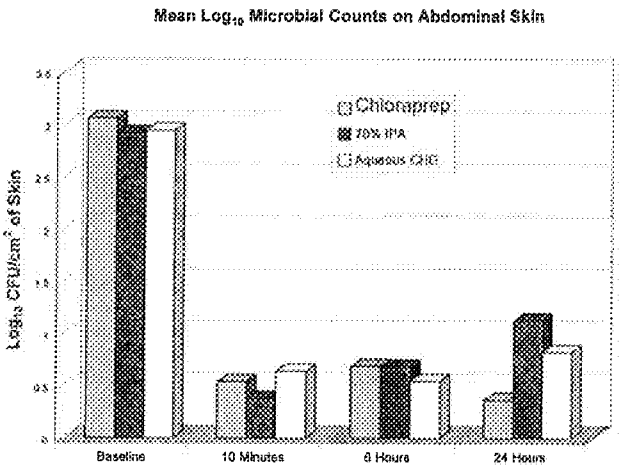


FIGURE 1.
Mean colony-forming units per square centimeter (CFUs/cm^2) of abdominal skin. All three antiseptics at all time points versus baseline, $P = .0001$. CHG + IPA versus IPA at 24 hours, $P = .0031$. CHG + IPA versus CHG at 24 hours, $P = .0280$. IPA, isopropyl alcohol; CHG, chlorhexidine gluconate.

Safety

No drug-related skin irritations were reported or observed during the study. Six adverse events were reported: four involved skin irritation under the tape area of the Tegaderm dressing used to hold the gauze in place over the treatment site, one subject was cut by scissors during treatment, and one subject had dryness

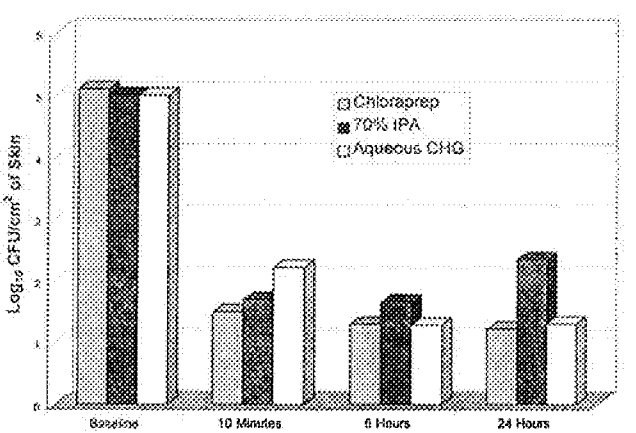


FIGURE 2.
Mean colony-forming units per square centimeter (CFUs/cm^2) of groin skin. All three antiseptics at all time points versus baseline, $P = .0001$.

TABLE 3

Reduction in Colony-Forming Units per Square Centimeter on the Abdomen at 24 Hours

Drug	Log_{10} Reduction LS Mean*	*P* CHG + IPA
CHG + IPA	2.7173	NA
IPA	1.8641	.0031†
CHG	2.1194	.0280†

CHG, chlorhexidine gluconate; IPA, isopropyl alcohol.
*LS = least square means adjusted for baseline.
†Significantly greater log_{10} reduction in colony-forming units countsobserved at 24 hours with CHG + IPA than with IPA or CHG.

TABLE 4

Reductions in Colony-Forming Units per Square Centimeter on the Groin Compared With Baseline

Drug *P* of Skin Sites	No.Mean R* Reduction From Baseline 10 Minutes	6 Hours	24 Hours
CHG + IPA	3.54	3.74	3.82
P	.0001†	.0001†	.0001†
n = 26	26	26	26
IPA	3.26	3.30	2.61
P	.0001†	.0001†	.0001†
n = 28	28	28	28
CHG	2.73	3.67	3.65
P	.0001†	.0001†	.0001†
n = 20	20	20	20

CHG, chlorhexidine gluconate; IPA, isopropyl alcohol.
*Log_{10} colony-forming units per square centimeter of skin.
†Significant reduction in bacterial counts compared with baseline.

and erythema in the groin area. The latter did not receive treatment in the groin area. No significant increases from baseline erythema, edema, rash, or dryness scores on the abdominal or groin treatment sites were reported with any treatment at any time point; nor were there significant differences among the three treatment groups in skin irritation scores.

DISCUSSION

The sharply increased incidence of nosocomial infections and evidence that bacteria from patients' own skin are a primary factor in the development of nosocomial infections indicates effective skin antisepsis is of paramount importance. Long-term and widespread use of CHG has established its exemplary efficacy and safety profile, and it has been recommended that CHG be considered as first-line antiseptic treatment for prevention of infection with percutaneous intravascular devices of all types.[2] Results of this study confirm the safety and antimicrobial efficacy of a new CHG formulation: 2% CHG in 70% IPA (ChloraPrep). This CHG formulation exceeded the FDA's proposed criteria for adequate antisepsis in patient preoperative skin preparation without causing skin irritation or adverse events.

In this study, CHG + IPA demonstrated immediate (10-minute) antimicrobial activity equivalent to 70% IPA or aqueous 2% CHG; however, CHG + IPA produced significantly better, more persistent (24-hour) antimicrobial activity on the abdomen than either of its components alone (CHG $P = .0280$ and IPA $P = .0031$). These results suggest that CHG + IPA might reduce the likelihood of infection by exerting longer, more persistent bactericidal activity, especially at more frequently used subclavian sites. Moreover, although differences between CHG + IPA, IPA, or CHG on the groin were not statistically significant at 24 hours, a clear trend toward more persistent antimicrobial activity with CHG + IPA (and aqueous CHG) versus IPA alone was observed (Figure 2). The lack of statistical significance may be due in part to the fact that more sites were sampled on the abdomen (42-43) than on the groin (20-28), giving greater statistical power to analyses of the abdominal samples.

Each of the three antiseptics tested in this trial reduced mean CFU counts on abdominal sites to an extent that exceeded the FDA's proposed criteria for patient preoperative skin preparation (microbial counts reduced ≥ 2.0 log_{10} per CFU/cm^2 of skin at 10 minutes after antiseptic application and maintained below baseline levels for at least 6 hours). On the groin, CHG + IPA and IPA alone also exceeded the FDA's proposed criteria (≥ 3.0 log_{10} per CFU/cm^2 of skin at 10 minutes after antiseptic application with counts remaining below baseline levels at 6 hours). However, at 24 hours after application, IPA alone showed a decrease in antimicrobial activity and CHG + IPA did not (Figure 2). Immediate microbial reductions with 2% aqueous CHG on the groin were <3 log_{10} per CFU/cm^2 of skin (2.73 at 10 minutes).

Safety findings from this study concur with results of skin sensitivity research that demonstrate chlorhexidine is not a primary skin irritant.[10] For example, results of a comparative antiseptic hand-washing trial indicated that intensive care unit staff tolerance of chlorhexidine was significantly superior to povidone-iodine, which caused skin irritation in approximately 50% of intensive care unit personnel ($P < .001$ versus chlorhexidine).[11] Sensitization reactions to chlorhexidine have been rarely reported.[12] Absorption of chlorhexidine through the skin does not occur or occurs at such minimal levels as to be undetectable; in any case, there is no evidence of toxicity resulting from chlorhexidine absorption.[5,13]

In conclusion, although all three antiseptics demonstrated significant immediate reductions in microbial counts compared with baseline, 2% CHG in 70% IPA continued to provide persistent antimicrobial activity on the abdomen that was statistically significant at 24 hours compared with 70% IPA ($P = .031$) and aqueous CHG ($P = .0280$). Additionally, CHG + IPA was not associated with skin irritation. The results of this study suggest ChloraPrep will help reduce the incidence of nosocomial infection.

REFERENCES

1. Clemence M, Walker D, Farr B. Central venous catheter practices: results of a survey. *Am J Infect Control.* 1995;23:5-12.
2. Maki D, Ringer M, Alvarado C. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet.* 1991;338:339-343.
3. Mimoz O, Pieroni L, Lawrence C, et al. Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. *Crit Care Med.* 1996;24:1818-1823.
4. Kirkland K, Briggs J, Trivette S, et al. The impact of surgical site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol.* 1999;725-730.
5. Denton G. Disinfection, sterilization, and preservation. In: *Chlorhexidine.* Philadelphia, Pa: Lea and Febiger; 1991:274.
6. Sukeyuki S, Sakuragi T, Dan K. Human skin flora as a potential source of epidural abscess. *Anesthesiology.* 1996;85:1276-1282.
7. Davies G, Francis J, Martin A, et al. 1:6-DI -4'-chlorophenyldiguanidohexane ("Hibitane"): laboratory investigation of a new antibacterial agent of high potency. *Br J Pharmacol.* 1954;9:192-196.
8. Lilly H, Lowbury E, Lilkins M. Detergents compared with other and with antiseptics as skin "degerming" agents. *J Hyg (Camb).* 1979;82:89-93.
9. Lowbury E, Lilly H. The effect of blood on disinfection of surgeon's hands. *Br J Surg.* 1974;61:19-21.
10. Aly R, Maibach H. Comparative evaluation of chlorhexidine gluconate (Hibiclens®) and povidone-iodine (E-Z Scrub®) sponge/brushes for presurgical hand scrubbing. *Curr Ther Res.* 1983;34:740-745.
11. Maki D, Hecht J. Antiseptic-containing handwashing agents reduce nosocomial infections: a prospective study. Presented at: the 29th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 1989; Houston, Texas.
12. Okano M, Nomura M, Hata S, et al. Anaphylactic symptoms due to chlorhexidine gluconate. *Arch Dermatol.* 1989;125:50-52.
13. Case DE, McAinsh J, Rushton A, Winrow MJ. Chlorhexidine: attempts to detect percutaneous absorption in man. In: Williams JD, Geddes AM, eds. *Chemotherapy.* Vol 3. New York, NY: Plenum; 1976:367-374.

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ORIGINAL ARTICLE

Chlorhexidine-based antiseptic solutions effectively reduce catheter-related bacteremia

Ali Mirza Onder · Jayanthi Chandar · Anthony Billings · Rosa Diaz · Denise Francoeur · Carolyn Abitbol · Gaston Zilleruelo

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Abstract The aim of this retrospective study was to investigate if the application of chlorhexidine-based solutions (ChloraPrep®) to the exit site and the hub of long-term hemodialysis catheters could prevent catheter-related bacteremia (CRB) and prolong catheter survival when compared with povidone–iodine solutions. There were 20,784 catheter days observed. Povidone–iodine solutions (Betadine®) were used in the first half of the study and ChloraPrep® was used in the second half for all the patients. Both groups received chlorhexidine-impregnated dressings at the exit sites. The use of Chloraprep® significantly decreased the incidence of CRB (1.0 vs 2.2/1,000 catheter days, respectively, P=0.0415), and hospitalization due to CRB (1.8 days vs 4.1 days/1,000 catheter days, respectively, P=0.0416). The incidence of exit site infection was similar for the two groups. Both the period of overall catheter survival (207.6 days vs 161.1 days, P=0.0535) and that of infection-free catheter survival (122.0 days vs 106.9 days, P=0.1100) tended to be longer for the catheters cleansed with ChloraPrep®, with no statistical significance. In conclusion, chlorhexidine-based solutions are more effective for the prevention of CRB than povidone–iodine solutions. This positive impact cannot be explained by decreased number of exit site infections. This study supports the notion that the catheter hub is the entry site for CRB.

Keywords Catheter survival · Catheter-related bacteremia · Chlorhexidine · Povidone–iodine · Children

A. M. Onder
Department of Pediatrics, Division of Pediatric Nephrology,
West Virginia University, School of Medicine,
Morgantown, West Virginia, USA

J. Chandar · R. Diaz · D. Francoeur · C. Abitbol · G. Zilleruelo
Department of Pediatrics, Division of Pediatric Nephrology,
University of Miami, Holtz Children's Hospital,
Miller School of Medicine,
Miami, Florida, USA

A. Billings
Department of Statistics, West Virginia University,
Morgantown, West Virginia, USA

A. M. Onder (✉)
Division of Pediatric Nephrology,
West Virginia University/Health Sciences Center,
P.O. Box 9214, Morgantown, WV 26506-9214, USA
e-mail: aonder@hsc.wvu.edu

Introduction

Catheter-related bacteremia (CRB) and catheter malfunction are the two common complications of tunneled-cuffed hemodialysis catheters (TCCs) [1, 2]. CRB strongly contributes to patient morbidity, death and loss of vascular access [3]. In our previous report, we found that CRB was the most important risk factor for shorter catheter survival [4]. The reported incidence of CRB varies from 1.1–4.2/1000 catheter days, with a mortality rate of 5% for the adult hemodialysis population [5–7]. For the cuffed catheters, the colonization of the intraluminal space through the catheter hub or following a bacteremia episode is accepted as the more likely pathogenesis of CRB (intraluminal hypothesis) [8]. For the temporary catheters, the entry of the pathogen to the catheter can be through the exit site and the tunnel around the catheter (extraluminal hypothesis) [9–11]. Among the well-known preventive measures for CRB are the use of strict hygiene measures during placement and maintenance of the catheters, the application of preventive antimicrobial ointments/solutions at the exit site, the

eradication of a *Staphylococcus aureus* nasal/skin carrier state, the cleansing of catheter hubs with antimicrobial solutions, the use of antimicrobial-coated catheters, and the intraluminal application of antibiotic lock solutions (ABLs) [5, 11–16].

ChloraPrep® (Enturia, Inc., Leawood, KS, USA) is a local cleansing agent with a mixture of chlorhexidine gluconate 2% and isopropyl alcohol 70%. The use of chlorhexidine-based solutions for the care of catheter exit sites has successfully decreased the incidence of CRB for the non-cuffed temporary catheters [17–21]. Although the importance of meticulous catheter care is emphasized in several guideline papers, there are still unsettled debates about which antiseptic solution would be the best choice [22–24]. Povidone–iodine solutions (Betadine®, Bruce Medical Supply, Waltham, MA, USA), on the other hand, have historically been used as the standard of exit site and hub care for TCCs [25–27].

The aim of this study was to investigate if the application of chlorhexidine-based solutions (ChloraPrep®) to the exit site and the hub of tunneled-cuffed hemodialysis catheters would have any beneficial impact on the prevention of CRB and catheter survival times when compared with the use of povidone–iodine solutions. Since both treatment groups received chlorhexidine-impregnated dressings at the exit sites, and prophylaxis with tobramycin–tissue plasminogen activator (TPA) antibiotic locks was used for the population at high risk for CRB, the major differentiating intervention between the two groups was the catheter hub care. The tested hypothesis was that the catheter hubs are the major entry site for CRB-causing microorganisms for long-term catheters. With strict surveillance using a broad-spectrum antiseptic at the hub, CRB may be prevented more effectively. It was unclear whether this would translate into longer catheter survival times, since none of the previous studies had focused on catheter survival times. The study was designed as a retrospective chart review.

Patients and methods

This study was approved by the University of Miami, School of Medicine Institutional Review Board (IRB). A retrospective review was performed on the charts of 59 children on long-term hemodialysis in the pediatric dialysis unit at the University of Miami/Holtz Children's Hospital, USA, from September 2004 to June 2006. All consecutive patients were included in the study. During this period, 51/59 (86%) children were using tunneled–cuffed catheters as vascular access, at least for some portion of the study. Standard tunneled–cuffed, silicone, double-lumen, hemodialysis catheters (Hemocath®; Medcomp, Harleysville, PA, USA) were used for vascular access and were placed percutaneously by the interventional radiologist or by the pediatric surgeon in children weighing fewer than 15 kg. Two pediatric surgeons and three interventional radiologists were involved in the placement and exchange of the catheters. The sizes and lengths of the catheters were based on the patient's size and ranged from 8 French, 18 cm, to 14 French , 40 cm. The right internal jugular vein was used whenever possible.

Hemodialysis protocol and catheter care

Patients underwent dialysis three to four times per week, with hollow-fiber dialyzers appropriate for body size, on Cobe® (Gambro Inc., Lakewood, Colorado, USA) or Baxter® (Deerfield, Illinois, USA) hemodialysis machines. A standard bicarbonate bath was used as dialysate. Antibiotics, vitamin D analogs, erythropoietin, and iron supplements were infused towards the end of dialysis as needed, through the catheter. Hemodialysis catheters were handled only during dialysis, with no intervention between treatments. The exit site was cleaned with chlorhexidine-based solution or povidone–iodine solution, and a chlorhexidine-impregnated dressing was applied weekly. At the end of each hemodialysis session, each port of the catheter was filled with 5,000 units/ml of heparin solution, according to the volume of the ports. Patients with high-risk for recurrent CRB were treated with tobramycin–tissue plasminogen activator (5 mg/dl tobramycin, 2 mg/2 ml TPA) antibiotic lock solutions 1–3 times per week (definition F, see below). Catheter malfunction was diagnosed when goal blood flow rate could not be maintained or when urea reduction rate (URR) was less than 65%. Catheter malfunction was initially treated by the instillation of 2 mg/2 ml TPA into each lumen for 1–2 h.

Definitions

(A) Catheter-related bacteremia (CRB) was defined as the occurrence of a positive blood culture from the catheter with or without a positive peripheral blood culture in a child with systemic symptoms (fever, chills, vomiting, hypotension) and no other source of infection identified. There were no surveillance blood cultures obtained from the catheters during the study period.

(B) Exit site infection was defined as the presence of purulent discharge, swelling, erythema and tenderness at the exit site with or without a positive swab culture.

(C) Polymicrobial CRB was defined as the documented growth of at least two or more microorganisms in the first or sequential blood cultures during the index CRB.

(D) Infection-free survival of a catheter was defined as the period between the placement of the catheter and the

first positive blood culture obtained from that catheter. All blood cultures were obtained when CRB was clinically suspected. Censored events were removal of that catheter for malfunction, obstruction, transfer to another facility, elective removal of the catheter [arteriovenous (AV) fistula, AV graft, kidney transplantation] or end of study with a functional non-infected catheter.

(E) Overall survival of a catheter was defined as the period between the insertion of the catheter and its removal. Censored events were the same as the ones for infection-free survival.

(F) High-risk for recurrent CRB was defined in children who had a previous history of more than ten episodes of CRB per 1,000 catheter days or life-threatening CRB with septic shock. In order to fulfill the criterion for high-risk, the new-onset hemodialysis children had to have experienced either two episodes of CRB in their first 200 catheter days or one episode of CRB with septic shock. Long-term hemodialysis patients were evaluated by their cumulative CRB history to qualify for high risk.

The povidone–iodine (Betadine®) era

During this era, all the patients in the unit had their exit sites cleansed with 10% povidone–iodine solution (Betadine®) at each hemodialysis session. The chlorhexidine-impregnated dressing (Biopatch®; Johnson&Johnson Medical Inc., Arlington, Tx, USA) was applied to the exit site once a week after cleansing with Betadine® and was then covered with a transparent dressing by the sterile technique. The exit site was not disturbed in-between hemodialysis treatments. The catheter hubs were immersed in 10% povidone–iodine soaked sterile gauze for 5 min prior to connection to the hemodialysis lines. Before all interventions, and at the end of the treatment sessions, the hubs were again cleansed with 10% povidone–iodine solution.

The chlorhexidine-based solution (Chloraprep®) era

In this era the exit sites were cleansed with chlorhexidine-based solution (chlorhexidine gluconate 2% and isopropyl alcohol 70%, ChloraPrep®). The chlorhexidine-impregnated dressing (Biopatch®) was applied to the exit site once a week after cleansing with chlorhexidine-based solution and was then covered with transparent dressing by the sterile technique. The exit site was not disturbed in-between hemodialysis treatments. The catheter hubs were cleansed with chlorhexidine-based solution for 1–3 min prior to connection to the hemodialysis lines. Before all interventions, and at the end of the treatment session, the hubs were again cleansed with chlorhexidine-based solution.

The diagnosis and management of CRB

Blood was obtained for culture from both ports of the catheter when children presented with fever, chills, hypotension or emesis during treatment. Peripheral blood was cultured whenever possible. All symptomatic children were examined for a clear source of infection, and, if none was found, they were presumed to have CRB. Urine for culture and chest X-rays were obtained whenever indicated. The initial empiric treatment was systemic levofloxacin and vancomycin along with tobramycin–TPA locks or tobramycin–heparin locks. The systemic antibiotics and the locks were tailored according to the sensitivities of the CRB. Symptomatic CRB after 48–72 h of protocol was treated by wire-guided exchange of catheter. Non-symptomatic CRB was treated for 2 weeks until two consecutive blood cultures 1 week apart showed no growth.

Outcome parameters

The primary end point was the occurrence of CRB. Secondary end points were infection-free catheter survival and overall catheter survival.

Data were obtained on serum albumin, ferritin and hemoglobin levels from the samples collected for monthly laboratory tests without underlying CRB for all children during the protocol period. Each patient's age, gender, etiology of end-stage renal disease, cumulative catheter days when entering the protocol, previous CRB incidence and oral treatment with methylprednisolone (Medrol®) were also documented. Type of CRB/exit site infection (Gram-positive, Gram-negative or polymicrobial) and specific microorganisms causing infections were recorded.

Statistical methods

Mean, standard deviation (SD) and percentage values were used to summarize baseline characteristics and outcome data. All results were expressed as mean±SD. P values of less than 0.05 were considered significant. Chi-square tests were used to compare proportions. Paired t test and Fischer exact test were used to compare outcomes in the two groups. Survival analysis for the catheter outcomes were performed with Kaplan–Meier curves. Graphpad® software (San Diego, CA, USA) was used to generate the survival curves. SAS 9.1 (SAS institute, Cary, NC, USA) was used for statistical analysis.

Results

There were 59 children on hemodialysis in our center during this study. Fifty-one (86%) of these children

underwent hemodialysis using a long-term catheter for at least for part of the study period. Eight patients were using an arteriovenous graft/fistula as their vascular access throughout the study. There were 24 male patients (41%) and 35 female patients (59%). Their mean age was 13.4± 8.2 years (range 2–21 years). Their racial distribution was 31 African-American, 22 Hispanic and six Caucasian. The primary etiology for end-stage renal disease was obstructive nephropathy/renal dysplasia–hypoplasia/neurogenic bladder in 21 patients, chronic glomerulonephritis in 14 patients, lupus nephritis/vasculitis in 12 patients, human immunodeficiency virus (HIV) nephropathy in eight patients, and unknown/other in four patients.

Table 1 describes the patients' comparative demographic characteristics during the Betadine® era and the ChloraPrep® era. There was no statistically significant difference when the two groups were compared for age, gender, primary etiology, the use of immunosuppressive agents, previous catheter days prior to the study or the previous CRB rates. Serum hemoglobin levels were higher in the ChloraPrep® group (10.6 g/dl vs 10.8 g/dl, P=0.0281). The ChloraPrep® group also had significantly lower serum ferritin levels than the Betadine® group (509.9 mg/dl vs 664.4 mg/dl, P=0.0034). Serum albumin concentrations were not statistically different between the two groups.

There were 116 catheters used in the study period. Ninety-six were in the right internal jugular, 18 in the left internal jugular, and two were in the right subclavian. Fourteen of the catheters were first time catheters for patients with newly diagnosed end-stage renal disease (six in the Betadine® era and eight in the Chloraprep® era).

This study involved a total of 20,784 catheter days. There were 34 episodes of CRB in 51 children. The overall incidence of CRB was 1.6/1,000 catheter days during this period. Sixteen were Gram-positive, 12 were Gram-negative and six were polymicrobial. Coagulase-negative *Staphylococcus* species were the most common Gram-positive isolates (38%). The most frequent Gram-negative isolate was *Klebsiella pneumoniae* (25%). There was no difference in the prevalence of Gram-positive, Gram-negative and polymicrobial CRB between the two groups. There was a statistically significant difference in the incidence of CRB between the Betadine® era and the ChloraPrep® era (2.2 vs 1.0/1,000 catheter days, P= 0.0415). Table 2 provides information on the distribution of CRB types.

The most common reason for patients to lose their catheters was CRB (47/116; 41%). Thirteen catheters were replaced by wire-guided exchange in the first 48–72 h of the CRB (8/64 for the Betadine® and 5/52 for the Chloraprep® eras, P>0.05). The mean overall period of catheter survival was longer for the Chloraprep® era, without reaching statistical significance (207.6 days for Chloraprep® vs 161.1 days for Betadine®; P=0.0535). There was no difference in infection-free survival time between the two groups. The comparative infection-free and overall catheter survival times for the two eras are demonstrated by Kaplan–Meier survival analysis curves in Figs. 1 and 2, respectively. The two groups had very similar incidences of exit-site infections (ESI), but CRB rate was lower for the Chloraprep® group. The Chloraprep® group had fewer hospitalization days due to CRB than did the Betadine® group (1.8 days vs 4.1 days/1,000 catheter days; P=0.0416). The incidence of catheter malfunction and breakdown requiring catheter exchange were similar for the two eras. Table 3 compares the two eras for the primary and secondary end-points of the study.

There were no allergic reactions/contact dermatitis with either Betadine® or Chloraprep® application during this study period.

Discussion

To our knowledge, this retrospective study was the first to investigate the effect of catheter cleansing method on overall and infection-free catheter survival times for tunneled-cuffed hemodialysis catheters. Our study demon-

Table 1 Comparative demographic characteristics in the Betadine® era and the ChloraPrep® era. Twenty-two patients overlapped in both treatment groups (*n* number of patients, *GN* glomerulonephritis, *NS* not significant)

Characteristic	Betadine® era (n= 39)	ChloraPrep® era (n=35)	P
Age (years)	13.9±4.7	12.8±4.3	NS 0.1789
Gender; male (%)	14 (36%)	19 (54%)	NS 0.1152
Primary etiology (HIV%)	7 (18%)	5 (14%)	NS 0.6746
Primary etiology (GN, vasculitis)	18 (46%)	15 (43%)	NS 0.7794
Immunosuppressant use	10 (26%)	12 (34%)	NS 0.4236
Previous catheter days	345.1±597.7	457.9±699.8	NS 0.4116
Previous CRB rate	5.0±2.2	4.6±2.9	NS 0.4843
Serum hemoglobin (g/dl)	10.6±1.7	10.83±1.6	0.0281
Serum albumin (g/dl)	3.4±0.7	3.4±0.5	NS 0.6746
Serum ferritin (mg/dl)	664.4±715.4	509.9±442.7	0.0034

Table 2 Incidence of different CRB types between the Betadine® era and the ChloraPrep® era (*n* number of CRBs, *NS* not significant, *NA* not applicable)

Type	Betadine® era (*n*=24)	ChloraPrep® era (*n*=10)	*P*
Gram-positive CRB	12 (50%)	4 (40%)	NS 0.6076
Gram-negative CRB	8 (33%)	4 (40%)	NS 0.7210
Polymicrobial CRB	4 (17%)	2 (20%)	NS 0.8230
Total CRB	24 (100%)	10 (100%)	NA

strated that the application of ChloraPrep® significantly decreased the incidence of CRB in long-term catheter use. There was no difference in the distribution of the types of CRB. ChloraPrep® improved the overall survival period of the catheters, not reaching statistical significance. If there had been more catheters involved in this study and a longer observation period, statistical differences might have been observed for both overall and infection-free survival of the catheters. These positive effects cannot be explained by the use of ChloraPrep® at the exit site, since there was no difference in the incidence of exit site infection between the two groups.

The success of chlorhexidine-based solutions can be explained by some of its characteristics. It is a purely topical agent, with minimal to no absorption by the skin, and without any reported systemic toxic effects. After its initial application, the residual antimicrobial effect of chlorhexidine is longer than that of povidone–iodine [28]. Moreover, chlorhexidine gluconate is a cationic biguanide with a broad spectrum of antimicrobial activity. When it is combined with an alcohol solution, it is shown to be active against most of the pathogens that are known to be responsible for ESI and CRB in long-term catheter usage for hemodialysis patients [18–20, 29]. As a last point, different body solutions can deactivate povidone–iodine solutions, which has not been described in chlorhexidine [30, 31]. There have been very few reports for the resistance patterns for chlorhexidine gluconate [32].

The overall CRB rate in this study period was lower than that reported in the literature. It was also the lowest CRB rate reported from our institution. The beneficial effects of the use of prophylactic antibiotic locks for patients at high-risk for CRB, the treatment of all CRB episodes with appropriate systemic antibiotics and antibiotic lock solutions, the use of chlorhexidine-impregnated dressings at the exit site and the appropriate length of catheter hub care at every treatment all contributed to this decreased CRB rate. This made the task of reaching statistical significance between the two groups even harder. Therefore, if the use of chlorhexidine can decrease the CRB rate for a population with an already low CRB incidence, it potentially may have more significant impact in hemodialysis units with higher baseline CRB rates.

The overall and infection-free survival times of the catheters during this study period seemed shorter than those in our previous reports [2, 4]. The two major differences in the current periods were the aggressive use of prophylactic antibiotic locks and then the use of Chloraprep®. But surprisingly, the significant improvement in CRB incidence did not generate its expected impact on the catheter survival times. When we re-analyzed our data, one important factor was the increased number of catheters that were censored

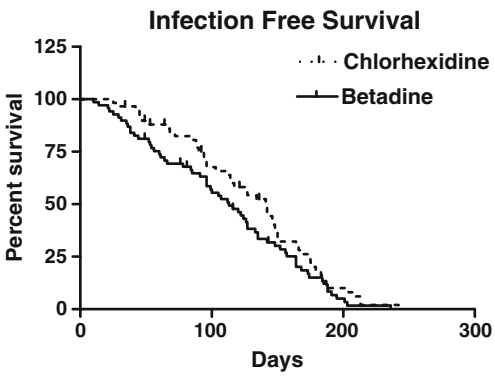

Fig. 1 Kaplan–Meier curves for infection-free survival times of the catheters in the chlorhexidine-based (Chloraprep®) and povidone–iodine based (Betadine®) cleansing eras. The infection-free survival periods were not statistically different, even though the chlorhexidine group's survival time tended to be longer than that of the Betadine® group (122.0±54.3 days vs 106.9±56.7 days, *P*=0.1100 by the log-rank test)

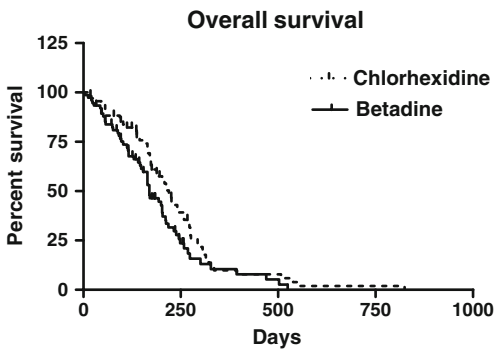

Fig. 2 Kaplan–Meier curves for the overall survival time of the catheters in the chlorhexidine-based (Chloraprep®) and povidone–iodine based (Betadine®) cleansing eras. The overall survival times of the catheters used in the Chloraprep® group were longer than those used in the Betadine® group, but it did not reach statistical significance (207.6±136.0 days vs 161.1±107.2 days, *P*=0.0535 by the log-rank test)

Table 3 Comparison of outcomes for the two different treatment groups. Twenty-two patients overlapped in both treatment groups (*n* number, *NS* not significant, *ESI* exit-site infections)

Parameter	Betadine® era (*n*=39)	ChloraPrep® era (*n*=35)	*P*
Total number of catheter days	10,960 days	9,824 days	NS 0.9866
Total number of CRB episodes	24	10	0.0041
CRB/1,000 catheter days	2.2	1.0	0.0415
Exit site infections	3 infections/2 patients infected	2 infections/2 patients infected	NS 0.9129
ESI/1,000 catheter days	0.3	0.2	NS 0.7393
Hospitalization for CRB/1,000 catheter days	4.1 days/7 patients admitted	1.8 days/3 patients admitted	0.0416
Overall catheter survival time (days±SD)	161.1±107.2	207.6±136.0	NS 0.0535
Infection-free catheter survival time (days±SD)	106.9±56.7	122.0±54.3	NS 0.1100
Number of catheters lost to malfunction/breakage	21/64 (33%)	20/52 (38%)	NS 0.5309

from the statistical analysis because their use had been terminated while they were functioning. More patients underwent kidney transplantation, more patients went through AV fistula surgeries, unfortunately with primary or secondary failures, and, lastly, many functioning catheters were censored because they had been functional at the end of the study. During the period reported here, there were also more children less than 10 years old. The advantage of a study that involves a longer observation period is that more catheters reach their natural endpoints, be it because of CRB, thrombosis or malfunction. In fact, when we analyzed all the catheter survival times within the study period without any censorship, we observed longer survival times in both groups and both eras. Furthermore, the difference in overall survival time was statistically significant, and the difference in infection-free survival was with a smaller *P* value. Therefore, we speculate that, with longer observation periods, not only would we observe longer survival periods but also we might be able to demonstrate the survival advantage of aggressive surveillance against CRB.

There are no clear data on whether the antimicrobial effect of chlorhexidine is more prominent in certain microorganisms/CRB types than in others. In this study there was a slight increase in the percentage of Gram-negative CRB during the ChloraPrep® era. It did not reach statistical significance, but, in larger numbers and with longer observation periods, this finding or similar other findings might reach statistical significance. An alternative explanation could be a more pronounced decrease in Gram-positive CRB. This was previously demonstrated in adult intensive care patients with uncuffed central venous catheters [20]. This selection characteristic of any antimicrobial/disinfectant would be an unwanted effect. This point is a very important one that needs to be investigated in a prospective trial.

This study, surprisingly, demonstrated improved serum hemoglobin levels and decreased serum ferritin levels during the ChloraPrep® era. We do not have the values for total iron infusion doses or the Epogen doses during the two periods to check if there is another explanation for this finding. However, that is unlikely, because, during the study time, both the approach to anemia and the methods of treating it were literally the same in the two eras. This improvement could also be an indirect sign of better controlled inflammation, which is now considered to be a hidden component of end-stage renal disease/chronic renal replacement therapy. The less frequent hospitalization during this era gives further support to the idea that the micro-inflammation might have been better controlled. One simple explanation for this impact may be less incidence of CRB.

There are several short-comings to our study. The retrospective nature and the overlapping patient populations are the two main limitations. There might have been unique and unaccounted for characteristics of either of the treatment periods that might have affected the outcomes, other than the cleansing methods used. Despite the fact that there was no study protocol, the daily practice in the hemodialysis unit was strictly followed by the nurses and the clinicians for each of the eras. Limited surveillance data from the monthly laboratory reports is another limitation of our study. If it were possible to assess the level of micro-inflammation by the conventional inflammatory markers, the effect of cleansing technique to control the inflammation could be assessed more precisely.

In conclusion, chlorhexidine-based solutions are more effective for the prevention of CRB than are povidone–iodine solutions. This positive impact cannot be explained by decreased number of exit site infections. The use of chlorhexidine as the hub cleanser has the potential to offer longer catheter survival times. Improved serum hemoglobin concentrations and ferritin levels may suggest better controlled inflammation. This study supports the hypothesis that the catheter hub is the more likely entry site in CRB during long-term catheter usage. Persistent and more effective surveillance at the catheter hub may offer decreased CRB rates and even longer catheter survival.

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References

1. Hoen B, Paul-Dauphin A, Hestin D, Kessler M (1998) EPIBAC-DIAL: a multicenter prospective study of risk factors for bacteremia in chronic hemodialysis patients. J Am Soc Nephrol 9:869–876
2. Onder AM, Chandar J, Coakley S, Abitbol C, Montane B, Zilleruelo G (2006) Predictors and outcome of catheter-related bacteremia in children on chronic hemodialysis. Pediatr Nephrol 21:1452–1458
3. Powe NR, Jaar B, Furth SL, Hermann J, Briggs W (1999) Septicemia in dialysis patients: incidence, risk factors and prognosis. Kidney Int 55:1081–1090
4. Onder AM, Chandar J, Saint-Vil M, Lopez-Mitnik G, Abitbol C, Zilleruelo G (2007) Catheter survival and comparison of catheter exchange methods in children on hemodialysis. Pediatr Nephrol 22:1355–1361
5. Dogra GK, Herson H, Hutchison B, Irish AB, Heath CH, Golledge C, Luxton G, Moody H (2002) Prevention of tunneled hemodialysis catheter related infections using catheter-restricted filling with gentamicin and citrate: a randomized controlled study. J Am Soc Nephrol 13:2133–2139
6. Klevens RM, Tokars JI, Andrus M (2005) Electronic reporting of infections associated with hemodialysis. Nephrol News Issues 19:37–39
7. Weijmer MC, Van den Dorpel MA, Van de Ven PJ, Wee PM, van Geelen J, Groeneveld JO, van Jaarsveld BC, Koopmans MG, le Poole CY, Schrander-Van der Meer AM, Siegert CEH, Stas KJF, for the CITRATE Study Group (2005) Randomized, clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in hemodialysis patients. J Am Soc Nephrol 16:2769–2777
8. Cheesbrough JS, Finch RG, Burden RP (1986) A prospective study of the mechanisms of infection associated with hemodialysis catheters. J Infect Dis 154:579–589
9. Linares J, Sitges-Serra A, Garau J, Perez JL, Martin R (1985) Pathogenesis of catheter sepsis: a prospective study with quantitative and semiquantitative cultures of catheter hub and segments. J Clin Microbiol 21:357–360
10. Raad I, Costerton W, Sabharwal, Sacilowski M, Anaissie E, Bodey G (1993) Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. J Infect Dis 168:400–407
11. Safdar N, Maki DG (2004) The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. Intensive Care Med 30:62–67
12. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C (2006) An intervention to decrease catheter-related blood stream infections in the ICU. N Engl J Med 355:2725–2732
13. Sesso R, Barbosa D, Leme IL, Sader H, Canziani ME, Manfredi S, Draibe S, Pignatari AC (1998) Staphylococcus aureus prophylaxis in hemodialysis patients using central venous catheter: effect of mupirocin ointment. J Am Soc Nephrol 9:1085–1092
14. Lok CE, Stanley KE, Hux JE, Richardson R, Tobe SW, Conly J (2003) Hemodialysis infection prevention with Polysporin ointment. J Am Soc Nephrol 14:169–179
15. Segura M, Alvarez-Lerma F, Tellado JM, Jimenez-Ferreres J, Oms L, Rello J, Baro T, Sanchez R, Morera A, Mariscal D, Marrugat J, Sitges-Serra A (1996) A clinical trial on the prevention of catheter-related sepsis using a new hub model. Ann Surg 223:363–369
16. Luna J, Masdeu G, Perez M, Claramonte R, Forcadell I, Barrachina F, Panisello M (2000) Clinical trial evaluating a new hub device designate to prevent catheter-related sepsis. Eur J Clin Microbiol Infect Dis 19:655–662
17. Langgartner J, Linde HJ, Lehn N, Reng M, Scholmerich J, Gluck T (2004) Combined skin disinfection with chlorhexidine/propanol and aqueous povidone-iodine reduces bacterial colonization of central venous catheters. Intensive Care Med 30:1081–1088
18. Bleasdale SC, Trick WE, Gonzalez IM, Lyles RD, Hayden MK, Weinstein RA (2007) Effectiveness of chlorhexidine bathing to reduce catheter-associated bloodstream infections in medical intensive care unit patients. Arch Intern Med 167:2073–2079
19. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S (2002) Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 136:792–801
20. Mimoz O, Villeminey S, Ragot S, Dahyot-Fizelier C, Laksiri L, Petitpas F, Debaene B (2007) Chlorhexidine-based antiseptic solution vs alcohol-based povidone-iodine for central venous catheter care. Arch Intern Med 167:2066–2072
21. Carson SM (2004) Chlorhexidine versus povidone-iodine for central venous catheter site care in children. J Pediatr Nurs 19:74–80
22. NKF K/DOQI Guidelines. Clinical Practice Guidelines for Vascular Access, 2006 Update. Available at www.kidney.org
23. O'Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, Masur H, McCormick RD, Mermel LA, Pearson ML, Raad II, Randolph A, Weinstein RA; Healthcare Infection Control Practices Advisory Committee (2002) Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control 30:476–489
24. Centers for Disease Control and Prevention (2001) Issues in healthcare settings: CDC's 7 healthcare safety challenges. Atlanta, GA. US Department of Health and Human Services, Centers for Disease Control and Prevention. http://www.cdc.gov/ncidod/dhqp/about_challenges.html. Accessed June 28, 2008
25. Levin A, Mason AJ, Jindal KK, Fong IW, Goldstein MB (1991) Prevention of hemodialysis subclavian vein catheter infections by topical povidone-iodine. Kidney Int 40:934–938
26. Kessler M, Hoen B, Mayeux D, Hestin D, Fontenaille C (1993) Bacteremia in patients on chronic hemodialysis. A multicenter prospective survey. Nephron 64:95–100
27. Krein SL, Hofer TP, Kowalski CP, Olmsted RN, Kauffman CA, Forman JH, Banaszak-Holl J, Saint S (2007) Use of central venous catheter-related bloodstream infection prevention practices by US hospitals. Mayo Clin Proc 82:672–678
28. Smylie HG, Logie JR, Smith G (1973) From Phisohex to Hibiscrub. Br Med J 4:586–589
29. Mimoz O, Pieroni L, Lawrence C (1996) Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. Crit Care Med 24:1818–1823
30. Zamora JL, Price MF, Chuang P, Gentry LO (1985) Inhibition of povidone-iodine's bactericidal activity by common organic substances: an experimental study. Surgery 98:25–29
31. Lowbury EJ, Lilly HA (1974) The effect of blood on disinfection of surgeons' hands. Br J Surg 61:19–21
32. Sticker DJ, Thomas B, Clayton CL (1985) Studies of the genetic basis of chlorhexidine resistance. Br J Clin Prac 25 (Suppl):23–30

Andrews Orthopedic &Sports Medicine Cente; ChloraPrep highly effective for presurgical pathogen removal

Abstract (Abstract): "In the DuraPrep group, bacteria grew on culture of specimens obtained from 65% of the hallux sites, 45% of the toe sites, and 23% of the control sites," while in the ChloraPrep group, "bacteria grew on culture of specimens from 30% of the hallux sites, 23% of the toe sites, and 10% of the control sites," test results showed. "ChloraPrep was the most effective agent for eliminating bacteria from the halluces and the toes (p<0.0001)."

Full text: 2005 JUL 9 - (LawRx.com) -- ChloraPrep skin-preparation solution is highly effective for eliminating infectious bacteria prior to foot and ankle surgery.

"Previous studies have demonstrated higher infection rates following orthopedic procedures on the foot and ankle as compared with procedures involving other areas of the body," surgeons in Florida explained.

In addition, the "difficulty of eliminating bacteria from the forefoot prior to surgery" has been well-documented, noted R.V. Ostrander and colleagues at the Andrews Orthopaedic and Sports Medicine Center in Gulf Breeze. They conducted their own study, to compare the "efficacy of three different surgical skin-preparation solutions in eliminating potential bacterial pathogens from the foot."

"A prospective study was undertaken to evaluate 125 consecutive patients undergoing surgery of the foot and ankle," the investigators said. "Each lower extremity was prepared with one of three randomly selected solutions: DuraPrep (0.7% iodine and 74% isopropyl alcohol), Techni-Care (3.0% chloroxylenol), or ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol)."

"After preparation, quantitative culture specimens were obtained from three locations: the hallux nailfold (the hallux site), the web spaces between the second and third and between the fourth and fifth digits (the toe site), and the anterior part of the tibia (the control site)," according to the report. "In the Techni-Care group, bacteria grew on culture of specimens obtained from 95% of the hallux sites, 98% of the toe sites, and 35% of the control sites."

"In the DuraPrep group, bacteria grew on culture of specimens obtained from 65% of the hallux sites, 45% of the toe sites, and 23% of the control sites," while in the ChloraPrep group, "bacteria grew on culture of specimens from 30% of the hallux sites, 23% of the toe sites, and 10% of the control sites," test results showed. "ChloraPrep was the most effective agent for eliminating bacteria from the halluces and the toes (p<0.0001)."

"The use of effective preoperative preparation solution is an important step in limiting surgical wound contamination and preventing infection, particularly in foot and ankle surgery. Of the three solutions tested in the present study, the combination of chlorhexidine and alcohol (ChloraPrep) was most effective for eliminating bacteria from the forefoot prior to surgery," the researchers concluded."

Ostrander and coauthors published the results of their study in the Journal of Bone and Joint Surgery - American Volume (Efficacy of surgical preparation solutions in foot and ankle surgery. J Bone Joint Surg Am, 2005;87A(5):980-985).

For additional information, contact R.V. Ostrander, Andrews Orthopaedic and Sports Medicine Center, 1118 Gulf Breeze Parkway, Suite 100, Gulf Breeze, FL 32561, USA.

The publisher of the Journal of Bone and Joint Surgery - American Volume can be contacted at: Journal of Bone and Joint Surgery Inc., 20 Pickering St., Needham, MA 02192, USA.

Keywords: Gulf Breeze, Florida, United States, Anti-infectives, Bacteriology, Foot and Ankle Surgery, Orthopedic Surgery, Surgical Technology.

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Medi-Flex, Inc.; ChloraPrep provides non-linting application

Abstract (Abstract): Center for Disease Control and Prevention (CDC) Guidelines for the Prevention of Intravascular Catheter-Related Infections state that for cutaneous antisepsis, "a 2% chlorhexidine-based preparation is preferred." ChloraPrep is the only 2% chlorhexidine gluconate/ 70% isopropyl alcohol patient preoperative skin prep approved by the FDA that meets the CDC's guidelines.

Full text: 2005 JUL 19 - (LawRx.com) -- Utilizing an innovative design that creates a new standard for excellence in swabstick technology, the ChloraPrep Swabstick is now available in single and triple applicators with a design that provides significant improvement in performance over traditional swabsticks.
The reinforced handle provides friction while the new polyester, polyurethane foam tip provides non-linting application.
"The ChloraPrep Swabstick is clearly a superior product combining advanced design technology with the best antiseptic available for infection prevention," said Cynthia T. Crosby, vice president of clinical affairs for Medi-Flex.
Center for Disease Control and Prevention (CDC) Guidelines for the Prevention of Intravascular Catheter-Related Infections state that for cutaneous antisepsis, "a 2% chlorhexidine-based preparation is preferred." ChloraPrep is the only 2% chlorhexidine gluconate/ 70% isopropyl alcohol patient preoperative skin prep approved by the FDA that meets the CDC's guidelines.
Clinical studies comparing chlorhexidine to povidone iodine consistently demonstrate reduction rates of 50% for catheter- related bloodstream infections. Furthermore in clinical practice ChloraPrep has consistently demonstrated a reduction in healthcare associated infections when replacing alcohol and iodine.
The ChloraPrep family of products is manufactured by Medi-Flex, Inc., a Leawood, Kansas-based company.

Company: Medi-Flex Inc

Publication title: Pharma Law Weekly

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Country of publication: United States

Publication subject: Law--Corporate Law

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Last updated: 2010-06-10

Database: ProQuest Research Library

Medi-Flex, Inc.; Availability of preoperative antibacterial skin preparation announced

Abstract (Abstract): ChloraPrep 26 mL with scrub teal tinting technology is the first U.S. Food and Drug Administration (FDA)-approved preoperative skin prep that contains the U.S. Centers for Disease Control and Prevention (CDC)-preferred amount of chlorhexidine gluconate. Compared to iodophors, ChloraPrep 26 mL demonstrates superior antibacterial activity and is the most rapid-acting, and persistent preoperative skin preparation available in the operating room.

Full text: 2005 NOV 18 - (LawRx.com) -- Medi-Flex, Inc. announced the availability of a new preoperative skin prep for use in the surgical suite.

ChloraPrep 26 mL with scrub teal tinting technology is the first U.S. Food and Drug Administration (FDA)-approved preoperative skin prep that contains the U.S. Centers for Disease Control and Prevention (CDC)-preferred amount of chlorhexidine gluconate. Compared to iodophors, ChloraPrep 26 mL demonstrates superior antibacterial activity and is the most rapid-acting, and persistent preoperative skin preparation available in the operating room.

Surgical site infections (SSIs) are a major cause of healthcare- associated infections (HAIs). Most of these debilitating, sometimes deadly surgical infections are caused by bacteria on the patient's own skin.

Reducing targeted surgical adverse events by 50% is one of the CDC's "Seven Healthcare Safety Challenges" for the next 5 years.

ChloraPrep is manufactured in Medi-Flex's FDA-approved facility in El Paso, Texas. The facility is ISO-9001:2000 and ISO:13488 certified and has the received four consecutive audits without an FDA observation.

Medi-Flex was founded in 1985 and has a 20-year history of developing antiseptic skin products.

Company / organization: Name: Food & Drug Administration; NAICS: 922190; SIC: 9400; DUNS: 13-818-2175 ; Name: Centers for Disease Control; NAICS: 923120; SIC: 9400;

Publication title: Food & Drug Law Weekly

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Database: ProQuest Career and Technical Education

Correct use of chlorhexidine in intravenous practice

Scales K (2009) Correct use of chlorhexidine in intravenous practice. *Nursing Standard*. 24, 8, 41-46. Date of acceptance: September 10 2009.

Summary

This article reviews the routes by which microorganisms may contaminate vascular access devices, and examines the role of chlorhexidine in the prevention of catheter-related bloodstream infections. Chlorhexidine-based cleansing products for use in intravenous therapy are reviewed and their correct use is discussed, with reference to clinical guidelines.

Author

Katie Scales, consultant nurse in critical care, Imperial College Healthcare NHS Trust, London.
Email: katie.scales@imperial.nhs.uk

Keywords

Chlorhexidine, infection control, intravenous therapy, vascular access devices

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VASCULAR ACCESS DEVICES (VADs) play an important role in modern health care, but are associated with an increased risk of infection (Department of Health (DH) 2007). Infection is a potentially life-threatening complication of intravenous (IV) therapy and may be localised, for example infective phlebitis, or systemic, for example septicaemia (Elliott *et al* 1995). Central venous catheters are the major cause of hospital-acquired bacteraemia (Coello *et al* 2003), resulting in increased hospitalisation and healthcare costs (Blot *et al* 2005). Chlorhexidine gluconate has been shown to reduce the risk of catheter-related bloodstream infections by 50% when compared with povidone-iodine for skin cleansing (Chaiyakunapruk *et al* 2002). A range of chlorhexidine-based cleansing products are now available and it is important that nurses and other healthcare professionals select the correct product for use in clinical practice.

Mechanisms of intravenous infection

Bacteraemia directly linked with a VAD is termed a catheter-related bloodstream infection (C-RBSI) and is associated with an increase in morbidity and mortality (Maki and Crnich 2003). There are five main mechanisms by which VADs may become infected (Figure 1) (Elliott and Faroqui 1992):

- Intraluminal migration via catheter hubs.
- Extraluminal migration via catheter insertion sites.
- Contaminated infusates.
- Contamination of the catheter tip during insertion.
- Haematogenous seeding.

Intraluminal migration This refers to contamination of the internal lumen of the VAD, which occurs when the catheter hub has become infected (Casey and Elliott 2007). Contamination of a VAD or the equipment connected to the VAD, for example multi-way connectors, three-way taps or administration sets, is usually from the patient's skin bacteria (flora) or by cross-infection from the hands of healthcare workers. Prevention relies on strict handwashing, appropriate glove use, aseptic technique and the use of sterile equipment. It is also important to keep manipulations of the VAD to a minimum (Hart 2008).

Extraluminal migration Contamination of the VAD from bacteria that migrate from the insertion site along the external surface of the device is known as extraluminal migration (Hart 2008). Bacterial contamination may be from the patient's own skin flora or by cross-infection from the hands of healthcare workers. The use of skin antisepsis before VAD insertion and during dressing changes is important in the prevention of extraluminal contamination (Pratt *et al* 2007).

Contaminated infusates This involves the administration of contaminated IV fluids or drugs through the VAD. This is a relatively rare occurrence, and the risks can be further reduced

by the use of pre-mixed solutions and the avoidance of IV additives prepared in ward environments where sterile conditions cannot be maintained. Careful inspection of IV fluids before use is essential (Hart 2008). Before administrating any IV fluids nurses should check that:

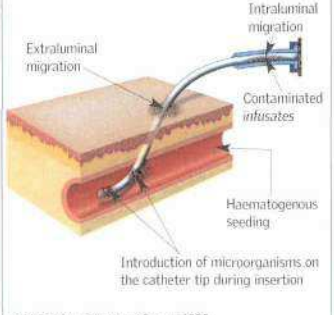
- The protective cover on fluid bags is intact.
- Protective caps on fluid bottles are in place.
- Fluid solutions are clear and free from particles.
- Bottles are free from cracks and bags are free from holes or damage.
- Fluids are within their expiry date.

Contamination of the catheter tip during insertion Contamination can occur from inadequate skin antisepsis before insertion. This allows skin organisms to be transferred to the VAD and introduced into the bloodstream. Contamination of the VAD may also happen before insertion through poor handling or an inadequate sterile field. It can also occur if the skin is re-palpated after skin cleansing, for example during peripheral cannulation using non-sterile gloves.

Haematogenous seeding This is the migration of microorganisms from another site in the body to the VAD via the bloodstream. There are many potential sources of haematogenous seeding. Organisms may migrate from the lung, the bowel, an abscess or another focus of infection.

FIGURE 1

Access routes of microorganisms that cause intravenous catheter-related infection



(Modified from Elliott and Faroqui 1992, Adams and Elliott 2007)

Infection prevention

Prevention of infection associated with VADs focuses on the following key areas of nursing practice:

- Thorough hand hygiene to prevent cross-infection.
- Appropriate use of personal protective equipment, for example gloves and aprons.
- Thorough skin disinfection before VAD insertion.
- Thorough decontamination of the VAD access port before and after the administration of drugs and fluids.
- Observation and monitoring of insertion sites and dressings.
- Correct dwell times for VADs.
- Timely removal of the VAD when it is no longer required.

The management of infusion systems also plays an important part in the prevention of infection. To administer fluids and drugs, or to obtain a blood sample, infusion systems can be accessed in one of three ways (Casey and Elliott 2007):

- Via an open system.
- Via a traditional closed system.
- Via a needleless device.

An IV system is described as 'open' if the interior of the system comes into direct contact with the environment. The removal of a cap from a three-way tap to expose the internal lumen of the IV device is an example of an open system. The use of an open IV system increases the risk of intraluminal contamination (Casey and Elliott 2007).

Traditional closed systems involve the use of luer caps with an injectable membrane that can be accessed with a fine needle, thereby keeping the system closed (Casey and Elliott 2007). This potentially carries a greater risk of needlestick injury in comparison to a traditional open system but has the advantage of reducing infection risks from intraluminal contamination.

Needleless devices were introduced in an attempt to reduce needlestick injuries while retaining the concept of a closed IV system. There are three types of needleless device available: split septum devices, mechanical valves, and mechanical valves with positive displacement technology (Casey and Elliott 2007). Technology continues to evolve and needleless devices are now marketed with additional technology to prevent contamination of the access port. For example, the Baxter V-link

luer-activated device incorporates silver nanotechnology to inhibit bacterial growth on the exterior and interior surfaces of the device.

Any action that exposes the internal lumen of the IV device is high risk and should be avoided.

Chlorhexidine and infection prevention

Chlorhexidine has been used as a topical disinfectant since the mid-1970s (Kessler 1998). Chlorhexidine is an effective antimicrobial agent and its mode of action is now thought to be through the disruption of bacterial cell membranes resulting in cellular dysfunction or cell death (Shalomanov 2005). Unlike other topical antiseptics, its antimicrobial effects are sustained because it binds to proteins in the skin and mucosa (Lim and Kam 2008). Chlorhexidine has been shown to exert an antimicrobial effect for up to six hours after application (Scales 2008).

Chlorhexidine is available in a number of different preparations, including surgical scrub solutions, topical creams and gels, toothpaste and mouthwash, and disinfectant solutions. Because of its widespread use, people have often had previous exposure to chlorhexidine before receiving chlorhexidine as part of their medical care.

Allergy to chlorhexidine has been reported and health professionals must be alert to potential allergy or anaphylaxis associated with its use. Delayed skin reactions, such as contact dermatitis, were first reported in 1965 (Birdwood 1965). Anaphylaxis is thought to be relatively rare, with only 50 cases reported worldwide over a ten-year period (Beaudouin *et al* 2004). The true incidence of chlorhexidine allergy may not be known because chlorhexidine is not classified as a drug. It is usually considered as a disinfectant or antiseptic and, therefore, the recognition of chlorhexidine as the cause of anaphylaxis may be overlooked. Chlorhexidine allergy has been reported more commonly in patients of Japanese origin (Oda T *et al* 1997). However, Stephens *et al* (2001) reported anaphylaxis in a European patient following the insertion of a chlorhexidine-sulphadiazine-coated central venous catheter. The use of chlorhexidine in neonates remains controversial with a range of adverse effects reported, including bradycardia (Quinn and Bini 1989) and skin reactions (Garland *et al* 1996). However, some recent studies have shown efficacy in neonates (Darmstadt *et al* 2007).

More recently, the importance of chlorhexidine in reducing infections associated with IV therapy has been recognised (Maki *et al* 1991, LeBlanc and Cobbett 2000, Mermel 2000, Pratt *et al* 2007), and products have been developed specifically for use in IV therapy. Early research into the use of chlorhexidine for skin preparation before VAD insertion was undertaken with 2% aqueous (water-based) chlorhexidine and demonstrated superior skin antisepsis when compared to povidone-iodine or 70% isopropyl alcohol (Maki *et al* 1991). A meta-analysis comparing aqueous chlorhexidine, alcoholic chlorhexidine and povidone iodine showed that aqueous and alcoholic chlorhexidine were more effective than povidine iodine in reducing C-RBSI, but only alcoholic chlorhexidine was shown to be statistically significant in reducing C-RBSI (Chaiyakunapruk *et al* 2002, Pratt *et al* 2007).

As the benefits of chlorhexidine have become more widely recognised, an increasing number of chlorhexidine-based products have entered the healthcare market. To be marketed in the UK each product must be CE marked and be licensed by the Medicines and Healthcare products Regulatory Agency. The licence determines how the product should be used in practice, for example whether the product is for use on skin as an antiseptic or for use on medical devices for decontamination. It is important that medical products and devices are used within their licence. Failure to do so may have consequences for the patient and for the practitioner.

The epic2 guidelines recommend the use of 'individual single-use sachets of antiseptic solution or individual packages of single-use antiseptic impregnated swabs or wipes' (Pratt *et al* 2007), rather than large containers for multiple-patient use. Despite the increasing evidence for the use of alcoholic chlorhexidine, a licensed product for single patient use skin disinfection was not available in the UK until November 2006, when ChloraPrep was launched by Enturia Inc. ChloraPrep is the only licensed single-use product available in the UK for skin disinfection. ChloraPrep contains 2% chlorhexidine gluconate in 70% isopropyl alcohol and is available in a range of pre-filled applicators. ChloraPrep devices contain an internal ampoule that must be broken to release the chlorhexidine solution on to the applicator. It is important not to touch the sponge of the applicator as this will contaminate the device (Enturia 2009).

ChloraPrep is not yet used in all UK hospitals and some organisations still rely on multi-use bottles of antiseptic. To date, 2% chlorhexidine in 70% isopropyl alcohol is not available in a multi-use bottle, and centres that do not use ChloraPrep may rely on 0.5% chlorhexidine in alcohol or povidone-iodine, both of which are proven to be less effective than 2% chlorhexidine in alcohol (Pratt *et al* 2007). Studies have shown that multi-use containers can become contaminated with bacteria, thereby reducing efficacy and increasing the risks to patients. Birnbach *et al* (1998) found that 40% of previously opened povidone-iodine

containers were contaminated with bacteria and recommended that only single-use containers should be used.

Skin disinfection before peripheral vascular access device insertion

Peripheral cannulae should be inserted by trained and competent staff using strict aseptic techniques (DH 2003). LeBlanc and Cobett (2000) demonstrated that 0.5% chlorhexidine gluconate in 70% isopropyl alcohol was more effective than 10% povidone-iodine and 70% isopropyl alcohol when used for skin antisepsis before peripheral cannulation.

ChloraPrep is available as a 0.67ml Sepp applicator (Figure 2) and as a 1.5ml Frepp applicator (Figure 3). Both are suitable for skin antisepsis before venepuncture, peripheral cannulation or subcutaneous device insertion (Enturia 2009). The Frepp applicator is also recommended for use before obtaining peripheral blood cultures. Mimoz *et al* (1999) demonstrated a significant reduction in the contamination rate of blood cultures when comparing chlorhexidine skin antisepsis with povidone-iodine.

When using the Sepp or Frepp applicator it is recommended that the applicator is gently pressed against the skin and that the applicator is applied in an 'up and down, back and forth motion for 30 seconds' (Enturia 2009). The solution must then be allowed to dry completely before VAD insertion or venepuncture (Enturia 2009). The applicator should be disposed of in a sharps container.

Skin disinfection before central venous catheter insertion

Central venous catheters (CVCs) are associated with an increased risk of C-RBSI in comparison to peripheral devices. Skin antisepsis of the insertion site before CVC insertion has been shown to play an important part in reducing C-RBSI (Pearson 1996). The epic2 guidelines recommend that 2% chlorhexidine in 70% isopropyl alcohol is used to decontaminate the skin before CVC insertion because this was found to be the most effective agent in preventing C-RBSI associated with CVC insertion (Pratt *et al* 2007).

ChloraPrep is available in larger applicators that provide sufficient solution to decontaminate large areas of skin before CVC insertion. The 3ml ChloraPrep applicator (Figure 4) provides enough solution to cleanse an area of skin that is 15cm x 15cm and is recommended for skin preparation before CVC or midline insertion (Enturia 2009). Elliott *et al* (1994) emphasised the need to clean beyond the intended CVC insertion site, suggesting that for

FIGURE 2
Sepp applicator

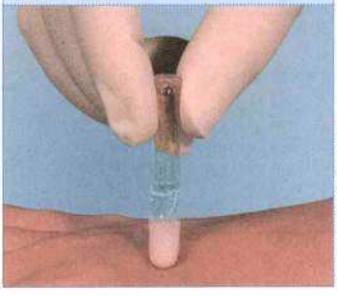


FIGURE 3
Frepp applicator

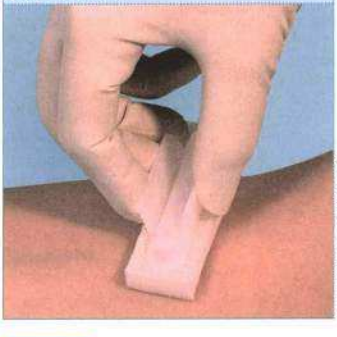


FIGURE 4
ChloraPrep 3ml applicator

jugular or subclavian access the skin preparation should extend to the neck, shoulders and top of the chest. If a large insertion site is to be prepared then the 10.5ml ChloraPrep applicator may be more appropriate because this contains enough solution to cover an area of 25cm x 30cm.

When using ChloraPrep to prepare a vascular insertion site, the manufacturer recommends that the solution is applied for 30 seconds, provided that the treatment area is completely wet with antiseptic solution. It should then be allowed to dry for at least 30 seconds (Enturia 2009).

ChloraPrep is a clear solution and it can be difficult to identify which areas of skin have been cleaned during the skin cleansing process. To improve visibility of the prepared area, an orange tinted version of ChloraPrep is available in the United States (Enturia 2009) and this will also be launched in the UK.

Skin cleansing during intravenous dressing changes

It is important to clean the skin around VAD insertion sites during IV dressing changes (Pratt *et al* 2007). Ideally, the cleansing solution should be 2% chlorhexidine in 70% isopropyl alcohol (Pratt *et al* 2007). The ChloraPrep, Sepp or Frepp applicators are suitable for use during dressing changes, but the Sepp applicator may be easier to direct around VAD insertion sites.

A 2% chlorhexidine alcoholic disposable skin disinfection wipe – the Clinell Alcoholic 2% Chlorhexidine Skin CA2CSKIN (Blue Skin Wipes) – is also available. It is suitable for use on small areas of dirty skin after dressing or plaster removal. This product is not sterile and is not licensed for use during IV dressing changes or insertion site care. The use of this product for IV site care is not permitted under the terms of its product licence and is against the manufacturer's advice.

Decontamination of catheter hubs and injection sites

The epic2 guidelines (Pratt *et al* 2007) recommend the use of a single patient application of 2% chlorhexidine in 70% isopropyl alcohol to decontaminate catheter hubs, injection ports and needlefree devices before and after use. It is important to know that this solution is compatible with the VAD that is being decontaminated. Nurses should refer to manufacturer guidelines if they are unsure. If the VAD is not compatible with alcohol then 2% aqueous chlorhexidine or aqueous povidone-iodine should be used (Pratt *et al* 2007).

Gama Healthcare Ltd provides an alcoholic 2% chlorhexidine wipe, the Clinell Alcoholic 2% Chlorhexidine CA2C200 (Green Medical Device Wipe), which was launched in response to the epic2 guidelines (Gama Healthcare Ltd 2009). This wipe is specifically designed to decontaminate catheter hubs of central, peripheral and arterial VADs and to decontaminate injection sites, needleless

References

Adams D, Elliott TS (2007) Skin antiseptics used prior to intravascular catheter insertion. *British Journal of Nursing.* 16, 5, 278-280.

Beaudouin E, Kanny G, Morisset M *et al* (2004) Immediate hypersensitivity to chlorhexidine: literature review. *European Annals of Allergy and Clinical Immunology.* 36, 4, 123-126.

Birdwood B (1965) Reaction to chlorhexidine and cetrimide. *The Lancet.* 1, 7386, 651-652.

Birnbach DJ, Stein DJ, Murray O, Thys DM, Sordillo EM (1998) Povidone iodine and skin disinfection before initiation of epidural anesthesia. *Anesthesiology.* 88, 3, 668-672.

Blot SI, Depuydt P, Annemans L *et al* (2005) Clinical and economic outcomes in critically ill patients with nosocomial catheter-related bloodstream infections. *Clinical Infectious Diseases.* 41, 11, 1591-1598.

Casey AL, Elliott TS (2007) Infection risks associated with needleless intravenous access devices. *Nursing Standard.* 22, 11, 38-44.

Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S (2002) Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Annals of Internal Medicine.* 136, 11, 792-801.

Coello R, Charlett A, Ward V *et al* (2003) Device-related sources of bacteraemia in English hospitals – opportunities for the prevention of hospital-acquired bacteraemia. *Journal of Hospital Infection.* 53, 1, 46-57.

Darmstadt GL, Hossain MM, Choi Y *et al* (2007) Safety and effect of chlorhexidine skin cleansing on skin flora of neonates in Bangladesh. *The Pediatric Infectious Disease Journal.* 26, 6, 492-495.

Department of Health (2003) *Winning Ways: Working Together to Reduce Healthcare Associated Infection in England.* The Stationery Office, London.

Department of Health (2007) *Saving Lives: A Delivery Programme to Reduce Healthcare Associated Infection Including MRSA. High Impact Intervention No2b: Peripheral Intravenous Cannula Care Bundle.* The Stationery Office, London.

Elliott TS, Faroqui MH (1992) Infections and intravascular devices. *British Journal of Hospital Medicine.* 48, 8, 496-497, 500-503.

Elliott TS, Faroqui MH, Armstrong RF, Hanson GC (1994) Guidelines for good practice in central venous catheterization. *Journal of Hospital Infection.* 28, 3, 163-176.

Elliott TS, Faroqui MH, Tebbs SE, Armstrong RF, Hanson GC (1995) An audit programme for central venous catheter-associated infections. *Journal of Hospital Infection.* 30, 3, 181-191.

devices and the tops of blood culture bottles (Gama Healthcare Ltd 2009). This wipe is not sterile and is not licensed for use on skin. Its use as a skin cleanser before venepuncture or peripheral cannulation is against manufacturer's advice and outside the product's licensed use.

The Sani-Cloth CHG 2% is also available for the decontamination of catheter hubs, connection ports and other medical devices (PDI 2009). It is not licensed for use on skin.

Conclusion

The evidence for alcoholic chlorhexidine gluconate in the prevention of IV-related infection is compelling, and current guidelines recommend its use (Pratt *et al* 2007). It is essential that nurses and other healthcare professionals incorporate this evidence into their clinical practice to protect patients from the potentially fatal effects of IV-related infection.

The availability of products containing 2% chlorhexidine in 70% isopropyl alcohol is increasing in the UK. Healthcare professionals should be aware of the licensed use of each product and ensure that products are used correctly. Cleansing solutions or wipes must be compatible with individual VADs to prevent complications, such as device cracking. Patient allergies and sensitivities must be checked to prevent anaphylaxis in those sensitive to chlorhexidine.

The use of alcoholic chlorhexidine is only one element of infection prevention in IV therapy. Strict attention to hand hygiene, aseptic handling of VADs, the use of closed systems and attention to VAD dwell times are essential to good IV therapy practice **NS**

Enturia Inc (2009) *ChloraPrep Product Education and Usage Information.* www.chloraprep.co.uk/productUsage Download.html (Last accessed: October 14 2009.)

Gama Healthcare Ltd (2009) *Clinell Alcoholic 2% Chlorhexidine CA2C200 – Green Medical Device Wipe: Frequently asked questions.* www.gamahealthcare.com/products-alcoholic-2percent-disinfection-faq.asp (Last accessed: October 14 2009.)

Garland JS, Alex CP, Mueller CD, Cisler-Kahill LA (1996) Local reactions to a chlorhexidine gluconate-impregnated antimicrobial dressing in very low birth weight infants. *Pediatric Infectious Disease Journal.* 15, 10, 912-914.

Hart S (2008) Infection control in intravenous therapy. In Dougherty L, Lamb J (Eds) *Intravenous Therapy in Nursing Practice.* Second edition. Blackwell Publishing, Oxford, 87-116.

Kessler LG (1998) FDA Alert: Hypersensitivity Reactions to Central Venous Catheters. *American Society of Anesthesiologists Newsletter.* 62. www.asahq.org/Newsletters/1998/05_98/FDA_0598.html (Last accessed: October 14 2009.)

LeBlanc A, Cobbett S (2000) Traditional practice versus evidence-based practice for IV skin preparation. *Canadian Journal of Infection Control.* 15, 1, 9-14.

Lim KS, Kam PC (2008) Chlorhexidine: pharmacology and clinical applications. *Anaesthesia and Intensive Care.* 36, 4, 502-512.

Maki DG, Crnich CJ (2003) Line sepsis in the ICU: prevention, diagnosis, and management. *Seminars in Respiratory and Critical Care Medicine.* 24, 1, 23-36.

Maki DG, Ringer M, Alvarado CJ (1991) Prospective randomised trial of povidone-iodine, alcohol and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *The Lancet.* 338, 8763, 339-343.

Mermel LA (2000) Prevention of intravascular catheter-related infections. *Annals of Internal Medicine.* 132, 5, 391-402.

Mimoz O, Karim A, Mercat A *et al* (1999) Chlorhexidine compared with povidone-iodine as skin preparation before blood culture: A randomized, controlled trial. *Annals of Internal Medicine.* 131, 11, 834-837.

Oda T, Hamasaki J, Kanda N, Mikami K (1997) Anaphylactic shock induced by an antiseptic-coated central venous catheter. *Anesthesiology.* 87, 5, 1242-1244.

Pearson ML (1996) Guideline for prevention of intravascular device-related infections. Hospital Infection Control Practices Advisory Committee. *Infection Control and Hospital Epidemiology.* 17, 7, 438-473.

PDI (2009) *Sani-Cloth CHG 2%.* www.pdi-europe.co.uk/en/range.asp?brandID=2&productID=13 (Last accessed: October 14 2009.)

Pratt RJ, Pellowe CM, Wilson JA *et al* (2007) epic2: National evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *Journal of Hospital Infection.* 65, Suppl 1, S1-S64.

Quinn MW, Bini RM (1989) Bradycardia associated with chlorhexidine spray. *Archives of Disease in Childhood.* 64, 6, 892-893.

Scales K (2008) Vascular access in the acute care setting. In Dougherty L, Lamb J (Eds) *Intravenous Therapy in Nursing Practice.* Second edition. Blackwell Publishing, Oxford, 271-320.

Shalomanov DS (2005) Chlorhexidine gluconate-induced morphological changes in Gram negative microorganisms. *Biotechnology and Biotechnological Equipment.* 19, 1, 121-124.

Stephens R, Mythen M, Kallis P, Davies DW, Egner WL, Rickards A (2001) Two episodes of life-threatening anaphylaxis in the same patient to a chlorhexidine-sulphadiazine-coated central venous catheter. *British Journal of Anaesthesia.* 87, 2, 306-308.

Intraoperative Patient Skin Prep Agents: Is There a Difference?

JENNIFER ZINN, RN, MSN, CNS-BC, CNOR; **JEANNE B. JENKINS,** RN, MSN, MBA; **VANGELA SWOFFORD,** RN, BSN; **BEVERLY HARRELSON,** RN, MSN, CPAN; **SHARON McCARTER,** RN, BSN, CNOR

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ABSTRACT

For health care institutions, intraoperative prep agents are a critical link in combating surgical site infections and the associated economic burden. The question remains, is there an intraoperative prep agent that is truly superior to the others? We conducted a literature review to examine available empirical evidence related to intraoperative prep agents used in our health system for open abdominal, general surgery procedures: povidone-iodine, chlorhexidine gluconate, parachoroxylenol, and iodine povacrylex in 74% isopropyl alcohol. Intraoperative surgical skin prep studies were limited in providing empirical evidence to support one superior prep agent. Each prep agent has a specific mechanism of action along with specific advantages and disadvantages. We concluded that no one perioperative skin prep agent is superior in all clinical situations. Factors to consider when choosing an appropriate intraoperative skin prep agent include contraindications, environmental risks, the patient's allergies and skin condition, the surgical site, the manufacturer recommendations for the prep agent, and surgeon preference. *AORN J* 92 (December 2010) 662-671. © AORN, Inc, 2010. doi: 10.1016/j.aorn.2010.07.016

Key words: *surgical site infection, infection prevention, intraoperative prep agents, antiseptic skin prep, chlorhexidine gluconate, povidone-iodine, parachoroxylenol, isopropyl alcohol.*

Surgical-site infections (SSIs) are the most common of all health care-associated infections in the surgical population, accounting for more than 6 million (38%) of all health care adverse events and 14% to 16% of all health care-associated infections.[1-3] According to the American College of Surgeons, SSIs annually result in 3.7 million additional hospital days with $845 million spent nationally,[4] which equates to 7.0 to 8.2 extra hospital days per case and a potential cost of more than $25,000 per event.[4-6]

Postoperative wound infections have fiscal ramifications for both the patient and the health

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care facility. An SSI can more than double the patient's health care-related expenses as well as adversely affect the patient's quality of life, functional status, and satisfaction.[7] An SSI can increase the hospital costs for major surgery fivefold; hospitals spend millions of dollars each year related to treatment costs and increased length of stay.[7]

As of October 2008, the revised Medicare reimbursement policy for health care facilities no longer includes the costs associated with treatment of specific SSIs.[1,8,9] This change in policy has challenged health care administrators and providers to thoroughly examine current internal SSI prevention measures.[1,8]

It is critical that health care providers acknowledge the effects of SSIs on patient outcomes and the associated economic burden. Intraoperative prep agents are a vital link in combating SSIs, but questions remain:

- Is there empirical research available that clearly identifies a superior prep agent?
- What is the best intraoperative prep agent to reduce the risk of SSI?

The purpose of this literature review was to examine the specific empirical evidence related to the intraoperative skin prep agents used for general surgical procedures. The information from this review expands the body of clinical nursing knowledge and evidence-based practice, particularly for perioperative nurses. Health care institutions may use these findings as a foundation for formulating recommendations focused on patient-centered care topics, such as quality of care, safe patient outcomes, length of stay, and reimbursement.

BACKGROUND

The patient's own floras are the most common source of an SSI.[3,5,8,10,11] Intact patient skin inherently provides resistance to infection by creating a protective barrier.[8] A surgical incision intentionally compromises intact patient skin, unavoidably allowing a portal of entry for endogenous and exogenous contaminate sources.[3,8,10] Resident bacteria on the skin are considered very difficult to remove, further highlighting the significance of effective skin asepsis.[12] An increase in wound infection risk occurs when the microbial counts on the surface of the skin are more than 10^5 microorganisms per gram of tissue.[3,8] Therefore, strict adherence to the basic principles of aseptic technique is a crucial responsibility of perioperative nurses that directly affects the potential for a postoperative SSI.[8] Intraoperative skin preparation is critical in reducing microbial counts and killing microorganisms.[5,8,11,13]

AORN publishes recommendations annually for standards of practice for perioperative nurses. According to AORN, the purpose of intraoperative skin preparation is to provide antisepsis of the surgical site.[10] Skin preparation limits the risk for SSI by

- removing bioburden (ie, soil and transient microorganisms) from the patient's skin,
- decreasing resident microorganism counts quickly while not irritating tissue, and
- preventing regrowth and rebound of microorganisms.[10]

Perioperative nurses play an integral role in decreasing the risk of SSI by using rigorous adherence to aseptic technique and by using impeccable skin preparation technique.[10]

METHODS

We searched the PubMed® and the Cumulative Index of Nursing and Allied Health Literature (CINAHL®) Plus databases and limited our results to articles published in English. Key words searched included *intraoperative, perioperative, skin, prep, prepping, preparation, skin preparation, surgical, Techni-Care®, DuraPrep™, chlorhexidine, povidone-iodine,* and *surgical wound infection/prevention and control.* To yield a greater number of articles related to intraoperative prep agents, we expanded the inclusive dates from five years to 15 years. In addition,

we reviewed the reference lists of the selected articles to identify primary literature of interest dating back to 1978. The articles yielded information on a variety of available intraoperative surgical prep agents, each agent having a different mechanism of action and specific advantages and disadvantages.

ANALYSIS

At the time of this literature review, the prep agents in our health system included povidone-iodine, chlorhexidine gluconate (CHG), parachoroxylenol (PCMX), and iodine povacrylex (0.7% available iodine) in 74% isopropyl alcohol (DuraPrep). Relevant articles from the literature searches were distributed among the research team members for review, analysis, and synthesis. Each team member used a literature review grid to facilitate consistency in data collection and article review. Two examples of use of the review grid are shown in Table 1. Research team members met biweekly to discuss the articles and to identify gaps in the literature related to SSIs and skin prep agents.

RESULTS

The literature review resulted in 89 "hits," and we chose and analyzed 29 of the articles based on relevance to the topic. The excluded articles involved animal studies and nonpertinent patient populations. All the studies reviewed clearly demonstrated a link between appropriate surgical skin preparation and the incidence of SSI.[8,10,13] Only a limited number of research reports focused on the four skin prep agents used at our facility; therefore, we also included surgical hand scrub studies in this literature review. Surgical hand scrubs have the same goal of removing microorganisms and inhibiting rebound and regrowth.[12,14] We found studies that compared two or three of the prep agents but not a direct comparison of all four intraoperative prep agents. The studies were all published between 1978 and 2010.

Povidone-iodine (Betadine®)

Povidone-iodine, commonly referred to as scrub and paint, was discovered in 1812 by a French chemist and is documented to have been first used on wounds in 1839.[15] Povidone-iodine was quickly recognized for its antimicrobial activity[15] and was introduced as an antiseptic agent in 1953.[16] Although it is one of the longest established and widely used antiseptic agents in the surgical domain,[16] povidone-iodine has the potential to cause local pain and skin irritation.[17]

Povidone-iodine has been studied both as a surgical hand scrub and as a surgical skin prep. The mechanism of action of povidone-iodine is the release of free iodine that binds to bacteria.[3,8,10,16] This agent has excellent activity against gram-positive bacteria and good activity against gram-negative bacteria.[3,8,10] Povidone-iodine's free iodine attracts and binds with organic substances, thus modifying or decreasing its antiseptic effectiveness in the presence of blood.[16] Povidone-iodine is classified as moderate in relation to the rapidity of action and provides minimal persistent and residual activity.[3,8,10]

Povidone-iodine has been shown to decrease the incidence of wound infection[18] and is considered a highly effective skin preparation for surgery.[19] Povidone-iodine is a broad-spectrum agent, which is a key component of an effective skin preparation.[3] Removing organic substances such as blood, pus, or fat from the surgical site yields optimal results with use of a povidone-iodine agent.[16]

The disadvantages of povidone-iodine as an intraoperative prep agent are difficult to determine because of the longevity of this agent, which has resulted in a lack of recent empirical studies. Povidone-iodine is a US Food and Drug Administration (FDA) approved, fast-acting, broad-spectrum agent that has beneficial and desirable characteristics as an intraoperative prep agent. Without conclusive evidence to demonstrate otherwise, povidone-iodine will remain a viable

TABLE 1. Literature Review Grid

Article	Participants	Design	Results	Strengths and weaknesses	Evidence and/or implications for a practice change?	Level of evidence*
Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis[27]	Adult surgical patients 18 years or older undergoing clean-contaminated surgery	■ Randomly assigned skin prep of chlorhexidine-alcohol or povidone-iodine ■ Setting: 6 hospital sites ■ Followed patients for 30 days after surgery for development of surgical site infection (SSI)	■ N = 849 with ■ 409 in the chlorhexidine-alcohol group ■ 440 in the povidone-iodine group ■ Significantly fewer SSIs in the chlorhexidine-alcohol group (9.5% v 16.1%; *P* = .004) ■ Chlorhexidine-alcohol group had fewer superficial incisional infections (4.2 v 8.6; *P* = .008), chlorhexidine-alcohol group had fewer deep incision infections (1% v 3%; *P* = .05) ■ Chlorhexidine-alcohol and povidone-iodine group had similar results related to organ/space infections (4.4% v 4.5%)	■ Strengths: ■ Randomized study ■ Adequate sample size ■ Statistically significant results ■ Weaknesses: ■ Limited to just comparing chlorhexidine-alcohol to povidone-iodine; a better comparison would be against iodine-base with alcohol solution ■ More than 50% of the researchers received monies or education grants from the manufacturer of the prep agent used in the study	This article suggests that chlorhexidine-alcohol is a superior product to povidone-iodine for wound class 2 procedures	A = Prospective, randomized clinical trial

(*table continued*)

TABLE 1. *(continued)* Literature Review Grid

Article	Participants	Design	Results	Strengths and weaknesses	Evidence and/or implications for a practice change?	Level of evidence*
Effects of preoperative skin preparation on postoperative wound infections rates: a prospective study of 3 skin preparation protocols[28]	■ Adult surgical patients 18 years or older undergoing general surgery ■ Elective or emergent cases, inpatients and outpatients	■ Placed in one of the 3 prep agent groups being studied based on the date of surgery: ■ 01/01/06 to 06/30/06: povidone-iodine ■ 07/01/06 to 12/31/06: 2% chlorhexidine and 70% isopropyl alcohol ■ 01/01/07 to 06/30/07: iodine povacrylex in isopropyl alcohol ■ Setting: single large academic medical center ■ Followed patients for 30 days after surgery for development of SSI	■ N = 3,209 with ■ 987 in the povidone-iodine group ■ 994 in the chlorhexidine and 70% isopropyl alcohol group ■ 1,228 in the povacrylex in isopropyl alcohol group ■ SSI lowest in the povacrylex in isopropyl alcohol group (3.9%) compared to povidone-iodine group (6.4%); the highest rates were observed in the 2% chlorhexidine and 70% isopropyl alcohol group (7.1%) (P = .002) ■ Greatest difference in SSI observed in the incidence of superficial SSIs ■ SSIs related to surgical wound classification similar results, with SSI lowest in the povacrylex in isopropyl alcohol group (5.9%) compared to povidone-iodine group (8.7%) and highest with 2% chlorhexidine and 70% isopropyl alcohol group (10.7%) (P = .021) ■ No difference observed related to the incidence of deep or organ/space SSIs	■ Strengths: ■ Compared commonly used prep agents for surgical patients ■ Scientific rationale for non-randomization (to analyze the effects of a widespread implementation of a protocol commonly seen in hospital practice; maximize consistency of prep application; shorten time frame to control for other variables) ■ Adequate sample size ■ Statistically significant results ■ Weaknesses: ■ Non-randomized study design ■ Sample size of the isopropyl alcohol group was larger based on the opening of additional ORs	This article suggests that both iodophor-based prep agents are superior products when compared to 2% chlorhexidine and 70% isopropyl alcohol and concludes, based on the results of this study, that surgeons and the institution prefer iodine povacrylex in isopropyl alcohol for intraoperative skin preparation	A = Single center, prospective, phase 4, unblinded protocol implementation comparison study

** A = strong randomized clinical trial (RCT); B = strong case control, cohort studies, weak RCT; C = case control, cohort; D = expert opinion, case study.*

intraoperative prep agent and remains a common agent used in intraoperative prep.

Chlorhexidine Gluconate

Chlorhexidine gluconate with and without alcohol has been studied extensively as a surgical hand scrub and surgical skin preparation. The mechanism of action for this broad-spectrum agent is disruption of the cell membranes by cytologic and physiologic changes that lead to cell death, specifically targeting vegetative gram-positive and gram-negative bacteria. This agent has excellent activity against gram-positive bacteria and good activity against gram-negative bacteria.[3,8,10,11] Chlorhexidine gluconate has been shown to remain effective in the presence of serum and protein-rich biomaterial, such as blood.[5,11] Chlorhexidine gluconate is classified as moderate in relation to the rapidity of action and has excellent persistent and residual activity.[3,8,10,11,20]

Extensive studies have demonstrated that CHG lowers bacteria counts compared with povidone-iodine and parachoroxylenol as a surgical hand scrub.[12,14,21,22] Because of CHG's persistent and residual activity, it is considered a highly effective surgical hand scrub,[11,14,21,22] consistently demonstrating log reductions below baseline criteria as defined by the FDA.[1,2,21] Hibiclens®, a brand of CHG, was the first surgical hand scrub approved as safe and effective by the Topical Antimicrobials Committee of the FDA and continues to be commonly used throughout health care settings. Results of numerous studies have supported CHG as effective in decreasing bacteria on the skin,[1,5,23] which correlates with decreased bloodstream and central line infections. These findings support the use of CHG as beneficial with repeated applications over an extended period of time.[1,21,23]

Research results also support bathing or showering twice before surgery with a 4% CHG agent as an effective measure to decrease the potential for postoperative infections.[1,8,10,11] Given the reported findings of the effectiveness of the 2% CHG cloth in decreasing bloodstream and central line infections, two interesting questions arise:

- Is a 2% CHG cloth as effective as the established 4% CHG bath/shower application to decrease the potential for SSIs?
- If yes, would one application of the 2% CHG cloth be adequate to achieve the same results as the twice bathing or showering with the 4% CHG agent?

These questions highlight an additional gap in evidence and warrant further exploration.

The disadvantages of CHG are specific contraindications for use. Chlorhexidine gluconate contact may cause corneal damage, ototoxicity, and neurotoxicity.[10,11,15] Furthermore, because of potential toxicities, CHG is not recommended for use on eyes, ears, brain and spinal tissues, mucus membranes, or genitalia, or for individuals with a known sensitivity.[10,11,15] Chlorhexidine gluconate has been reported to be inactivated by saline solution[24] and may have a drying effect on the skin.[15]

Parachoroxylenol

Parachoroxylenol, also known as PCMX, is considered to be a broad-spectrum agent with a mechanism of action that disrupts cell membranes by preventing the uptake of essential amino acids. This agent demonstrates good activity against vegetative gram-positive bacteria and fair activity against gram-negative bacteria.[3,8,10,15] Results of previous studies of parachoroxylenol have suggested it is 99.9% effective against methicillin-resistant *Staphylococcus aureus* and other common organisms.[15] Parachoroxylenol is classified as moderate with regard to the rapidity of action and persistent and residual activities.[3,8,10] Parachoroxylenol immediately bonds with the dermis and is not denatured by organic material, thus parachoroxylenol has a tolerance for organic material, such as blood, and remains active in saline solution.[15] Parachoroxylenol is considered nontoxic, with no tissue contraindications.[8,10,15] Although this review yielded limited evidence to support parachoroxylenol as a first choice

antimicrobial agent, it has been introduced as a safe intraoperative skin prep alternative for surgical sites that involve mucus membranes.

The disadvantages of parachoroxylenol are not well documented in the literature. Among the studies available that evaluated parachoroxylenol as a surgical hand scrub, the agent has demonstrated less effective results than other agents included in this review.[11,14,21,22] As an intraoperative skin prep agent, parachoroxylenol also demonstrates less effective results than other skin prep agents.[20] Currently, there is not an abundance of data regarding this prep agent and thus, additional investigation is needed.[3,8]

Iodine-base With Alcohol (DuraPrep)

Alcohol alone is considered to have excellent gram-positive and gram-negative activity with a mechanism of action to denature proteins.[3,8,10] Alcohol is considered immediately germicidal, classified excellent with regard to rapidity of action but does not demonstrate persistent residual activity.[3,8,10] However, the combination of alcohol and iodine (DuraPrep) has demonstrated greater effectiveness than each of these agents used independently in combating SSIs.[20] This increased effectiveness may be a result of the immediate germicidal action of alcohol and the residual activity of iodine.

The majority of DuraPrep research focuses on orthopedic procedures. The purpose of this literature review was to explore prep agents specifically used in open abdominal, general surgery procedures, therefore we did not include research articles that focused on DuraPrep in orthopedic procedures. We found limited research that addressed the use of DuraPrep in open abdominal, general surgery procedures, thus demonstrating a gap in the knowledge and evidence specific to this prep agent and population.

A disadvantage of DuraPrep is the product's potential for causing surgical fires because it has an alcohol base. The alcohol content in this skin prep agent is an undesirable catalyst in the OR because of its flammability.[1,3] Along with specific SSIs, surgical fires are considered "never events" (ie, preventable events that may cause serious injury or death) by the Centers for Medicare and Medicaid Services and are considered 100% preventable.[9,25] An overview of the advantages and disadvantages of the prep agents included in this literature review is provided in Table 2.

DISCUSSION

Several factors must be considered when choosing an appropriate intraoperative skin preparation, including a nursing assessment of contraindications. Advantages and disadvantages of the prep agents must be weighed carefully to facilitate positive patient outcomes, specifically, to decrease the incidence of SSIs. Given the current status of the economy, hospitals must consider the cost:benefit ratio for each prep agent and ask the question, "Are health care systems paying for a product whose performance is evidence based?"

Environmental risks are another factor to consider when choosing an appropriate intraoperative skin preparation. Although rare, surgical fires are a significant risk in any OR. Ignition sources (eg, electrosurgery, lasers) are used commonly in surgery; therefore, the potential of a surgical fire is increased any time alcohol-based or flammable skin prep agents are used.[25,26] According to a 2009 ECRI Institute guidance report, 70% of surgical fires are caused by an electrosurgery unit and 10% are related to laser use, both of which are common ignition sources in any OR setting.[26] Furthermore, surgical fires rank third on the ECRI Institute's technology hazard alerts.[26]

Health care providers are responsible for choosing an appropriate intraoperative prep agent for each patient. An ideal prep agent should

- decrease the microorganism count,
- be effective against a broad spectrum of microorganisms,
- be fast acting, and
- have a persistent effect against rebound and regrowth.[8,10]

TABLE 2. Comparison of Prep Solutions

	Advantages	Disadvantages
Povidone-iodine (Betadine®)	■ Excellent gram-positive activity ■ Good gram-negative activity ■ Broad spectrum ■ Moderate rapidity of action ■ Long established as an effective agent	■ Minimal persistent and residual activity ■ Decreased effectiveness in the presence of blood and organic material ■ Lack of recent empirical evidence
Chlorhexidine gluconate (Hibiclens®)	■ Excellent gram-positive activity ■ Good gram-negative activity ■ Broad spectrum ■ Moderate rapidity of action ■ Excellent persistent and residual activity	■ Contraindicated for use on eyes, ears, brain and spinal tissue, genitalia, mucus membranes ■ Inactivated in the presence of saline solution ■ Drying effect on the skin
Parachoroxylenol (PCMX)	■ Good gram-positive activity ■ Good/fair gram-negative activity ■ Broad spectrum ■ Moderate rapidity of action ■ Moderate persistent/residual activity ■ Considered nontoxic with no tissue contraindications ■ Remains effective in the presence of blood and organic material and in the presence of saline solution	■ Has demonstrated less effective results in studies for hand scrubs ■ Not well documented in the literature as an intraoperative prep solution
Iodine-base with alcohol (DuraPrep™)	■ Excellent gram-positive activity ■ Excellent gram-negative activity ■ Broad spectrum ■ Moderate rapidity of action ■ Long established as an effective agent ■ Alcohol provides immediately germicidal activity	■ Highly flammable ■ Limited research related to application in general surgery

Before making a final decision on a surgical skin prep agent, health care providers should consider the patient's allergies and skin condition, the surgical site, the manufacturer recommendations for the prep agent, and surgeon preference.[8,10] Based on this literature review for intraoperative skin preparations specific to general surgical procedures, and considering all the advantages and disadvantages, we concluded that there is not one superior skin prep agent for use in abdominal procedures.

LIMITATIONS

Intraoperative surgical skin prep studies were limited in providing empirical evidence to support one superior prep agent. Each prep agent has a specific mechanism of action along with specific advantages and disadvantages to consider when selecting a prep agent to use for surgery. Many factors must be considered when choosing a prep agent, such as patient allergy, surgical site, and surgeon preference. All prep agents are FDA approved and meet requirements for efficacy. No prep agent is categorized as superior. The Centers for Disease Control and Prevention has not made formal recommendations for the use of intraoperative prep agents, citing a lack of well-controlled studies related to skin preparation and SSIs on specific surgical procedures. Rather, the Centers for Disease Control and Prevention focuses on the intent of the aseptic skin preparation, the

environment in the OR, staff attire, drapes, and the technique used to prep the patient.[1,3] In other words, there is no published gold standard related to a superior prep agent to decrease the incidence of SSIs. In addition, a variety of products must be available to meet the needs of the diverse patient populations encountered in the perioperative setting.[10]

The team did not evaluate the literature exclusively pertaining to 2% CHG with 70% isopropyl alcohol (ChloraPrep®) because this product was not available in our hospital system at the time of our literature review. A recent study[27] claimed superior results for patients who underwent intraoperative surgical preparation with ChloraPrep versus povidone-iodine. This study did not include all of the four prep agents used in our hospital system, which was one reason we did not use it in our literature review. In addition, more than half of the researchers in this study disclosed receiving monetary considerations from the manufacturer of ChloraPrep.[27] In another recent study,[28] ChloraPrep was not found to be a superior prep agent compared with povidone-iodine and iodine povacrylex in isopropyl alcohol (DuraPrep). The findings indicated that compared with ChloraPrep both iodophor-based compounds performed better and resulted in lower SSI rates.[28]

IMPLICATIONS FOR NURSING

Nurses are participating in multidisciplinary collaboration in many hospitals to provide knowledge and recommendations for evidenced-based clinical practice issues. The findings of this literature review provide the foundation for future retrospective and prospective studies to empirically evaluate surgical skin agents. Information gained from future research may be used to help formulate surgical prep solution recommendations for perioperative nurses, surgeons, infection prevention practitioners, other health care providers, policy makers, administrators, third-party payers, and the general population interested in SSIs. AORN

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References

1. DeBaun B. Evaluation of the antimicrobial properties of an alcohol-free 2% chlorhexidine gluconate solution. *AORN J.* 2008;87(5):925-933.
2. Bratzler DW, Hunt DR. The Surgical Infection Prevention and Surgical Care Improvement Projects: national initiatives to improve outcomes for patients having surgery. *Clin Infect Dis.* 2006;43(3):322-330.
3. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR; Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. Guideline for Prevention of Surgical Site Infection, 1999. *Infect Control Hosp Epidemol.* 1999; 20(4):250-278.
4. The Surgical Infection Prevention and Surgical Care Improvement Projects: national initiatives to improve surgical care [PowerPoint presentation]. March 18, 2006. http://www.hsag.com/App_Resources/.../B_Bratzler_SCIP_WebEx.ppt. Accessed September 12, 2010.
5. Hibbard JS, Mulberry GK, Brady AR. A clinical study comparing the skin antisepsis and safety of ChloraPrep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. *J Infus Nurs.* 2002;25(4):244-249.

6. Jarvis WR. Selected aspects of the socioeconomic impact of nosocomial infections: morbidity, mortality, cost, and prevention. *Infect Control Hosp Epidemol.* 1996;17(8):552-557.
7. Lee JT. Not just another guideline. *Infect Control Hosp Epidemol*. 1999;20(4):231-232.
8. Wanzer L, Vane E. Prepping and draping. In: Rothrock JC, Seifert PC, eds. *Assisting In Surgery: Patient-Centered Care*. Denver, CO: Competency and Credentialing Institute; 2009:38-73.
9. Eliminating serious, preventable, and costly medical errors—never events [news release]. Baltimore, MD: Centers for Medicare and Medicaid Services; May 18, 2006. http://www.cms.hhs.gov/apps/media/press/release.asp?Counter=1863. Accessed September 16, 2006.
10. Recommended practices for preoperative patient skin antisepsis. In: *Perioperative Standards and Recommended Practices*. Denver, CO: AORN, Inc; 2010:351-370.
11. Denton GW. Chlorhexidine. In: Block SS, ed. *Disinfection, Sterilization and Preservation*. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2000:321-336.
12. Aly R, Maibach HI. Comparative evaluation of chlorhexidine gluconate (Hibiclens®) and povidone-iodine (E-Z Scrub®) sponge/brushes for presurgical hand scrubbing. *Curr Ther Res Clin Exp.* 1983;34(4II):740-745.
13. Fry DE. Surgical site infection: pathogenesis and prevention. February 13, 2003. MedscapeCME. http://cme_medscape.com/viewarticle/448981. Accessed August 9, 2010.
14. Paulson DS. Comparative evaluation of five surgical hand scrub preparations. *AORN J.* 1994;60(2):246-256.
15. Techni-Care® surgical scrub [package insert]. St Louis, MO: Care-Tech Laboratories; 2009.
16. Zamora JL, Price MF, Chuang P, Gentry LO. Inhibition of povidone-iodine's bactericidal activity by common organic substances: an experimental study. *Surgery.* 1985;98(1):25-29.
17. Gulliver G. Wound care. Arguments over iodine. *Nurs Times*. 1999;95(27):68-70.
18. Sherlock DJ, Ward A, Holl-Allen RTJ. Combined preoperative antibiotic therapy and intraoperative topical povidone-iodine: reduction of wound sepsis following emergency appendectomy. *Arch Surg.* 1984;119(8):909-911.
19. Shindo K. Antiseptic effect of povidone-iodine solution on abdominal skin during surgery and on thyroid-gland-related substances. *Dermatology.* 1997;195(Suppl 2):78-84.
20. Ostrander RV, Botte MJ, Brage ME. Efficacy of surgical preparation solutions in foot and ankle surgery. *J Bone Joint Surg Am.* 2005;87(5):980-985.
21. Aly R, Malbach HI. Comparative antibacterial efficacy of a 2-minute surgical scrub with chlorhexidine gluconate, povidone-iodine, and chloroxylenol sponge-brushes. *Am J Infect Control.* 1988;16(4):173-177.
22. Peterson AF, Rosenberg A, Alatary SD. Comparative evaluation of surgical scrub preparations. *Surg Gynecol Obstet.* 1978;146(1):63-65.
23. Maki DG, Ringer M, Alverado CJ. Prospective randomised trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet.* 1991;338(8763):339-343.
24. Manz EA. Antimicrobials: the right active ingredient for the right application [electronic media presentation]. St Paul, MN: 3M Product Information Center; 2006. http://solutions.3m.com/wps/portal/3M/en_US/essentials-edu/home/edu/in-service-articles/0106. August 9, 2010.
25. Watson DS. Surgical fires: 100% preventable, still a problem. *AORN J.* 2009;90(4):589-593.
26. ECRI. New clinical guide to surgical fire prevention. *Health Devices.* 2009;38(10):314-332.
27. Darouiche R, Wall MJ Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone iodine for surgical-site antisepsis. *N Engl J Med.* 2010;362(1):18-26.
28. Swenson BR, Hendrick TL, Metzger R, Bonatti H, Pruett TL, Sawyer RG. Effects of preoperative skin preparation on postoperative wound infection rates: a prospective study of 3 skin preparation protocols. *Infect Control Hosp Epidemiol.* 2009; 30(10):964-971.

Jennifer Zinn, RN, MSN, CNS-BC, CNOR, is a clinical nurse specialist for Perioperative Services at Moses Cone Health System, Greensboro, NC. *Ms Zinn has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.*

Jeanne B. Jenkins, RN, MSN, MBA, is a doctoral candidate in the School of Nursing, University of North Carolina at Greensboro, NC. *Ms Jenkins has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.*

Vangela Swofford, RN, BSN, is a surgical clinical nurse reviewer at Moses Cone Health System, Greensboro, NC. *Ms Swofford has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.*

Beverly Harrelson, RN, MSN, CPAN, is a clinical nurse specialist for Perioperative Services at Moses Cone Health System, Greensboro, NC. *Ms Harrelson has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.*

Sharon McCarter, RN, BSN, CNOR, is an assistant director at Moses Cone Main Operating Room, Greensboro, NC. *Ms McCarter has no declared affiliation that could be perceived as posing a potential conflict of interest in the publication of this article.*

EXAMINATION

CONTINUING EDUCATION PROGRAM

2.2 CE

www.aorn.org/CE

Intraoperative Skin Prep Agents: Is There a Difference?

PURPOSE/GOAL

To educate perioperative nurses about the properties of different surgical skin prep solutions used to help prevent surgical site infections.

OBJECTIVES

1. Discuss the purpose of intraoperative skin preparation.
2. Explain how four common surgical skin prep agents work.
3. Identify the advantages associated with four common surgical skin prep agents.
4. Identify the disadvantages associated with four common surgical skin prep agents.
5. Discuss health care provider considerations for choosing a particular surgical skin prep agent.

The Examination and Learner Evaluation are printed here for your convenience. To receive continuing education credit, you must complete the Examination and Learner Evaluation online at *http://www.aorn.org/CE*.

QUESTIONS

1. The patient's floras are is the most common source of a surgical site infection.
a. true *b.* false

2. The purpose of intraoperative skin preparation is to
1. provide antisepsis of the surgical site.
2. remove bioburden from the patient's skin.
3. decrease resident microorganisms counts quickly.
4. prevent regrowth and rebound of microorganisms.
a. 1 and 3 *b.* 2 and 4
c. 1, 2, and 4 *d.* 1, 2, 3, and 4

3. The mechanism of action of povidone-iodine is the
a. disruption of cell membranes by cytologic and physiological changes.
b. release of free iodine that binds to bacteria.
c. denaturation of proteins.
d. disruption of cell membranes by preventing the uptake of amino acids.

4. Povidone-iodine
1. attracts and binds to organic substances.
2. has excellent activity against gram-positive bacteria.
3. is a broad-spectrum agent.
4. is inactivated by saline solution.
a. 1 and 4 *b.* 2 and 4
c. 1, 2, and 3 *d.* 1, 2, 3, and 4

5. Chlorhexidine gluconate has been shown to remain effective in the presence of serum and protein-rich biomaterial, such as blood.
a. true *b.* false

6. Disadvantages of chlorhexidine gluconate include that it
1. is not effective against gram-positive bacteria.
2. is not recommended for use on brain and spinal tissues.
3. may cause corneal damage.
4. may be inactivated by saline solution.
a. 1 and 2 *b.* 1 and 4
c. 2, 3, and 4 *d.* 1, 2, 3, and 4

7. Some studies have suggested that _____ is 99.9% effective against methicillin-resistant *Staphylococcus aureus* and other common organisms.
a. chlorhexidine gluconate
b. iodine-base with alcohol
c. parachoroxylenol
d. povidone-iodine

8. The combination of alcohol and iodine has demonstrated greater effectiveness in combating surgical site infections than each of the agents used independently, which may be a result of the
1. immediate germicidal action of alcohol.
2. residual activity of iodine.
3. immediate bond of iodine with the dermis.
4. residual activity of alcohol.
a. 1 and 2 *b.* 3 and 4
c. 1, 2, and 3 *d.* 1, 2, 3, and 4

9. Before making a final decision about which skin prep agent to use, health care providers should consider
1. the patient's allergies and skin condition.
2. the surgical site.
3. manufacturer recommendations of the prep product.
4. surgeon preference.
a. 1 and 2 *b.* 3 and 4
c. 1, 2, and 3 *d.* 1, 2, 3, and 4

10. The Centers for Disease Control and Prevention has not made formal recommendations for the use of intraoperative prep agents.
a. true *b.* false

The behavioral objectives and examination for this program were prepared by Rebecca Holm, MSN, RN, CNOR, clinical editor, with consultation from Susan Bakewell, MS, RN-BC, director, Center for Perioperative Education. Ms Holm and Ms Bakewell have no declared affiliations that could be perceived as potential conflicts of interest in publishing this article.

LEARNER EVALUATION

CONTINUING EDUCATION PROGRAM

Intraoperative Patient Skin Prep Agents: Is There a Difference?

2.2 CE

www.aorn.org/CE

This evaluation is used to determine the extent to which this continuing education program met your learning needs. Rate the items as described below.

OBJECTIVES

To what extent were the following objectives of this continuing education program achieved?

1. Discuss the purpose of intraoperative skin preparation. *Low 1. 2. 3. 4. 5. High*
2. Explain how four common surgical skin prep agents work. *Low 1. 2. 3. 4. 5. High*
3. Identify the advantages associated with four common surgical skin prep agents. *Low 1. 2. 3. 4. 5. High*
4. Identify the disadvantages associated with four common surgical skin prep agents. *Low 1. 2. 3. 4. 5. High*
5. Discuss health care provider considerations for choosing a particular surgical skin prep agent. *Low 1. 2. 3. 4. 5. High*

CONTENT

6. To what extent did this article increase your knowledge of the subject matter? *Low 1. 2. 3. 4. 5. High*
7. To what extent were your individual objectives met? *Low 1. 2. 3. 4. 5. High*
8. Will you be able to use the information from this article in your work setting? *1. Yes 2. No*
9. Will you change your practice as a result of reading this article? (If yes, answer question #9A. If no, answer question #9B.)

9A. How will you change your practice? *(Select all that apply)*

1. I will provide education to my team regarding why change is needed.
2. I will work with management to change/implement a policy and procedure.
3. I will plan an informational meeting with physicians to seek their input and acceptance of the need for change.
4. I will implement change and evaluate the effect of the change at regular intervals until the change is incorporated as best practice.
5. Other: _____

9B. If you will not change your practice as a result of reading this article, why? *(Select all that apply)*

1. The content of the article is not relevant to my practice.
2. I do not have enough time to teach others about the purpose of the needed change.
3. I do not have management support to make a change.
4. Other: _____

10. Our accrediting body requires that we verify the time you needed to complete the 2.2 continuing education contact hour (132-minute) program: ___

This program meets criteria for CNOR and CRNFA recertification, as well as other continuing education requirements.

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AORN recognizes these activities as continuing education for registered nurses. This recognition does not imply that AORN or the American Nurses Credentialing Center approves or endorses products mentioned in the activity.

AORN is provider-approved by the California Board of Registered Nursing, Provider Number CEP 13019. Check with your state board of nursing for acceptance of this activity for relicensure.

Event: #10505; **Session:** #4052 **Fee:** Members $11, Nonmembers $22

The deadline for this program is December 31, 2013.

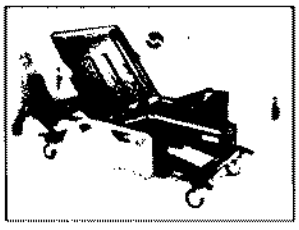
A score of 70% correct on the examination is required for credit. Participants receive feedback on incorrect answers. Each applicant who successfully completes this program can immediately print a certificate of completion.

New Products
Anonymous
Critical Care Nurse; Aug 2006; 26, 4; ProQuest Career and Technical Education
pg. 56

NewProducts

Lightweight bed ideal for acute care environments

HUNTLEIGH HEALTHCARE has introduced the Enterprise hospital bed, an electric bed with unique features designed to improve efficiency and reduce risks in the acute care environment. The Enterprise bed promotes fall prevention because of its low height of 12 inches, it is easy to maneuver, and it is easy to clean and decontaminate. In addition, the patented Bio-Contour profiling system has been proven to give better pressure reduction than other profiling beds, helping to reduce the risk of pressure ulcer development.

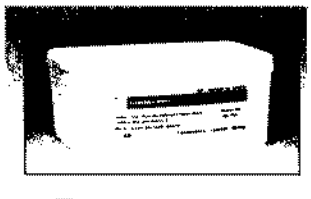


For more information, call (888) 223-1218.

Effective transdermal estradiol gel decreases hot flashes in menopausal women

BIOSANTE PHARMACEUTICALS has introduced a gel formulation of estradiol (bioidentical human estrogen) called Bio-E-Gel. This gel is quickly absorbed through the skin after topical application on the arms, shoulders, abdomen, or thighs, delivering estradiol to the bloodstream evenly over time at minimal dosage and in a noninvasive, painless manner. Results from a clinical study show that Bio-E-Gel can decrease the number of hot flashes by 88% in menopausal women.

For more information, call (847) 478-0500 or visit www.biosantepharma.com.



Easy-to-use flushable wipes

THE HYGEA WIPES BY PROFESSIONAL DISPOSABLES INTERNATIONAL are the first and only flushable bathroom wipes available for the hospital and long-term care markets. These wipes are soft enough for the most sensitive skin, providing fresher cleansing than dry bathroom tissue alone. The Hygea wipes are alcohol and latex free, they are convenient, and they allow the patient the ability to maintain personal hygiene with dignity.

The Hygea Flushable Wipes are available in 48-count wipe tubs, and are safe for sewer and septic systems.

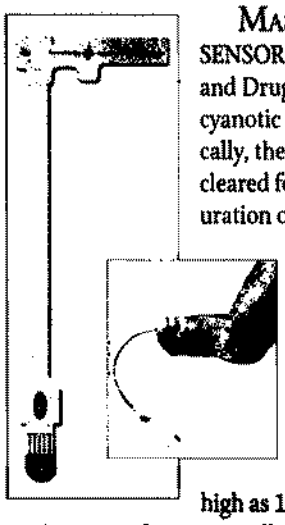
For more information, visit www.pdipdi.com.

Superior antibacterial activity in surgical skin preparation

MEDI-FLEX HAS ANNOUNCED the introduction of ChloraPrep, a preoperative skin preparation that has been approved by the Food and Drug Administration and contains the Centers for Disease Control and Prevention preferred amount of chlorhexidine gluconate. ChloraPrep's unique formulation of 2% chlorhexidine and 70% isopropyl alchol is the first of its kind in the surgical suite. Clinical evidence demonstrates that this combination possesses superior, immediate, residual, and cumulative antibacterial activity than current standard antiseptics such as alcohol.

For more information, call (800) 523-0502 or visit www.medi-flex.com.

First pulse oximeter sensor to accurately monitor cyanotic infants



MASIMO'S SET LNOP BLUE SENSOR has been cleared by the Food and Drug Administration for care of cyanotic infants and children. Specifically, the LNOP Blue Sensor has been cleared for measuring the oxygen saturation of arterial blood in pediatric patients with cardiac lesions, with accuracy of 3% from 100% to 80% and accuracy of 4% from 80% to 60%. Before the introduction of Masimo's SET LNOP Blue Sensor, the inaccuracy of pulse oximeters were as high as 15% in cyanotic patients.

For more information, call (949) 297-7000 or visit www.masimo.com.

System reduces time receiving ventilation and infection potential

SMARTCARE, A KNOWLEDGE-BASED ventilation system, has been cleared by the Food and Drug Administration for use in the United States. This weaning system, manufactured by Draeger Medical, is developed to improve the efficiency and effectiveness of the weaning process by automating the weaning process on the basis of the user's input. As the level of ventilator support is adjusted automatically, the patient's response and ability to adapt to each change in support is evaluated.

Unlike traditional, intermittent methods of weaning, SmartCare continuously monitors the patient, interprets the data, and adjusts the level of ventilator in 2- or 5-minute intervals.

For more information, visit www.draegermedical.com.

Superior foot protection at an affordable price

AVAILABLE IN 2 SIZES, the Podus Boot, produced by Posey, is made with moisture-wicking material to help keep patients' feet dry. The inner shell of the boot completely isolate the heel to hetter prevent and treat heel ulcers, and the boot accommodates up to a 45-degree plantar flexion contracture. Standard features include a padded, detachable toe post that keeps bed linens off of toes and is secured by 2 anhors that help prevent unwanted rotation, and a sturdy, adjustable antirotation bar that helps prevent any internal or external hip rotation and larger foot securement flaps.

For more information, call (800) 44-POSEY or visit www.posey.com.

Improving Quality of Surgical Care and Outcomes: Factors Impacting Surgical Site Infection after Colorectal Resection

VIRGINIA OLIVA SHAFFER, M.D., CAITLIN D. BAPTISTE, B.S., YUAN LIU, PH.D., JAHNAVI K. SRINIVASAN, M.D., JOHN R. GALLOWAY, M.D., PATRICK S. SULLIVAN, M.D., CHARLES A. STALEY, M.D., JOHN F. SWEENEY, M.D., JOE SHARMA, M.D., THERESA W. GILLESPIE, PH.D., M.A

From Emory University School of Medicine, Atlanta, Georgia

Surgical site infections (SSIs) result in patient morbidity and increased costs. The purpose of this study was to determine reasons underlying SSI to enable interventions addressing identified factors. Combining data from the American College of Surgeons National Surgical Quality Improvement Project with medical record extraction, we evaluated 365 patients who underwent colon resection from January 2009 to December 2012 at a single institution. Of the 365 patients, 84 (23%) developed SSI. On univariate analysis, significant risk factors included disseminated cancer, ileostomy, patient temperature less than 36°C for greater than 60 minutes, and higher glucose level. The median number of cases per surgeon was 36, and a case volume below the median was associated with a higher risk of SSI. On multivariate analysis, significant risks associated with SSI included disseminated cancer (odds ratio [OR], 4.31; $P < .001$); surgery performed by a surgeon with less than 36 cases (OR, 2.19; $P = .008$); higher glucose level (OR, 1.06; $P = .017$); and transfusion of five units or more of blood (OR, 3.26; $P = .029$). In this study we found both modifiable and unmodifiable factors associated with increased SSI. Identifying modifiable risk factors enables targeting specific areas to improve the quality of care and patient outcomes.

SURGICAL SITE INFECTIONS (SSIs) lead to tremendous morbidities in patients and increased costs for hospitals. Infection rates after colorectal surgery have been noted to be as high as 30 per cent.[1] Several initiatives have aimed to reduce the risk of SSIs.[2–4] Factors such as choice of perioperative antibiotics have been shown to be important in reducing SSIs.[5] Other factors such as normothermia have been shown to have an inverse relationship to SSIs.[6] In this single-institution evaluation of SSI, 22 per cent of readmissions were the result of SSIs. Based on data from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP), which compares infection rates at similar hospitals, this institution was a high outlier in SSIs after colectomy when compared with peer institutions. The exact reasons for this higher rate are unclear. The goal of this study was to investigate the factors associated with developing a SSI. If these factors are identified and modifiable, then they can be potentially altered to decrease SSI rates after colon resection and improve patient outcomes.

The primary hypotheses were that certain factors contributed to higher risk of developing a SSI: males; body mass index (BMI), above normal; diabetes; low albumin; higher Charlson comorbidity score[7]; low hematocrit; having received a transfusion; or the presence of a colostomy or ileostomy at the beginning or end of the operation. We also hypothesized that hypothermia (patients who had body temperatures less than 36°C during the operation, continued at less than 36°C for longer than 60 minutes, or whose temperature was less than 36°C at the end of the case) increased the risk of developing a wound infection, and patients whose abdomen was prepped with something other than Chloraprep were at increased risk of developing a wound infection; and if they did not receive appropriate antibiotics or appropriate redosing, they were also at increased risk of developing a SSI. An additional hypothesis was that smokers, people with higher than American Society of Anesthesiologists (ASA) Class 3, and people on steroids have an increased risk of a wound infection, and that diabetics and patients with glucose values over 200 mg/dL are also at increased risk of SSI.

Presented at the Annual Scientific Meeting and Postgraduate Course Program, Southeastern Surgical Congress, Savannah, GA, February 22–25, 2014.

Address correspondence and reprint requests to Virginia Oliva Shaffer, M.D., Emory University, 1365 Clifton Road NE, Clinic A, Suite 3300, Atlanta, GA 30322. E-mail: voliva@emory.edu.

Methods

Patient Cohort

A retrospective cohort study of 365 patients who underwent a partial or total colon resection without proctectomy was conducted at a single institution using the American College of Surgeons NSQIP data representing January 2009 to December 2012. These data included 13 unique *Current Procedural Terminology (CPT)* descriptions: eight open and five laparoscopic procedure types. The primary outcome was developing a SSI by NSQIP criteria. NSQIP criteria are an infection that occurs within 30 days after the operation of the skin and subcutaneous tissue and at least one of the following: purulent drainage, organisms isolated from an aseptically obtained culture of fluid or tissue, and at least one the following: pain or tenderness, localized swelling, redness, or heat or an incision that was deliberately opened, unless the culture is negative, or diagnosed by the surgeon as having a SSI.

Procedural Details

The variables obtained from the NSQIP database included: SSI status (yes/no), age, gender, race, ASA class, smoking status, diabetes, presence of disseminated cancer, transfusion of at least 5 units of packed red blood cells within 72 hours perioperatively, steroid use, BMI, *CPT*, hematocrit, albumin, creatinine, and surgeon volume. Additional information for each patient was obtained through medical chart extraction. These variables were: ileostomy or colostomy presence at the beginning and/or end of the case, appropriate redosing antibiotics intraoperatively, appropriate use of preoperative antibiotics that include gastrointestinal micro-organism coverage, type of surgical preparation used on the abdomen, intraoperative body temperatures less than 36°C, length of time the patient was less than 36°C, temperature at the end of the case, the lowest postanesthesia care unit temperature recorded, Charlson comorbidity score, and glucose measurements within 48 hours postoperatively. The purpose of this data collection and analysis was to determine risk factors for SSI at one institution and target areas for improvement and risk prevention or reduction.

Statistical Analysis

The summary statistics were calculated for continuous variables and frequency table was used for categorical variables. The univariate association with wound infection was carried out by χ^2 test for categorical covariates and analysis of variance for continuous covariates. The unadjusted association with wound infection was also tested by univariate logistic regression to obtain an odds ratio. Logistic regression model was used to build multivariable model by backward elimination with stay criteria of $P < 0.2$. Receiver operating characteristic analysis was used to identify the optimal cut point for some continuous predictors to wound infection. The analysis was conducted using SAS 9.3 (SAS Institute, Cary, NC) and R 1.1 (http://CRAN.R-project.org/package = optimalcutpoints). Tables and figures were made using Microsoft Excel (Redmond, WA) and GraphPad Prism 4 (GraphPad Software, Inc., La Jolla, CA). Significant level was set at 0.05.

Results

Of 365 patients in the study population, 84 (23%) developed a SSI. Tables 1 and 2 summarize patient characteristics and demographics for the patients in the study.

In the univariate logistic regression analysis, the following variables were statistically significant with $P < 0.05$ (Fig. 1): disseminated cancer, ileostomy presence at the beginning of the case, surgeon volume, patient body temperature below 36°C for greater than 60 minutes, length of time patient temperature below 36°C, and highest glucose within 48 hours. In this study, a patient with disseminated cancer had a 3.99 increased odds of developing a SSI and the presence of an ileostomy at the beginning of the case conferred a 5.86 increased odds of developing a SSI. If the surgery was performed by a surgeon with less than 36 colectomies, the odds of developing a SSI increased by 1.72. For every 10 minutes the patient's temperature was less than 36°C, the odds of developing a SSI increased 1.03, but if the hypothermia lasted less than 60 minutes, the odds decreased by 44 per cent. When the highest glucose was examined as a continuous variable, for every 10-mg/dL increase in glucose, the odds of developing a SSI increased by 1.06.

In the multivariate logistic regression model, the following variables were statistically significant with $P < 0.05$ (Fig. 2): disseminated cancer, surgeon volume, highest glucose within 48 hours, and whether the patient had a transfusion of at least five units of packed red cells. A patient with disseminated cancer had a 4.31 increased odds of developing a SSI. A surgeon with less than 36 cases increased the odds of the patient developing a SSI by 2.19. When the highest glucose within 48 hours was examined as a continuous variable, for every 10-mg/dL increase in glucose, the patient had an additional 6 per cent increase chance of developing a SSI.

TABLE 1. *Patient Characteristics*

Variable		n = 365	Percent
Wound infection	No	281	77
	Yes	84	23
Gender	Male	190	52.1
Race	Asian	6	1.6
	Black	89	24.4
	Unknown	9	2.5
	White	261	71.5
ASA class	1	2	0.5
	2	126	34.6
	3	200	54.9
	4	33	9.1
	5	3	0.8
Smoker	Yes	58	15.9
Diabetes	No	320	87.7
	Noninsulin-dependent	25	6.8
	Insulin-dependent	20	5.5
Disseminated cancer	Yes	36	9.9
Transfusion (5 units)	Yes	21	5.8
Steroid use	Yes	43	11.8
Ileostomy_end	Yes	41	11.2
Colostomy_end	Yes	35	9.6
Ileostomy_beginning	Yes	8	2.2
Colostomy_beginning	Yes	5	1.4
Antibiotic redosing	Yes	352	98.6
Appropriate antibiotic coverage	Yes	329	90.1
Surgical preparation (Chloraprep)	Yes	298	81.6
Surgeon volume (median 36)	≤36	184	50.4
Temperature < 36°C for ≤ 60 minutes	Yes	198	56.6
Laparoscopy	Yes	127	34.8
Highest glucose (48 hours)	≤200	290	80.1

ASA, American Society of Anesthesiologists.

Discussion

In this study we looked at several factors and patient characteristics obtained from the American College of Surgeons NSQIP combined with medical chart extraction to develop a predictive model for SSIs. Both modifiable and unmodifiable factors were found to be associated with SSI. When adjusted for the other covariates, independent risk factors associated with developing a SSI included disseminated cancer, a surgeon with less than the median number of cases (36 cases), transfusion requirement of five units or greater packed red cells, and higher glucose levels within 48 hours of surgery.

Studies have indicated that the type of preoperative antibiotics given is an important risk factor in SSI[8]; however, this was not the case in our study population. A possible explanation is that there were 29 different antibiotic combinations used and thus diluted the possible effects of antibiotic type. Updated recommendations published in 2011 advice intraoperative redosing based on renal function to control surgical site infections.[9] This variable was not statistically significant in this study, likely because 98.6 per cent of

TABLE 2. *Patient Characteristics*

	Mean	Median	Range
Age (years)	56.8	57	19–92
BMI (kg/m^2)	27.5	26	13.7–53.3
Hematocrit (%)	35.2	35.8	15.2–48.9
Glucose within 48 hours (mg/dL)	166	153	75–463
Albumin (g/dL)	3.43	3.5	1.3–4.8
Creatinine (mg/dL)	1.01	0.89	0.4–8.67
Charlson comorbidity score	4.72	5	1 to 11
Surgeon volume (no. of cases)	45.1	36	1 to 95
Lowest body temperature (°C)	35.6	35.6	33.9–37.8
Temperature at end of case (°C)	36.6	36.6	35.0–39.7
Lowest PACU temperature (°C)	36.4	36.4	35.5–37.7

BMI, body mass index; PACU, postanesthesia care unit.

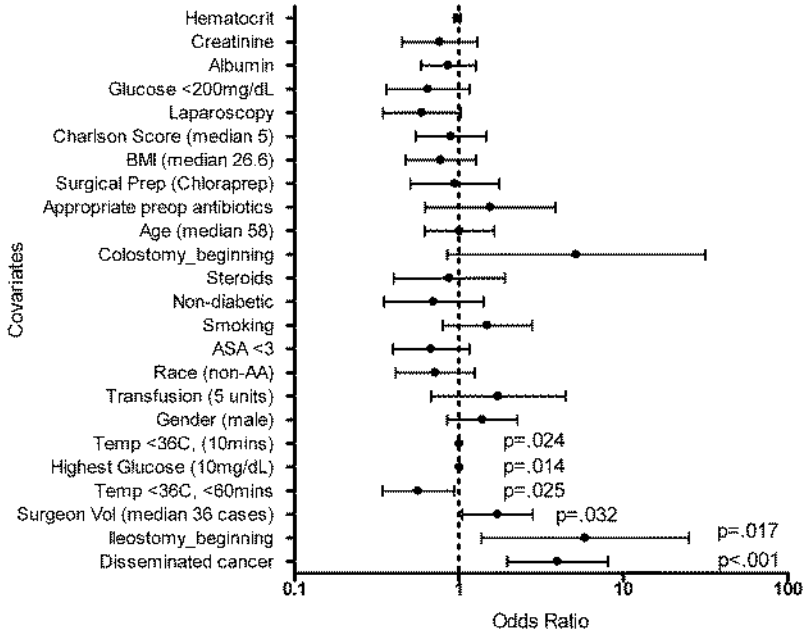


FIG. 1. Univariate regression analysis. Univariate regression analysis with odds ratio and 95 per cent confidence interval denoted by the lines. The scale is logarithmic. Only P values < 0.05 are shown. Dotted line shows X = 1.

patients were redosed with antibiotics in the operating room. In some studies, normothermia has been found to have an inverse relationship with SSI.[6] Our data suggest this is true in our patient population: for every 10 minutes longer a patient's body temperature was less than 36°C, he or she had an additional two per cent increase chance of developing an SSI. This was significant in our univariate regression analysis but did not hold statistical significance in our multivariate model. Confounding variables are likely contributing to this effect.

Hyperglycemia is associated with SSIs in diabetics.[10] This study found that, independent of diabetic status, for every 10-mg/dL increase, patients have an additional six per cent increase chance of developing an SSI. Perioperative blood transfusions are associated with SSIs.[11, 12] Our study results were consistent with this association from previous reports, and in our multivariate model, transfusion of five units or greater of packed red blood cell was associated with a 3.26 increased odds of developing an SSI. This may be the result of the immunosuppressive effects of blood transfusion or because it is a marker of disease severity. A recent study found inflammatory bowel disease to be associated with increased SSI;[13] we found disseminated cancer to be highly associated with developing an SSI (odds ratio, 4.3). Advanced tumor stage has been found to be an independent risk factor for infectious complications,[14] although we did not specifically look at tumor stage in our study.

There are conflicting data on the use of bowel preparation and the use of oral antibiotics with bowel preparation; however, recent studies have supported the use of oral antibiotics when using a bowel preparation. Unfortunately, our medical records were limited in this retrospective study and we were unable to accurately decipher which patients had been bowel prepped or the type of bowel preparation used. Future studies should encompass this variable.

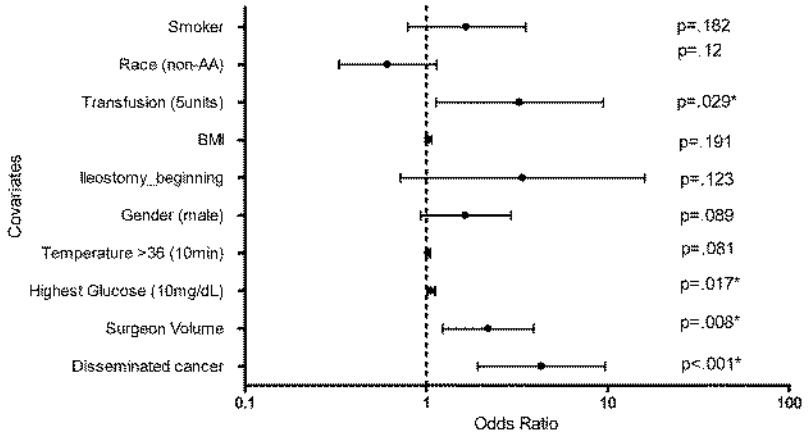


FIG. 2. Multivariate regression model. Multivariate regression analysis with odds ratio and 95 per cent confidence interval denoted by the lines. The scale is logarithmic. Dotted line shows X = 1. All P values are shown and asterisk shows P < 0.05.

Surgeon volume was found to be inversely related to SSI rate in our study. The exact reasons for this are unclear. Perhaps less experienced surgeons took longer to perform the surgery or do not have a "standard" way of doing the operation and thus introduce more variability. Future studies should further investigate the reasons for the importance of surgeon volume as it relates to SSI.

This study was limited by its retrospective, nonrandomized, and single-institution study design. In an attempt to overcome some of the limitations of a database study, a medical chart review was conducted as an adjunct to the NSQIP database information. This study was further limited by the information in the medical record. Temperature and glucose measurements were not done at standard intervals for all patients. This limited the type of analysis and conclusions we could make. Additionally, there were 23 surgeons and 29 different antibiotic combinations used during the 3-year study period. This decreased the ability to make reliable conclusions about the data. Because preoperative antibiotic choice has been shown to be an important factor in preventing SSI, standardizing antibiotic choices at our institution will be an important step. Future endeavors include implementing standardized protocols for clinical practice and standardized protocols for recordkeeping so better analysis can be done and ideally patients can be randomized to a control and experimental group.

The aim of this study was to determine the risk factors associated with SSI with the future goal of addressing these factors to decrease the institutional SSI rate after colon resection and improve patient outcomes. We found both modifiable and unmodifiable factors associated with SSI. Disseminated cancer was strongly associated with developing an SSI. Modifiable factors included surgeon volume, perioperative transfusion, and glucose control. These findings will guide our future steps in implementing standardized protocols for transfusion indications, temperature monitoring, and glucose monitoring and control. These protocols will need to be developed by a core group of experienced surgeons who perform the majority of colon resections in this patient population. Drawing from the evidence base that exists, along with expert opinion and group consensus, we will establish new guidelines to be followed to reduce SSI at this institution and compare findings with other NSQIP institutions.

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REFERENCES

1. Bull A, Wilson J, Worth LJ, et al. A bundle of care to reduce colorectal surgical infections: an Australian experience. J Hosp Infect 2011;78:297–301.

2. Berenguer CM, Ochsner MG, Jr., Lord SA, et al. Improving surgical site infections: using National Surgical Quality Improvement Program data to institute Surgical Care Improvement Project protocols in improving surgical outcomes. J Am Coll Surg 2010;210:737–743.

3. Smith RL, Bohl JK, McElearney ST, et al. Wound infection after elective colorectal resection. Ann Surg 2004;239:599–605; discussion 605–97.

4. Wick EC, Hobson DB, Bennett JL, et al. Implementation of a surgical comprehensive unit-based safety program to reduce surgical site infections. J Am Coll Surg 2012;215:193–200.

5. Hendren SK, Morris AM. Evaluating patients undergoing colorectal surgery to estimate and minimize morbidity and mortality. Surg Clin North Am 2013;93:1–20.

6. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996;334:1209–15.

7. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

8. Hendren S, Fritze D, Banerjee M, et al. Antibiotic choice is independently associated with risk of surgical site infection after colectomy: a population-based cohort study. Ann Surg 2013;257: 469–75.

9. Alexander JW, Solomkin JS, Edwards MJ. Updated recommendations for control of surgical site infections. Ann Surg 2011; 253:1082–93.

10. McConnell YJ, Johnson PM, Porter GA. Surgical site infections following colorectal surgery in patients with diabetes: association with postoperative hyperglycemia. J Gastrointest Surg 2009;13:508–15.

11. Tang R, Chen HH, Wang YL, et al. Risk factors for surgical site infection after elective resection of the colon and rectum: a single-center prospective study of 2,809 consecutive patients. Ann Surg 2001;234:181–9.

12. Halabi WJ, Jafari MD, Nguyen VQ, et al. Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program analysis. Am J Surg 2013; 206:1024–32; discussion 1032–3.

13. Drosdeck J, Harzman A, Suzo A, et al. Multivariate analysis of risk factors for surgical site infection after laparoscopic colorectal surgery. Surg Endosc 2013;27:4574–80.

14. Bot J, Piessen G, Robb WB, et al. Advanced tumor stage is an independent risk factor of postoperative infectious complications after colorectal surgery: arguments from a case-matched series. Dis Colon Rectum 2013;56:568–76.

ORIGINAL ARTICLE

Chlorhexidine–Alcohol versus Povidone–Iodine for Surgical-Site Antisepsis

Rabih O. Darouiche, M.D., Matthew J. Wall, Jr., M.D., Kamal M.F. Itani, M.D., Mary F. Otterson, M.D., Alexandra L. Webb, M.D., Matthew M. Carrick, M.D., Harold J. Miller, M.D., Samir S. Awad, M.D., Cynthia T. Crosby, B.S., Michael C. Mosier, Ph.D., Atef AlSharif, M.D., and David H. Berger, M.D.

ABSTRACT

BACKGROUND

Since the patient's skin is a major source of pathogens that cause surgical-site infection, optimization of preoperative skin antisepsis may decrease postoperative infections. We hypothesized that preoperative skin cleansing with chlorhexidine–alcohol is more protective against infection than is povidone–iodine.

METHODS

We randomly assigned adults undergoing clean-contaminated surgery in six hospitals to preoperative skin preparation with either chlorhexidine–alcohol scrub or povidone–iodine scrub and paint. The primary outcome was any surgical-site infection within 30 days after surgery. Secondary outcomes included individual types of surgical-site infections.

RESULTS

A total of 849 subjects (409 in the chlorhexidine–alcohol group and 440 in the povidone–iodine group) qualified for the intention-to-treat analysis. The overall rate of surgical-site infection was significantly lower in the chlorhexidine–alcohol group than in the povidone–iodine group (9.5% vs. 16.1%; P=0.004; relative risk, 0.59; 95% confidence interval, 0.41 to 0.85). Chlorhexidine–alcohol was significantly more protective than povidone–iodine against both superficial incisional infections (4.2% vs. 8.6%, P=0.008) and deep incisional infections (1% vs. 3%, P=0.05) but not against organ-space infections (4.4% vs. 4.5%). Similar results were observed in the per-protocol analysis of the 813 patients who remained in the study during the 30-day follow-up period. Adverse events were similar in the two study groups.

CONCLUSIONS

Preoperative cleansing of the patient's skin with chlorhexidine–alcohol is superior to cleansing with povidone–iodine for preventing surgical-site infection after clean-contaminated surgery. (ClinicalTrials.gov number, NCT00290290.)

From the Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine (R.O.D., S.S.A., A.A., D.H.B.), and Ben Taub General Hospital and Baylor College of Medicine (M.J.W., M.M.C., H.J.M.) — all in Houston; Veterans Affairs Boston Healthcare System and Boston University Medical School, Boston (K.M.F.I.); Veterans Affairs Medical Center and Medical College of Wisconsin, Milwaukee (M.F.O.); Veterans Affairs Medical Center, Atlanta (A.L.W.); and Cardinal Health, Leawood (C.T.C.), and Washburn University, Topeka (M.C.M.) — both in Kansas. Address reprint requests to Dr. Darouiche at the Center for Prostheses Infection, Baylor College of Medicine, 1333 Moursund Ave., Suite A221, Houston, TX 77030, or at rdarouiche@aol.com.

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Despite the implementation of preoperative preventive measures, which include skin cleansing with povidone–iodine, surgical-site infection occurs in 300,000 to 500,000 patients who undergo surgery in the United States each year.[1-6] Since the patient's skin is a major source of pathogens, it is conceivable that improving skin antisepsis would decrease surgical-site infections.[7] The Centers for Disease Control and Prevention (CDC) recommends that 2% chlorhexidine-based preparations be used to cleanse the site of insertion of vascular catheters.[8] However, the CDC has not issued a recommendation as to which antiseptics should be used preoperatively to prevent postoperative surgical-site infection in the 27 million operations performed annually in the United States.[9] Furthermore, no published randomized studies have examined the effect of one antiseptic preparation as compared with another on the incidence of surgical-site infection. The main objective of this study was to compare the efficacy of chlorhexidine–alcohol with that of povidone–iodine for preventing surgical-site infections.

METHODS

STUDY DESIGN

We conducted this prospective, randomized clinical trial between April 2004 and May 2008 at six university–affiliated hospitals in the United States. The institutional review board at each hospital approved the study protocol, and written informed consent was obtained from all patients before enrollment. This investigator-initiated trial was conceived by the first author, who also acted as the study sponsor, recruited the sites, gathered the data, wrote the first and final versions of the manuscript, and decided in consultation with the other authors to submit the paper for publication. All authors vouch for the completeness and accuracy of the data. One of the authors, who is a statistician, analyzed the data. The single author from Cardinal Health (manufacturer of the antiseptic agents studied) substantially contributed to the design and conception of the study and critically revised the manuscript but played no role in data collection or analysis. All other authors had full access to the data and substantially contributed to the analysis and interpretation of the data and the writing of the manuscript.

PATIENTS

Patients 18 years of age or older who were undergoing clean-contaminated surgery (i.e., colorectal, small intestinal, gastroesophageal, biliary, thoracic, gynecologic, or urologic operations performed under controlled conditions without substantial spillage or unusual contamination) were eligible for enrollment. Exclusion criteria were a history of allergy to chlorhexidine, alcohol, or iodophors; evidence of infection at or adjacent to the operative site; and the perceived inability to follow the patient's course for 30 days after surgery.

INTERVENTIONS

Enrolled patients were randomly assigned in a 1:1 ratio to have the skin at the surgical site either preoperatively scrubbed with an applicator that contained 2% chlorhexidine gluconate and 70% isopropyl alcohol (ChloraPrep, Cardinal Health) or preoperatively scrubbed and then painted with an aqueous solution of 10% povidone–iodine (Scrub Care Skin Prep Tray, Cardinal Health). More than one chlorhexidine–alcohol applicator was used if the coverage area exceeded 33 by 33 cm. To help match the two groups and address potential interhospital differences, randomization was stratified by hospital with the use of computer-generated randomization numbers without blocking.

EFFICACY OUTCOMES

The primary end point of the study was the occurrence of any surgical-site infection within 30 days after surgery. The operating surgeon became aware of which intervention had been assigned only after the patient was brought to the operating room. Both the patients and the site investigators who diagnosed surgical-site infection on the basis of criteria developed by the CDC[9] remained unaware of the group assignments. Secondary end points included the occurrence of individual types of surgical-site infections. These were classified as superficial incisional infection (which involved only skin and subcutaneous tissue and excluded stitch-related abscesses), deep incisional infection (which involved fascia and muscle), or organ-space infection (which involved any organ or space other than

the incised layer of body wall that was opened or manipulated during the operation).[9]

CLINICAL ASSESSMENT

Preoperative evaluation included a medical history taking, physical examination, and routine hematologic and blood chemical laboratory tests. The surgical site and the patient's vital signs were assessed at least once a day during hospitalization, on discharge, at the time of follow-up evaluation, and whenever surgical-site infection occurred. After discharge, the investigators called the patients once a week during the 30-day follow-up period and arranged for prompt clinical evaluation if infection was suspected. Whenever surgical-site infection was suspected or diagnosed, clinically relevant microbiologic samples were cultured. Investigators who were unaware of the patients' group assignments assessed the seriousness of all adverse events and determined whether they were related to the study.

STATISTICAL ANALYSIS

The average baseline rate of surgical-site infection at the six participating hospitals was 14% after clean-contaminated surgery with povidone–iodine skin preparation, and we estimated that substituting chlorhexidine–alcohol for povidone–iodine would reduce this rate to 7%. Therefore, we planned to enroll approximately 430 patients in each study group who could be evaluated in order for the study to have 90% power to detect a significant difference in the rates of surgical-site infection between the two groups, at a two-tailed significance level of 0.05 or less.

The criteria for including patients in the intention-to-treat analysis included randomization and the possibility of applying each of the study antiseptic preparations (which required performance of surgery). Inclusion in the per-protocol analysis required the application of the study preparation before clean-contaminated surgery and completion of the 30-day follow-up. An independent data and safety monitoring board composed of an infectious-disease physician, a surgeon, and a statistician met annually to review the conduct of the study. No formal criteria were set for stopping the study.

The significance of differences between the two study groups in terms of patient characteristics was determined with the use of the Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. For efficacy outcomes, we compared the proportions of patients in the two study groups who could be evaluated and who had any type of surgical-site infection, using Fisher's exact test and calculating the relative risk of infection and 95% confidence intervals. The consistency of the effects of the study intervention on infections across different types of surgery was examined with the use of an interaction test. To determine whether the results were consistent across the six participating hospitals, a prespecified Breslow–Day test for homogeneity was performed. To compare the proportions of patients in the two study groups who were free of surgical-site infection as a function of the length of time since surgery, we performed log-rank tests on Kaplan–Meier estimates based on analyses in which data for patients who did not have infections were censored 30 days after surgery. Both the frequency of isolating certain organisms and categories of organisms and the incidence of adverse and serious adverse events were compared between the study groups with the use of Fisher's exact test. All reported P values are based on two-tailed tests of significance and were not adjusted for multiple testing.

We conducted univariate and multivariate analyses to assess whether risk factors contributed to the occurrence of surgical-site infection. The univariate analysis for categorical factors was performed with the use of Fisher's exact test. For continuous factors, we used a single-variable logistic-regression model that involved generalized estimating equations (GEE) to account for hospital site as a random effect. A multivariate logistic-regression analysis that also adjusted for the hospital site as a random effect (by means of GEE) was performed to assess factors deemed significant ($P \leq 0.10$) by univariate analysis or considered clinically important. The assessed risk factors were prespecified in the protocol, and the statistical methods were preplanned except for the inclusion of hospital site as a random effect. Since some types of surgery did not result in infection in either study group, a dichotomous variable — "abdominal" surgery (including colorectal, biliary, small intestinal, and gastroesophageal operations) versus "nonabdominal" surgery (including thoracic, gynecologic, and urologic operations) — was created for the GEE logistic-regression model.

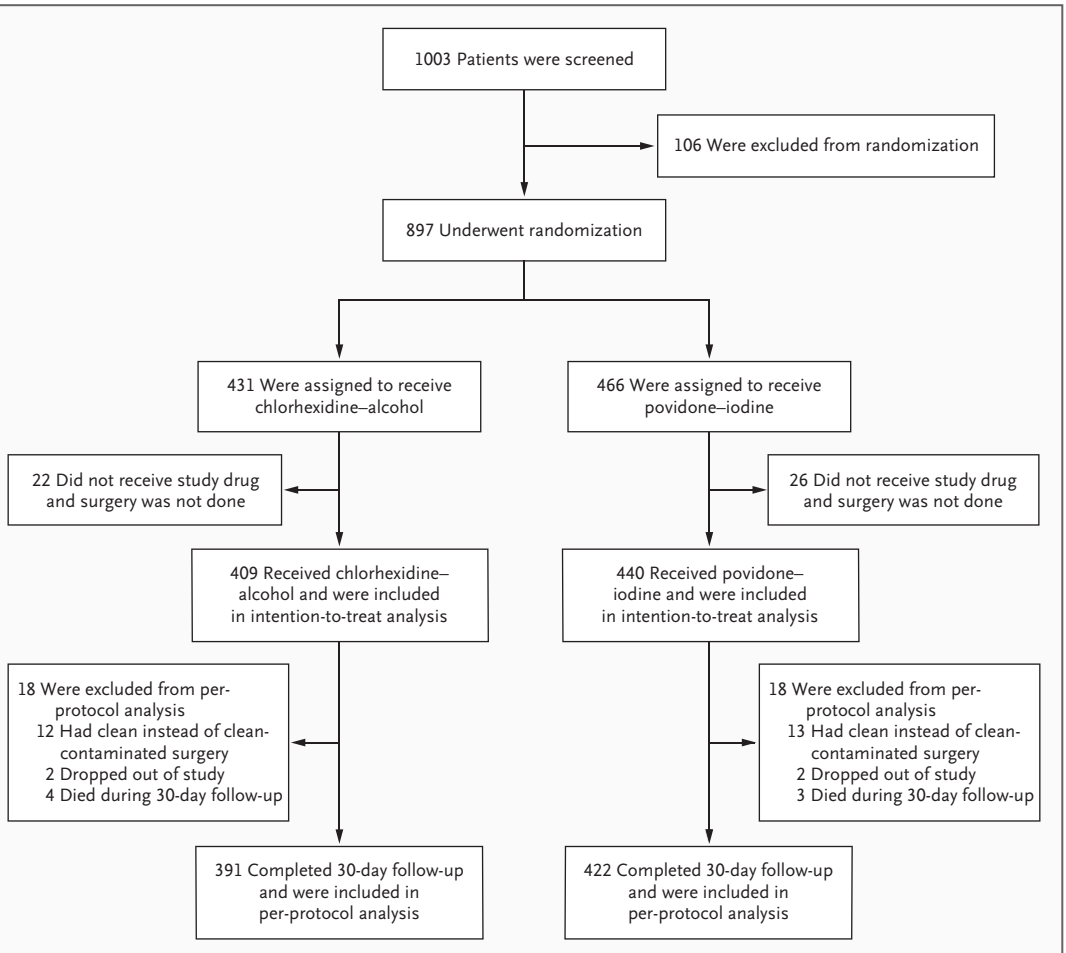

Figure 1. Screening, Randomization, and Follow-up of Study Participants.

RESULTS

PATIENTS

A total of 897 patients were randomly assigned to a study group: 431 to the chlorhexidine–alcohol group and 466 to the povidone–iodine group (Fig. 1). Of the 849 patients who qualified for the intention-to-treat analysis, 409 received chlorhexidine–alcohol and 440 received povidone–iodine. Thirty-six patients were excluded from the per-protocol analysis: 25 underwent clean rather than clean-contaminated surgery, 4 dropped out of the study 1 or 2 days after surgery, and 7 died before completion of the 30-day follow-up (4 in the chlorhexidine–alcohol group and 3 in the povidone–iodine group). Therefore, 813 patients (391 in the chlorhexidine–alcohol group and 422 in the povidone–iodine group) were included in the per-protocol analyses. The patients in the two study groups were similar with respect to demographic characteristics, coexisting illnesses, risk factors for infection, antimicrobial exposure, and duration and types of surgery (Table 1, and Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). All patients received systemic prophylactic antibiotics within 1 hour before the initial incision, and there were no significant differences in the type or number of antibiotics given to the two study groups, even when only patients who underwent colorectal surgery were considered (Table 2 in the Supplementary Appendix).

RATES OF INFECTION

For the patients in the intention-to-treat population, the overall rate of surgical-site infection was

Table 1. Baseline Characteristics of the Patients (Intention-to-Treat Population).*

Characteristic	Chlorhexidine–Alcohol (N=409)	Povidone–Iodine (N=440)	P Value
Male sex (%)	58.9	55.9	0.40
Age (yr)	53.3+14.6	52.9+14.2	0.87
Systemic antibiotics			
Initiated preoperatively (%)	100	100	>0.99
Duration of preoperative administration (days)			
Mean	1.1±1.2	1.1±0.8	>0.99
Range	1–20	1–11	
Received postoperatively (%)	51.7	48.9	0.41
Duration of surgery (hr)	3.0±1.5	3.0±1.5	>0.99
Abdominal surgery (%)	72.6	70.0	0.41
Colorectal	45.5	43.4	0.58
Biliary	10.8	12.3	0.52
Small intestinal	10.0	7.7	0.28
Gastroesophageal	6.4	6.6	0.89
Nonabdominal surgery (%)	27.4	30.0	0.41
Thoracic	10.8	13.0	0.34
Gynecologic	10.3	9.1	0.56
Urologic	6.4	8.0	0.42
Preoperative shower (%)	26.7	27.0	0.94
With 4% chlorhexidine gluconate (%)	16.1	18.9	0.32
With 10% povidone–iodine (%)	7.3	5.2	0.26
With 0.6% triclocarban soap bar (%)	3.2	3.0	>0.99

* Plus–minus values are means ±SD.

significantly lower in the chlorhexidine–alcohol group (9.5%) than in the povidone–iodine group (16.1%, P=0.004) (Table 2). The relative risk of any surgical-site infection among patients whose skin was preoperatively cleansed with chlorhexidine–alcohol versus povidone–iodine was 0.59 (95% confidence interval [CI], 0.41 to 0.85). Similarly, chlorhexidine–alcohol was associated with significantly fewer superficial incisional infections (relative risk, 0.48; 95% CI, 0.28 to 0.84) and deep incisional infections (relative risk, 0.33; 95% CI, 0.11 to 1.01). However, there were no significant differences between the two study groups in the incidence of organ-space infection (relative risk, 0.97; 95% CI, 0.52 to 1.80) or sepsis from surgical-site infection (relative risk, 0.62; 95% CI, 0.30 to 1.29).

The per-protocol analysis yielded similar efficacy results. The Kaplan–Meier estimates of the risk of surgical-site infection (Fig. 2) showed a significantly longer time to infection after surgery in the chlorhexidine–alcohol group than in the povidone–iodine group (P=0.004 by the log-rank test).

The interaction between treatment group and type of surgery (abdominal vs. nonabdominal) was included in a logistic-regression model with the main effects of group and surgery type and was found not to be significant (P=0.41). When considered separately in a subgroup analysis (Table 3), the rate of infection after abdominal surgery was 12.5% in the chlorhexidine–alcohol group versus 20.5% in the povidone–iodine group (95% CI for the absolute difference [chlorhexidine–alcohol minus povidone–iodine], –13.9 to –2.1 percentage points). For patients undergoing nonabdominal surgery, the rate of infection was 1.8% in the chlorhexidine–alcohol group versus 6.1% in the

Table 2. Proportion of Patients with Surgical-Site Infection, According to Type of Infection (Intention-to-Treat Population).

Type of Infection	Chlorhexidine–Alcohol (N=409)	Povidone–Iodine (N=440)	Relative Risk (95% CI)*	P Value†
	no. (%)			
Any surgical-site infection	39 (9.5)	71 (16.1)	0.59 (0.41–0.85)	0.004
Superficial incisional infection	17 (4.2)	38 (8.6)	0.48 (0.28–0.84)	0.008
Deep incisional infection	4 (1.0)	13 (3.0)	0.33 (0.11–1.01)	0.05
Organ-space infection	18 (4.4)	20 (4.5)	0.97 (0.52–1.80)	>0.99
Sepsis from surgical-site infection	11 (2.7)	19 (4.3)	0.62 (0.30–1.29)	0.26

* Relative risks are for chlorhexidine–alcohol as compared with povidone–iodine. The 95% confidence intervals were calculated with the use of asymptotic standard-error estimates.
† P values are based on Fisher's exact test.

povidone–iodine group (95% CI for the absolute difference, –7.9 to 2.6 percentage points).

Both the intention-to-treat analysis (Table 3) and the per-protocol analysis showed lower rates of surgical-site infection in the chlorhexidine–alcohol group than in the povidone–iodine group for each of the seven types of operations studied. Although the trial was not powered to compare the rates of infection for subcategories of patients, infection occurred significantly less often in the chlorhexidine–alcohol group than in the povidone–iodine group in the intention-to-treat analysis for patients who underwent small intestinal surgery (P=0.04) or abdominal surgery (P=0.009) or who did not shower preoperatively (P=0.02).

The Breslow–Day tests indicated homogeneity in showing no significant differences between hospitals with respect to the incidence of either any type of surgical-site infection (P=0.35) or individual types of infection (P≥0.19). Even so, we accounted for hospital site in all logistic-regression models by including this term as a random effect through the use of GEE.

ANALYSES OF RISK FACTORS

The multivariate logistic-regression analysis identified the following risk factors for surgical-site infection in the intention-to-treat population: use of povidone–iodine, abdominal surgery, alcohol abuse, liver cirrhosis, cancer, diabetes mellitus, malnutrition, gastrointestinal disease, longer duration of surgery, longer duration of placement of surgical drain, and preoperative shower with povidone–iodine (Table 3 in the Supplementary Appendix). Since an analysis of risk factors other than the assigned intervention constitutes an exploratory analysis, which involves multiple simultaneous statistical tests, it could inflate the probability of a false positive finding (type II error).

MICROBIOLOGIC CAUSES OF INFECTION

Culture of the surgical site in 60 of 61 infected patients yielded growth of organisms (a total of 107 isolates), and similar proportions of infected patients in the two study groups (23 of 39 [59%] in the chlorhexidine–alcohol group and 37 of 71 [52%] in the povidone–iodine group) had an identifiable microbiologic cause of infection (Table 4 in the Supplementary Appendix). Gram-positive aerobic bacteria (63 isolates) outnumbered gram-negative aerobic bacteria (25 isolates) by a factor of 2.5, and 38% of cultures were polymicrobial. There were no significant differences in the frequency of isolating certain categories of organisms or particular organisms in the chlorhexidine–alcohol group (total of 44 isolates) as compared with the povidone–iodine group (total of 63 isolates), with the exception of streptococci, which were less common in the former group (1 of 44 [2.3%] vs. 10 of 63 [15.9%], P=0.03).

ADVERSE EVENTS

In the intention-to-treat analysis, adverse events occurred in equal proportions among the patients in the chlorhexidine–alcohol group and the povidone–iodine group (228 of 409 [55.7%] and 256 of 440 [58.2%], respectively), as did serious adverse events (72 of 409 [17.6%] and 70 of 440 [15.9%],

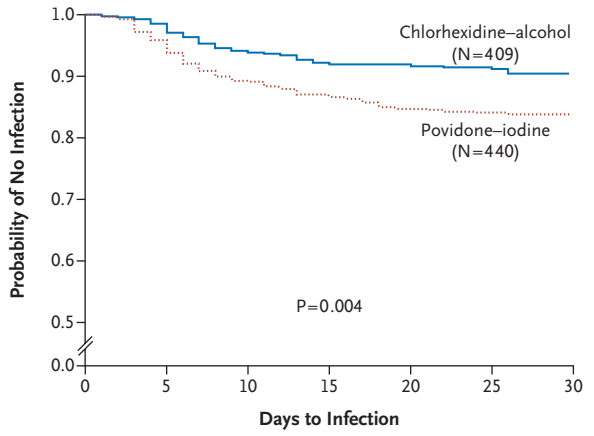

Figure 2. Kaplan–Meier Curves for Freedom from Surgical-Site Infection (Intention-to-Treat Population).

Patients who received chlorhexidine–alcohol were significantly more likely to remain free from surgical-site infection than were those who received povidone–iodine (P=0.004 by the log-rank test). In the chlorhexidine–alcohol group, 39 patients had events (9.5%) and data from 370 patients (90.5%) were censored; in the povidone–iodine group, 71 patients had events (16.1%) and data from 369 patients (83.9%) were censored.

respectively) (Table 4, and Table 5 in the Supplementary Appendix). Findings were similar in the per-protocol analysis. Three patients (0.7%) in each study group had an adverse event (pruritus, erythema, or both around the surgical wound) that was judged to be related to the study drugs; however, no serious adverse events were judged to be related to the study drugs. There were no cases of fire or chemical skin burn in the operating room. A total of seven patients died: four (1.0%) in the chlorhexidine–alcohol group who did not have surgical-site infections and three (0.7%) in the povidone–iodine group who died from sepsis due to organ-space infection.

DISCUSSION

Randomized studies have compared the efficacy of different types[10-13] or doses[14,15] of systemic antibiotics for preventing surgical-site infection but not the effect of preoperative skin antisepsis. In this randomized study, the application of chlorhexidine–alcohol reduced the risk of surgical-site infection by 41% as compared with the most common practice in the United States of using aqueous povidone–iodine.[7] This degree of protection is similar to the 49% reduction in the risk of vascular catheter–related bloodstream infection in a meta-analysis that showed the superiority of skin disinfection with chlorhexidine-based solutions versus 10% povidone–iodine.[16] Although the overall rates of surgical-site infection of 10 to 16% in this study are higher than those reported in some previous studies,[17,18] they are similar to the prestudy rates at the participating hospitals and those reported in other studies[13] and are lower than the rates reported in trials that used the CDC definition of infection and had adequate follow-up,[11,12,19] as we did in this trial. On the basis of our findings, the estimated number of patients who would need to undergo skin preparation with chlorhexidine–alcohol instead of povidone–iodine in order to prevent one case of surgical-site infection is approximately 17.

Although both the antiseptic preparations we studied possess broad-spectrum antimicrobial activity,[9] the superior clinical protection provided by chlorhexidine–alcohol is probably related to its more rapid action, persistent activity despite exposure to bodily fluids, and residual effect.[20] The superior clinical efficacy of chlorhexidine–alcohol in our study correlates well with previous microbiologic studies showing that chlorhexidine-based antiseptic preparations are more effective than iodine-containing solutions in reducing the bacterial concentration in the operative field for vaginal hysterectomy[21] and foot-and-ankle surgery.[22,23] Although the use of flammable alcohol-based products in the operating room poses the risk, though small, of fire or chemical skin burn, no such adverse events occurred in this study or the other studies.[21-23]

In this trial we universally enforced standard-of-care preventive measures (e.g., administering systemic prophylactic antibiotics within 1 hour before the first incision was made and, if needed, clipping hair immediately before surgery),[9,24] but hospitals were allowed to continue their preexisting practices, which offer potential but not established protective efficacy (e.g., preoperative showering).[25] However, we controlled the effect of differences in hospital practices by using hospital-stratified randomization, which ensured close matching of the two study groups as well as trial results that are applicable to a broadly representative population of hospitalized patients.

Because antiseptics act only against organisms

Table 3. Proportion of Patients with Surgical-Site Infection, According to Type of Surgery (Intention-to-Treat Population).

Type of Surgery	Chlorhexidine–Alcohol		Povidone–Iodine	
	Total No. of Patients	Patients with Infection	Total No. of Patients	Patients with Infection
		no. (%)		*no. (%)*
Abdominal	297	37 (12.5)	308	63 (20.5)
Colorectal	186	28 (15.1)	191	42 (22.0)
Biliary	44	2 (4.6)	54	5 (9.3)
Small intestinal	41	4 (9.8)	34	10 (29.4)
Gastroesophageal	26	3 (11.5)	29	6 (20.7)
Nonabdominal	112	2 (1.8)	132	8 (6.1)
Thoracic	44	2 (4.5)	57	4 (7.0)
Gynecologic	42	0	40	1 (2.5)
Urologic	26	0	35	3 (8.6)

Table 4. Clinical Adverse Events (Intention-to-Treat Population).

Clinical Adverse Event	Chlorhexidine–Alcohol (N=409)	Povidone–Iodine (N=440)	Absolute Difference*	P Value†
	no. (%)		*percentage points (95% CI)*	
Adverse events in ≥5% of patients in either group	228 (55.7)	256 (58.2)	–2.4 (–9.1 to 4.2)	0.49
Drug-related adverse events‡	3 (0.7)	3 (0.7)	0.1 (–1.1 to 1.2)	>0.99
Serious adverse events in >1% of patients in either group	72 (17.6)	70 (15.9)	1.7 (–3.3 to 6.7)	0.52
Serious drug-related adverse events	0	0	—	—
Death	4 (1.0)	3 (0.7)	0.3 (–0.9 to 1.5)	0.72

* The absolute difference is shown as the rate in the chlorhexidine–alcohol group minus the rate in the povidone–iodine group.
† P values were calculated with the use of Fisher's exact test.
‡ Drug-related adverse events included pruritus, erythema, or both around the surgical wound and are reported even though the rate was not 5% or higher in either group.

that reside on the patient's integument, the overall superior protection afforded by chlorhexidine–alcohol was attributed primarily to a reduction in the rates of superficial and deep incisional infections that were caused mostly by gram-positive skin flora. Since two thirds of surgical-site infections are confined to the incision,[9,11] optimizing skin antisepsis before surgery could result in a significant clinical benefit.

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REFERENCES

1. Wolf JS Jr, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ. Best practice policy statements on urologic surgery antimicrobial prophylaxis. J Urol 2008;179:1379-90. [Erratum, J Urol 2008;180:2262-3.]
2. Hawn MT, Itani KM, Gray SH, Vick CC, Henderson W, Houston TK. Association of timely administration of prophylactic antibiotics for major surgical procedures and surgical site infection. J Am Coll Surg 2008;206:814-9.
3. Belda FJ, Aguilera L, Garcia de la Asunción J, et al. Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. JAMA 2005;294:2035-42. [Erratum, JAMA 2005;294:2973.]
4. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. N Engl J Med 1996;334:1209-15.
5. Yasunaga H, Ide H, Imamura T, Ohe K. Accuracy of economic studies on surgical site infection. J Hosp Infect 2007; 65:102-7.
6. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. Infect Control Hosp Epidemiol 1999;20:725-30.
7. Napolitano LM. Decolonization of the skin of the patient and surgeon. Surg Infect (Larchmt) 2006;7:Suppl 3:S3-S15.
8. O'Grady NP, Alexander M, Dellinger EP, et al. Guidelines for the prevention of intravascular catheter-related infections. Infect Control Hosp Epidemiol 2002;23: 759-69.
9. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999: Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250-78.
10. Ishizaka K, Kobayashi S, Machida T, Yoshida K. Randomized prospective comparison of fosfomycin and cefotiam for prevention of postoperative infection following urological surgery. J Infect Chemother 2007;13:324-31.
11. Itani KMF, Wilson SE, Awad SS, Jensen EH, Finn TS, Abramson MA. Ertapenem versus cefotetan prophylaxis in elective colorectal surgery. N Engl J Med 2006; 355:2640-51.
12. Milsom JW, Smith DL, Corman ML, Howerton RA, Yellin AE, Luke DR. Double-blind comparison of single-dose alatrofloxacin and cefotetan as prophylaxis of infection following elective colorectal surgery. Am J Surg 1998;176:6A Suppl:46S-52S.
13. Arnaud JP, Bellissant E, Boissel P, et al. Single-dose amoxycillin-clavulanic acid vs. cefotetan for prophylaxis in elective colorectal surgery: a multicentre, prospective, randomized study. J Hosp Infect 1992; 22:Suppl A:23-32.
14. Fujita S, Saito N, Yamada T, et al. Randomized, multicenter trial of antibiotic prophylaxis in elective colorectal surgery: single dose vs 3 doses of a second-generation cephalosporin without metronidazole and oral antibiotics. Arch Surg 2007;142: 657-61.
15. Mohri Y, Tonouchi H, Kobayashi M, et al. Randomized clinical trial of single-versus multiple-dose antimicrobial prophylaxis in gastric cancer surgery. Br J Surg 2007;94:683-8.
16. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. Ann Intern Med 2002;136:792-801.
17. Uchiyama K, Takifuji K, Tani M, et al. Prevention of postoperative infections by administration of antimicrobial agents immediately before surgery for patients with gastrointestinal cancers. Hepatogastroenterology 2007;54:1487-93.
18. Greif R, Akça O, Horn E-P, Kurz A, Sessler DI. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. N Engl J Med 2000; 342:161-7.
19. Smith RL, Bohl JK, McElearney ST, et al. Wound infection after elective colorectal resection. Ann Surg 2004;239:599-605.
20. Denton GW. Chlorhexidine. In: Block SS, ed. Disinfection, sterilization, and preservation. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2001:321-36.
21. Culligan PJ, Kubik K, Murphy M, Blackwell L, Snyder J. A randomized trial that compared povidone iodine and chlorhexidine as antiseptics for vaginal hysterectomy. Am J Obstet Gynecol 2005; 192:422-5.
22. Ostrander RV, Botte MJ, Brage ME. Efficacy of surgical preparation solutions in foot and ankle surgery. J Bone Joint Surg Am 2005;87:980-5.
23. Bibbo C, Patel DV, Gehrmann RM, Lin SS. Chlorhexidine provides superior skin decontamination in foot and ankle surgery: a prospective randomized study. Clin Orthop Relat Res 2005;438:204-8.
24. Tanner J, Woodings D, Moncaster K. Preoperative hair removal to reduce surgical site infection. Cochrane Database Syst Rev 2006;2:CD004122.
25. Webster J, Osborne S. Preoperative bathing or showering with skin antiseptics to prevent surgical site infection. Cochrane Database Syst Rev 2007;2:CD004985.

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Evaluation of a 2% chlorhexidine gluconate in 70% isopropyl alcohol skin disinfectant

D. Adams[a,*], M. Quayum[b], T. Worthington[b], P. Lambert[b], T. Elliott[a]

[a]*Microbiology Research and Development Group, University Hospital Birmingham NHS Foundation Trust, The Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, UK*
[b]*Department of Pharmaceutical and Biological Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK*

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KEYWORDS
ChloraPrep®; Chlorhexidine; Disinfectant; Povidone iodine; Isopropanol; Skin antisepsis

Summary The efficacy of a new skin disinfectant, 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol (IPA) (ChloraPrep®), was compared with five commonly used skin disinfectants against *Staphylococcus epidermidis* RP62A in the presence or absence of protein, utilizing quantitative time-kill suspension and carrier tests. All six disinfectants [70% (v/v) IPA, 0.5% (w/v) aqueous CHG, 2% (w/v) aqueous CHG, 0.5% (w/v) CHG in 70% (v/v) IPA and 10% (w/v) aqueous povidone iodine (PI)] achieved a $\log_{10}$ reduction factor of 5, in colony-forming units/mL, in a suspension test (exposure time 30 s) in the presence and absence of 10% human serum. Subsequent challenges of *S. epidermidis* RP62A in a biofilm (with and without human serum) demonstrated reduced bactericidal activity. Overall, the most effective skin disinfectants tested against *S. epidermidis* RP62A were 2% (w/v) CHG in 70% IPA and 10% (w/v) PI. These results suggest that enhanced skin antisepsis may be achieved with 2% (w/v) CHG in 70% (v/v) IPA compared with the three commonly used CHG preparations [0.5% (w/v) aqueous CHG, 2% (w/v) aqueous CHG and 0.5% (w/v) CHG in 70% (v/v) IPA].

Introduction

Coagulase-negative staphylococci are frequently associated with catheter-related bloodstream infections.[1,2] A characteristic feature of these micro-organisms is their ability to adhere and form biofilms on prosthetic devices, resulting in resistance to antimicrobial agents. In order to reduce the risk of microbial colonization and subsequent sepsis of peripheral vascular catheters, it is recommended that the skin insertion site should be disinfected for 30 s with an antimicrobial solution.[3] A chlorhexidine preparation is preferred;

* Corresponding author. Tel.: +44 121 472 1311x3451; fax: +44 121 414 1682.
E-mail address: debbie.adams@uhb.nhs.uk

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however, povidone iodine (PI) or 70% isopropyl alcohol (IPA) may be used.[4-6] These agents use different modes of action to achieve antisepsis, which may be reduced in the presence of organic matter.[7,8] Two percent chlorhexidine gluconate (CHG) preparations have not been universally available in the UK. Recently, a 2% (w/v) CHG in 70% (v/v) IPA solution (ChloraPrep®: Medi-Flex® Incorporated; Kansas, USA) for skin decontamination has been developed and is currently under review for approval by the Medicines and Healthcare Products Regulatory Agency (UK) for marketing authorization. Clinical studies have demonstrated that this skin disinfectant provided a significantly better and more persistent antimicrobial activity than 70% (v/v) IPA or 2% (w/v) aqueous CHG at 24 h in patients receiving pre-operative skin antisepsis on abdominal and inguinal sites ($N=106$).[9] This enhanced residual antimicrobial activity may also potentially reduce the risk of subsequent phlebitis for patients requiring a peripheral vascular catheter.

The criterion for determining the antimicrobial activity of a disinfectant is usually the rate of reduction of the number of viable micro-organisms when exposed to the antiseptic agent. The most widely recognized definition with regards to bactericidal activity is a $\log_{10}$ reduction factor of 5.[10] Assessing the efficacy of a disinfectant may be undertaken by various quantitative in vitro methods including suspension tests and carrier tests.[11]

The aim of the present study was to determine the antimicrobial efficacy of 2% CHG in 70% (v/v) IPA, which has recently become available in the UK, and to compare it with 70% (v/v) IPA, 10% (w/v) aqueous PI, 0.5% (w/v) aqueous CHG, 2% (w/v) aqueous CHG and 0.5% (w/v) CHG in 70% (v/v) IPA utilizing quantitative in vitro time-kill tests against *S. epidermidis* RP62A at 30 s. Suspension tests were used to determine the effectiveness of the disinfectant in reducing the potential risk from impaction on insertion of vascular catheters. Although biofilm formation develops following medical device insertion, some disinfectants have residual activity. Therefore, in addition to the suspension tests, carrier tests were undertaken to evaluate the potential inhibition of biofilms on disinfectant activity.

Methods

Six skin disinfectants were evaluated: 70% (v/v) IPA (BDH; Poole, UK) was prepared by diluting 100% (v/v) IPA in sterile distilled water; 0.5% (w/v) and 2% (w/v) aqueous CHG (Sigma; St Louis, USA) were prepared by diluting 20% (w/v) CHG in sterile distilled water; 0.5% (w/v) CHG in 70% (v/v) IPA (Adams Healthcare; Leeds, UK); 2% (w/v) CHG in 70% (v/v) IPA (Medi-Flex® International; Kansas, USA) and 10% (w/v) aqueous PI (Seton Healthcare; Oldham, UK).

Evaluation of the efficacy of the antimicrobial agents was undertaken at 30 s; the recommended time for disinfecting the intended skin site of a peripheral vascular catheter prior to insertion.[3]

A neutralizing agent was prepared containing 2% (v/v) Tween 80 (BDH; Poole, UK), 1.17% (w/v) lecithin (Fisher Scientific; Loughborough, UK), 0.1% (v/v) Triton X-100 (Sigma; St Louis, USA) and 0.5% (w/v) sodium thiosulphate (BDH; Poole, UK) in sterile distilled water. This was sterilized at 121 °C for 15 min and then stored at 4 °C until required. Prior to commencing the antimicrobial time-kill studies, verification of the effectiveness and non-toxicity of the chosen neutralizing agent against the range of antimicrobial agents and the efficacy of the antimicrobial agents against the challenge micro-organisms were determined.

S. epidermidis RP62A stored on microbank beads (Pro-Lab Diagnostics; Ontario, Canada) was revived by placing one bead in 3 mL brain heart infusion (BHI) broth (Oxoid; Basingstoke, UK) and incubating at 37 °C in air for 24 h. *S. epidermidis* RP62A is a reference biofilm-positive strain and 'slime' producer, which was confirmed under current test conditions by Freeman *et al.*'s technique.[12]

In the suspension test, 10 μL broth containing 3×10^6 colony-forming units (cfu) *S. epidermidis* RP62A was added to 990 μL disinfectant and mixed. After 30 s contact time at room temperature, 100 μL suspension was removed and added to 900 μL neutralizing agent, mixed and left to dwell for 5 min. Serial dilutions were inoculated on to BHI agar plates which were incubated at 37 °C in air for up to 48 h. Further suspension tests were undertaken by adding 10% (v/v) human serum (Sigma; St Louis, USA) to the suspension prior to adding the disinfectant. The evaluations were carried out in triplicate.

To evaluate the efficacy of the disinfectants against a biofilm, a carrier test was undertaken with a 96-well polystyrene flat-bottomed microtitre tray (Immulon® 2HB Thermo Labsystems; Franklyn, MA, USA). A suspension of *S. epidermidis* RP62A was diluted in BHI to approximately 1×10^4. Two-hundred-microlitre aliquots of the suspension were inoculated into 16 wells of a sterile microtitre

tray. This was then covered with a microplate sealer (Greiner-Bio-One; Gloucester, UK) and incubated at 37 °C in air for 24 h. Confirmation of biofilm production was undertaken by O'Toole and Kolter's[13] technique. To determine the efficacy of the disinfectants against a biofilm in the presence of protein, the carrier test was repeated; a suspension of *S. epidermidis* RP62A was diluted in BHI to approximately 1×10^4 cfu/mL and 10% human (v/v) serum was added.

The cells in suspension in each well were removed by inversion of the plate; the wells were then washed with 250 μL phosphate-buffered saline (PBS). Two-hundred microlitres of the selected disinfectant was added to each well and allowed to dwell for 30 s. The disinfectant was aspirated and 250 μL neutralizing agent was added to each well and left for 5 min. The neutralizing agent was removed by inversion of the tray, and the microtitre wells were washed with PBS. Removal of the biofilm from the microtitre well was undertaken by adding a 200-μL aliquot of BHI to each inoculated well. With a sterile pipette tip, the walls of the microtitre wells and base were scraped 10 times and the BHI was removed from each well and collected. This procedure was repeated a further three times and the inoculum was mixed thoroughly. Previous studies had demonstrated that four consecutive scrapes were required to remove >99% of the micro-organisms in a biofilm attached to a microtitre well; successive scrapes failed to statistically reduce this number further. The numbers of viable *S. epidermidis* RP62A in suspension were enumerated by serial dilutions, and 100 μL of each dilution was inoculated on to BHI agar plates. The plates were then incubated at 37 °C in air for up to 48 h. Tests and controls were carried out 16 times.

Statistical analysis

Data were compared using the Mann–Whitney *U*-test. *P* values of equal to or less than 0.05 were regarded as significant.

Results

In all tests, the controls containing no disinfectant resulted in a complete recovery of the initial inocula.

Table I outlines the results of the suspension and carrier tests in both the presence and absence of protein. Efficacy of the disinfectant activity is represented as the $\log_{10}$ reduction factor of the initial cfu/mL. None of the skin disinfectants tested achieved a $\log_{10}$ reduction factor >5 in all four tests. Four disinfectants [70% (v/v) IPA, 0.5% (w/v) CHG in 70% (v/v) IPA, 2% (w/v) CHG in 70% (v/v) IPA and 10% (w/v) aqueous PI] achieved a $\log_{10}$ reduction factor >5 at 30 s in the suspension tests, both in the presence and absence of human serum, and in the carrier test when challenged with *S. epidermidis* RP62A in a biofilm.

When evaluating the effectiveness of the six disinfectants against *S. epidermidis* RP62A in a biofilm enriched with 10% (v/v) human serum, 70% (v/v) IPA, 0.5% (w/v) aqueous CHG, 2% (w/v) aqueous CHG and 0.5% (w/v) CHG in 70% (v/v) IPA achieved a $\log_{10}$ reduction factor between 2 and 4 at 30 s. In comparison, 2% (w/v) CHG in 70% (v/v) IPA and 10% (w/v) aqueous PI achieved a $\log_{10}$ reduction factor of between 4 and 5. There was no statistical difference between the two disinfectants on analysis ($P=0.28$).

Table I Comparing the efficacy of 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol (IPA) against five standard skin disinfectants on *Staphylococcus epidermidis* RP62A after 30 s of contact time utilizing suspension and carrier tests

Antiseptic	$\log_{10}$ reduction factor in cfu/mL of *S. epidermidis* RP62A			
	Suspension test	Suspension test with 10% human serum	Carrier test: biofilm	Carrier test: biofilm enriched with 10% human serum
2% (w/v) CHG in 70% (v/v) IPA	6.5	6.3	5.3	**4.7**
70% (v/v) IPA	6.5	6.3	5.4	**2.8**
0.5% (w/v) aqueous CHG	6.5	6.3	**4.1**	**2.3**
2% (w/v) aqueous CHG	6.5	6.3	**4.8**	**2.8**
0.5% (w/v) CHG in 70% (v/v) IPA	6.5	6.3	5.8	**3.6**
10% (w/v) aqueous povidone iodine	6.5	6.3	5.9	**4.4**

cfu, colony-forming units. Bold type indicates a failure to achieve a $\log_{10}$ reduction factor of 5.

Discussion

This study compared the antimicrobial effectiveness of 2% (w/v) CHG in 70% (v/v) IPA with five standard skin disinfectants. The findings demonstrated that the range of disinfectants tested were capable of achieving a $\log_{10}$ reduction factor of 5, in cfu/mL, when in suspension both in the presence and absence of protein. However, when challenged with *S. epidermidis* RP62A in a biofilm (with or without protein), the antimicrobial effectiveness was reduced, thus reflecting previous reports that disinfectants may be inhibited in the presence of organic matter.[7,8]

The application of effective skin antisepsis is essential in the strategy to reduce catheter-related sepsis. The Centers for Disease Control and Prevention[4] recommend the use of a 2% chlorhexidine-based preparation for skin decontamination prior to line insertion, but do not specify the use of either an aqueous solution or one in 70% IPA. Pratt *et al.*[5] and the National Institute for Clinical Excellence guidelines[6] recommend an alcoholic chlorhexidine solution but do not specify a concentration. This study supports the recommendation of a chlorhexidine in alcohol product. Indeed, the in vitro results suggest that 2% (w/v) CHG in 70% (v/v) IPA offers an improved antimicrobial effect compared with all three standard preparations of CHG currently available in the UK [0.5% (w/v) aqueous CHG, 2% (w/v) aqueous CHG and 0.5% (w/v) CHG in 70% (v/v) IPA] when challenged with *S. epidermidis* RP62A in a biofilm in the presence of 10% human serum ($P=0.0001$).

Further in vitro studies are required to assess the potential clinical effectiveness of 2% (w/v) CHG in 70% (v/v) IPA against a wider range of pathogens. In addition, assessment of the residual antiseptic activity on the skin compared with other commercially available chlorhexidine preparations needs to be studied. This study, however, suggests that 2% (w/v) CHG in 70% (v/v) IPA may offer advantages over the other chlorhexidine products available. In vivo studies are required to assess the effectiveness of this product in the clinical situation.

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References

1. Elliott TSJ, Faroqui MH, Armstrong RF, *et al*. Guidelines for good practice in central venous catheterization. *J Hosp Infect* 1994;**28**:163—176.
2. Mermel LA, Farr BM, Sherertz RJ, *et al*. Guidelines for the management of intravascular catheter-related infections. *J Intraven Nurs* 2001;**24**:180—205.
3. Infection Control Nurses Association. *Guidelines for preventing intravascular catheter-related infections*. Bathgate: Fitwise Publications; 2001.
4. Centers for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter related infections. *MMWR* 2002;**51**:1—26.
5. Pratt RJ, Pellowe CM, Loveday HP, *et al*. The EPIC project: developing national evidence-based guidelines for preventing healthcare associated infections. *J Hosp Infect* 2001; **47**(Suppl):S21—S37.
6. National Institute for Clinical Excellence. *Infection control: prevention of healthcare associated infection in primary and community care (clinical guideline 2)*. London: NICE; 2003.
7. Ayliffe GAJ, Coates D, Hoffman PN. *Chemical disinfection in hospital*. 2nd ed. London: PHLS; 1993.
8. Hugo WB, Russell AD. Types of antimicrobial agents. In: Russell AD, Hugo WB, Ayliffe GA, editors. *Principles and practice of disinfection, preservation and sterilization*. 3rd ed. Oxford: Blackwell Science; 1999. p. 8—106.
9. Hibbard JS, Mulberry GK, Brady AR. A clinical study comparing the skin antisepsis and safety of ChloraPrep®, 70% isopropyl alcohol and 2% aqueous chlorhexidine. *J Infus Nurs* 2000;**25**:244—249.
10. Cremieux A, Freney J, Davin-Regli A. Methods of testing disinfectants. In: Block S, editor. *Disinfection, sterilization and preservation*. 5th ed. London: Lippincott Williams and Wilkins; 2000. p. 1305—1327.
11. Reybrouck G. The evaluation of the antimicrobial activity of disinfectants. In: Russell AD, Hugo WB, Ayliffe GA, editors. *Principles and practice of disinfection, preservation and sterilization*. 3rd ed. Oxford: Blackwell Science; 1999. p. 134—157.
12. Freeman DJ, Falkiner FR, Keane CT. New method for detecting slime production by coagulase negative staphylococci. *J Clin Pathol* 1989;**42**:872—874.
13. O'Toole GA, Kolter R. Inititation of biofilm formation in *Pseudomonas fluorescens* WCS365 proceeds via multiple, convergent signalling pathways: a genetic analysis. *Mol Microbiol* 1998;**28**:449—461.

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Comparison of Chlorhexidine and Tincture of Iodine for Skin Antisepsis in Preparation for Blood Sample Collection

Joan Barenfanger,[1]* Cheryl Drake,[1] Jerry Lawhorn,[1] and Steven J. Verhulst[2]

Laboratory Medicine, Memorial Medical Center,[1] and Division of Statistics and Research Consulting, School of Medicine, Southern Illinois University,[2] Springfield, Illinois

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Rates of contamination of blood cultures obtained when skin was prepared with iodine tincture versus chlorhexidine were compared. For iodine tincture, the contamination rate was 2.7%; for chlorhexidine, it was 3.1%. The 0.41% difference is not statistically significant. Chlorhexidine has comparable effectiveness and is safer, cheaper, and preferred by staff, so it is an alternative to iodine tincture.

Contaminated blood cultures cause unnecessary costs and poor patient care and promote the use of unnecessary antibiotics. The current "gold standard" skin preparation is iodine tincture. A new less toxic product ChloraPrep, a one-step application of 2% chlorhexidine gluconate and 70% isopropyl alcohol, is now available. Several studies have established that for preparing the skin for insertion of intravenous lines, chlorhexidine is superior to povidone-iodine or alcohol alone (1, 4–6, 9; N. Chaiyakunapruk, D. L. Veenstra, S. Saint, and B. A. Lipsky, Abstr. 28th Annu. Meet. Assoc. Prof. Infect. Control Epidemiol., abstr. 99, 2001; D. G. Maki, V. Knasinski, L. L. Narans, and B. J. Gordon, Program Abstr. 11th Soc. Healthcare Epidemiol. Am., abstr. 142, 2001; D. G. Maki, V. Knasinski, L. L. Narans, and B. J. Gordon, Program Abstr. 11th Soc. Healthcare Epidemiol. Am., abstr. 142, 2001; G. Sheehan, K. Leicht, M. O'Brien, G. Taylor, and R. Rennie, Program Abstr. 33rd Intersci. Conf. Antimicrob. Agents Chemother. abstr. 1616, 1993) and that for preparing the skin prior to obtaining blood for culture, chlorhexidine is superior to povidone-iodine (8). However, only one smaller study compared the rates of blood culture contamination obtained with chlorhexidine versus those obtained with iodine tincture (10). To further document the efficacy of chlorhexidine, we compared the rates of blood culture contamination when iodine tincture was used to prepare the skin versus those obtained when chlorhexidine was used.

(This work was previously presented in part [103rd Gen. Meet. Am. Soc. Microbiol., abstr. C-095, p. 135, 2003].)

At Memorial Medical Center in Springfield, Ill., 11,738 blood cultures over two time periods (January 2002 to June 2002 and August 2002 to February 2003) were studied. The cultures were processed identically during each time period in an automated blood culturing instrument (BacT/Alert; Organon Teknika, Durham, N.C.). Both chlorhexidine and iodine tincture are manufactured by Medi-Flex Hospital Products, Inc. (Overland Park, Kans.). From January to June 2002, iodine tincture was used for antiseptic skin preparation. From August 2002 to February 2003, chlorhexidine was used. Since contiguous time periods were used to evaluate the products, a potential bias of seasonality was not accounted for. Therefore, to determine any effect of different time periods, we included contamination rates for the months of January to June 2003, during which time chlorhexidine alone was used. The procedures used for skin preparation with iodine tincture and chlorhexidine were in accordance with the package inserts.

Blood cultures were collected by a variety of hospital staff, including phlebotomists from the laboratory (who collect about one-third of the samples), staff in the Emergency Department, and nurses. Generally, the rates of contamination were lowest when the phlebotomy was done by the phlebotomy team and highest when it was done by the staff in the Emergency Department (1.5 to 3% higher). During each time period, two in-services about the importance of skin antisepsis were given. For adults, a blood culture consisted of a set of two (FAN Aerobic and FAN Anaerobic) bottles. A pediatric bottle could be used for children. Generally, the pediatric population (<18 years of age) was <5% of the patients. A blood culture was considered positive if either one or both bottles grew organisms. If a patient had more than two cultures taken and only one was positive for coagulase-negative staphylococci, viridans group streptococci, nutritionally deficient streptococci, *Peptostreptococcus* spp., diphtheroids, or *Propionibacterium*, *Bacillus*, or *Micrococcus* spp., then that culture was considered contaminated. If a patient had only one culture taken and one of the organisms named above was present in that single culture, then data from that culture were discarded. Data were retrieved by the Cerner laboratory information system. Questionnaires were distributed to assess phlebotomists' opinions of the two products.

From January 2002 to June 2002 (when iodine tincture was used), 32 positive blood cultures with potential contaminants were discarded; from August 2002 to February 2003 (when chlorhexidine was used), 30 were discarded. During the time when iodine tincture was used, the average contamination rate was 2.72% (158 contaminants in 5,802 cultures); during the time when chlorhexidine was used, the average contamination rate was 3.13% (186 contaminants in 5,936 cultures) (Fig. 1). The 0.41% (3.13% − 2.72%) difference was not statistically significant ($P = 0.188$, chi-square analysis). The contaminating organisms found with both iodine tincture and chlorhexidine were similar in distribution (Table 1). The most common or-

* Corresponding author. Mailing address: Laboratory Medicine, Memorial Medical Center, 701 N. First St., Springfield, IL 62781. Phone: (217) 788-3000. Fax: (217) 788-5577. E-mail: barenfanger.joan@mhsil.com.

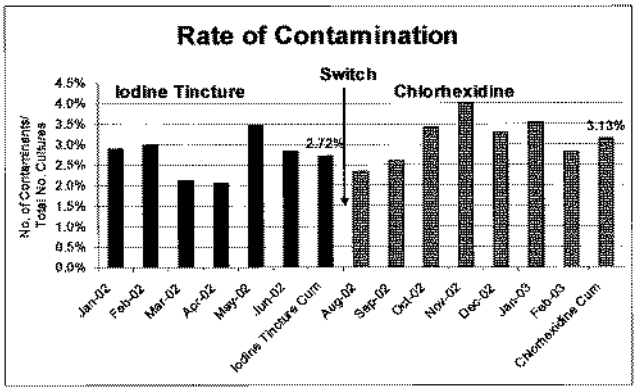

FIG. 1. Graph of contamination rates obtained with the two different skin preparations compared in this study. Cum, cumulative.

ganisms causing contamination were coagulase-negative staphylococci (125 of 158 or 79.1% with iodine tincture and 137 of 186 or 73.7% with chlorhexidine), followed by diphtheroids (12 of 158 or 7.6% with iodine tincture and 22 of 186 or 11.8% with chlorhexidine) and viridans group streptococci (9 of 158 or 5.7% with iodine tincture and 11 of 186 or 5.9% with chlorhexidine). Despite the use of the different products, there was minimal variation in the rates of contamination from month to month during different years (Table 2).

The cost of chlorhexidine in this hospital was 16 cents less per kit. The time required for skin antisepsis by chlorhexidine was 40 s less than that required for skin antisepsis by iodine tincture. Fifteen phlebotomists and nurses answered questionnaires about their subjective impressions. All but one preferred chlorhexidine. The reasons cited were that chlorhexidine was easier, faster, and less messy.

The study that directly compared iodine tincture to chlorhexidine for skin preparation for blood cultures had results similar to but slightly different from ours (10). The study by Trautner et al. of 430 blood cultures found a slightly higher contamination rate with iodine tincture, but the difference was not statistically significant ($P = 0.62$) (10).

Our findings are subject to at least two limitations. First, the use of different time frames is a theoretical problem. It is possible that the lack of a statistically significant difference observed was due to changes in patient population or seasonal trends. However, in subsequent months when chlorhexidine alone was used, the average contamination rate was 2.9% from January 2003 to June 2003, compared to the same time frame in the previous year in which iodine tincture was used with a contamination rate of 2.7% (Table 2). Second, a chart review was not done to determine if the isolate was really a true contaminant. However, we used the same widely used criteria in both arms of the study to determine contamination rates.

TABLE 1. Distribution of organisms causing contamination in the two time periods studied

Organisms	No. (%) of organisms	
	Iodine tincture	Chlorhexidine
Bacillus spp.	5 (3.2)	8 (4.3)
Coagulase-negative staphylococci	125 (79.1)	137 (73.7)
Diphtheroids	12 (7.6)	22 (11.8)
Micrococci	4 (2.5)	3 (1.6)
Nutritionally deficient streptococci	1 (0.6)	0
Propionibacteria	1 (0.6)	5 (2.7)
Peptostreptococci	1 (0.6)	0
Viridans group streptococci	9 (5.7)	11 (5.9)
All contaminant organisms	158 (100)	186 (100)

TABLE 2. Contamination rates during the same months in different years

Mo	Contamination rate with Iodine tincture in 2002 (%)	Contamination rate with chlorhexidine in 2003 (%)
January	2.9	3.0
February	3.0	2.6
March	2.1	3.5
April	2.1	2.7
May	3.5	2.1
June	2.8	3.5
Cumulative	2.7	2.9

Iodine tincture has the disadvantage of being toxic when used repeatedly (4). Toxicity or sensitization due to chlorhexidine is very uncommon (2–4, 7). In contrast, iodinated antiseptics alter thyroid function in newborns of low birth weight because of systemic absorption of iodine (5). After discussions with infectious disease physicians, infection control staff, and committee, we will continue using chlorhexidine for antiseptic preparation of skin prior to obtaining blood for culture at this institution.

In conclusion, since chlorhexidine has comparable effectiveness to iodine tincture and is safer, cheaper, and preferred by users, it is an alternative to iodine tincture.

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REFERENCES

1. **Cobett, S., and A. LeBlanc.** 1999. IV site infection: a prospective, randomized clinical trial comparing the efficacy of three methods of skin antisepsis; CINA conference '99. Off. J. Can. Intravenous Nurs. Assoc. **15:**48–49.
2. **Darmstadt, G. L.** 2000. Neonatal skin care. Pediatr. Clin. N. Am. **47:**757–782.
3. **Garland, J. S., C. P. Alex, C. D. Mueller, D. Otten, C. Shivpuri, et al.** 2001. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. Pediatrics **107:**1431–1436.
4. **Garland, J. S., R. K. Buck, P. Maloney, D. M. Durkin, S. Toth-Lloyd, M. Duffy; P. Szocik, T. L. McAuliffe, and D. Goldmann.** 1995. Comparison of 10% povidone-iodine and 0.5% chlorhexidine gluconate for the prevention of peripheral intravenous catheter colonization in neonates: a prospective trial. Pediatr. Infect. Dis. **14:**510–516.
5. **Kinirons, B., O. Mimoz, L. Lafendi, T. Naas, et al.** 2001. Chlorhexidine versus povidone iodine in preventing colonization of continuous epidural catheters in children. Anesthesiology **94:**239–244.
6. **Maki, D. G., M. Ringer, and C. J. Alvarado.** 1991. Prospective randomized trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. Lancet **338:**339–343.
7. **Metry, D. W.** 2000. Topical therapies and medications in the pediatric patient. Pediatr. Clin. N. Am. **47:**867–876.
8. **Mimoz, O., A. Karim, A. Mercat, M. Cosserson, et. al.** 1999. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. Ann. Int. Med. **131:**834–837.
9. **Mimoz, O., L. Pieroni, C. Lawrence, A. Edouard, Y. Costa, K. Samii, and C. Brun-Buisson.** 1996. Prospective, randomized trial of two antiseptic solutions for prevention of central venous or arterial catheter colonization and infection in intensive care unit patients. Crit. Care Med. **24:**1818–1823.
10. **Trautner, B., J. Clarridge, and R. O. Darouche.** 2002. Skin antisepsis kits containing alcohol and chlorhexidine gluconate or tincture of iodine are associated with low rates of blood culture contamination. Infect. Control Hosp. Epidemiol. **23:**397–401.

Eliminating catheter-related bloodstream infections in the intensive care unit*

Sean M. Berenholtz, MD, MHS; Peter J. Pronovost, MD, PhD; Pamela A. Lipsett, MD; Deborah Hobson, BSN; Karen Earsing, RN, MS; Jason E. Farley, MSN, MPH, CRNP; Shelley Milanovich, RN, MSN, ACNP; Elizabeth Garrett-Mayer, PhD; Bradford D. Winters, MD, PhD; Haya R. Rubin, MD, PhD; Todd Dorman, MD; Trish M. Perl, MD, MSc

LEARNING OBJECTIVES

On completion of this article, the reader should be able to:

1. Identify key elements of the insertion technique that will minimize catheter-related bloodstream infections in the intensive care unit.
2. Describe other interventions that will minimize catheter-related bloodstream infection in the intensive care unit.
3. Describe the application of this knowledge in the clinical environment.

Dr. Berenholtz has disclosed that he is a consultant to VHA, Inc. The remaining authors have disclosed that they have no financial relationships or interests in any commercial companies pertaining to this educational activity. The authors have disclosed that none of the proton pump inhibitors or histamine antagonists discussed in this article have been approved by the U.S. Food and Drug Administration for use in the prevention of stress-related mucosal bleeding except continuous infusion cimetidine.

Visit the *Critical Care Medicine* Online website (www.ccmjournal.com) for information on obtaining continuing medical education credit.

Objective: **To determine whether a multifaceted systems intervention would eliminate catheter-related bloodstream infections (CR-BSIs).**

Design: **Prospective cohort study in a surgical intensive care unit (ICU) with a concurrent control ICU.**

Setting: **The Johns Hopkins Hospital.**

Patients: **All patients with a central venous catheter in the ICU.**

Intervention: **To eliminate CR-BSIs, a quality improvement team implemented five interventions: educating the staff; creating a catheter insertion cart; asking providers daily whether catheters could be removed; implementing a checklist to ensure adherence to evidence-based guidelines for preventing CR-BSIs; and empowering nurses to stop the catheter insertion procedure if a violation of the guidelines was observed.**

Measurement: **The primary outcome variable was the rate of CR-BSIs per 1,000 catheter days from January 1, 1998, through December 31, 2002. Secondary outcome variables included adherence to evidence-based infection control guidelines during catheter insertion.**

Main Results: **Before the intervention, we found that physicians followed infection control guidelines during 62% of the procedures. During the intervention time period, the CR-BSI rate in the study ICU decreased from 11.3/1,000 catheter days in the first quarter of 1998 to 0/1,000 catheter days in the fourth quarter of 2002. The CR-BSI rate in the control ICU was 5.7/1,000 catheter days in the first quarter of 1998 and 1.6/1,000 catheter days in the fourth quarter of 2002 ($p = .56$). We estimate that these interventions may have prevented 43 CR-BSIs, eight deaths, and $1,945,922 in additional costs per year in the study ICU.**

Conclusions: **Multifaceted interventions that helped to ensure adherence with evidence-based infection control guidelines nearly eliminated CR-BSIs in our surgical ICU. (Crit Care Med 2004; 32:2014–2020)**

KEY WORDS: intensive care units; infection, nosocomial; catheterization, central venous; total quality management; organizational innovation

Catheter-related bloodstream infections (CR-BSIs) are associated with significant morbidity, mortality, and costs (1, 2). Patients in intensive care units (ICUs) are at an increased risk for CR-BSIs because 48% of ICU patients have indwelling central venous catheters, accounting for 15 million central catheter days per year in United States ICUs (1). Assuming an average CR-BSI rate of 5.3 per 1,000 catheter days and an attributable mortality of 18% (0% to 35%), as many as 28,000 ICU patients die of CR-BSIs annually in the United States alone (2–4). Therefore, efforts to decrease the rate of CR-BSIs and to improve the quality of ICU care are paramount.

Although the rates of CR-BSI are high, they are preventable. Numerous interventions have reduced the incidence of CR-BSI and the ensuing morbidity, mortality, and costs (5–8). In addition, the Centers for Disease Control and Prevention (CDC) (www.cdc.gov), the Society of Critical Care Medicine, the Society of Healthcare Epidemiologists of America, the Infectious Disease Society of America, and several other societies have recently developed evidence-graded guidelines for the prevention of catheter-related infections (9). Several of the guideline recommendations are supported by well-done clinical trials or systematic reviews and include the following: appropriate use of hand hygiene; chlorhexidine skin preparation; full-barrier precautions during central venous catheter insertion; subclavian vein placement as the preferred site; and maintaining a sterile field while inserting the catheter (1).

Despite this evidence, a gap exists between best evidence and best practice (10). The aim of this project was to eliminate CR-BSIs in our ICU. To accomplish this aim, we used a quality improvement model that can be broadly applied to other ICUs. We also estimated the number of CR-BSIs that we may have prevented and the potential savings as a result of our improvement.

MATERIALS AND METHODS

Study Setting. The Johns Hopkins Hospital is a 926-bed tertiary care hospital with seven ICUs and medical, surgical, psychiatric, and neurologic services. Two ICUs participated in this project. The intervention surgical ICU (SICU) is a 16-bed surgical ICU that cares for adult patients undergoing general, orthopedic, transplant, trauma, and vascular surgery. The concurrent control ICU is a 15-bed unit that cares for adult patients undergoing cardiac surgery.

Study Design. We designed a prospective cohort study with concurrent controls. Central venous catheters are routinely placed by the anesthesiologists in the operating room or by surgery, anesthesia, and critical care residents in the ICU. The decision to use a single or multilumen catheter was at the discretion of the intraoperative anesthesia or critical care team in the ICU. Both ICUs are a mandatory consult model in which the patient's surgeon remains the attending physician of record and all patients in the ICU are co-managed by an intensivist-led team, including ICU attending physicians and fellows, anesthesia and surgery residents, a pharmacist, and nurses. The intensivist-lead team visits every patient daily in the ICU to review patient information and to develop a care plan for the day. The nurse/patient staffing ratio is 1:1 or 1:2. The patient's primary nurse is routinely present during central catheter insertion in both ICUs. This patient care model did not change during the study period. The management of central venous catheters once they are inserted did not change during the study period, with the exception of the change in daily patient visits in the study SICU to ask whether catheters could be removed. We did not replace or exchange catheters over a guidewire at scheduled time intervals. The decision to replace or exchange catheters over a guidewire if the patient developed evidence of a systemic infection was at the discretion of the critical care team in the ICU. In general, we exchanged catheters over a guidewire if the patient demonstrated evidence of a systemic infection, the catheter malfunctioned, or we changed to a catheter with fewer lumens. If the patient developed significant hemodynamic instability, we generally replaced the catheters, established a new site, and sent the intradermal portion of the old central catheters for culture. The study population included all patients with a percutaneous central venous catheter in the ICU. All percutaneous central venous catheters for intravenous fluid, medication, dialysis, or administration of total parenteral nutrition were included. Our CR-BSI rates do not include tunneled catheter or central arterial catheter infections. The institutional review board at our institution approved the study and waived the need for informed consent.

Measures. The primary outcome variable was the rate of CR-BSIs per 1,000 catheter days. Hospital epidemiology and infection control (HEIC) at our institution defines catheter-related nosocomial bloodstream infections using National Nosocomial Infection Surveillance System (CDC)-based definitions (3). Surveillance is performed prospectively by trained infection control practitioners. Catheter-related infections are attributed to patients who have a central venous catheter and who have been in the ICU for at least 48 hrs. Patients with a central venous catheter who develop a bloodstream infection within 48 hrs of ICU discharge also have a CR-BSI. Secondary outcome variables included adherence to evidence-based infection control practices during central venous catheter insertion. We also interviewed SICU nurses to evaluate their perception of the burden of our intervention. Data were collected from January 1, 1998, through December 31, 2002.

Improvement Model. We created an interdisciplinary team including the SICU co-directors, ICU physicians, nurses, and infection control practitioners to gain visibility and credibility for this initiative. We based these interventions on the conceptual model for adhering to practice guidelines developed by Cabana et al. (11) that seeks to evaluate physician awareness, agreement, and ability to use a guideline. We also used principles from the human factors literature in patient safety to enhance physicians' ability to comply with the CDC guidelines (12). Specifically, we sought to enhance provider awareness, to reduce com-

***See also p. 2150.**

Assistant Professor, the Departments of Anesthesiology/CCM and Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD (SMB); Associate Professor, Medical Director, the Center for Innovations in Quality Patient Care, the Departments of Anesthesiology/CCM, Surgery, and Health Policy and Management, The Johns Hopkins University School of Medicine (PJP); Professor of Surgery, the Departments of Anesthesiology/CCM, Surgery, and Nursing, The Johns Hopkins University School of Medicine, Baltimore, MD (PAL); Performance Improvement Chair in SICU, Staff Nurse in SICU, the Department of Surgery, The Johns Hopkins Hospital, Baltimore, MD (DH); Nurse Manager, SICU, The Johns Hopkins Hospital, Baltimore, MD (KE); Adult Nurse Practitioner, The Johns Hopkins University, the Department of Hospital Epidemiology and Infection Control, The Johns Hopkins Hospital, Baltimore, MD (JEF); Acute Care Nurse Practitioner, Surgical Intensive Care, The Johns Hopkins Hospital, Baltimore, MD (SM); Assistant Professor, the Department of Oncology, The Johns Hopkins University School of Medicine, Baltimore, MD (EG-M); the Department of Anesthesiology/CCM, The Johns Hopkins University School of Medicine, Baltimore, MD (BDW); Professor of Medicine, the Departments of Medicine and Health Policy and Management, The Johns Hopkins University School of Medicine, Bloomberg School of Public Health, and the Center for Innovations in Quality Patient Care, Baltimore, MD (HRR); Associate Professor, the Departments of Anesthesiology/CCM, Surgery, Medicine, and Nursing, The Johns Hopkins Hospital, Baltimore, MD (TD); and Associate Professor of Medicine, the Departments of Medicine and Hospital Epidemiology and Infection Control, The Johns Hopkins University School of Medicine, Baltimore, MD (TMP).

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plexity, to create independent redundancies, and to empower nurses to enforce adherence to evidence-based infection control practices and to ensure patients receive those therapies that they ought to receive.

Our SICU team's improvement model included five interventions: a) implementing an educational intervention to increase provider awareness of evidence-based infection control practices for inserting and maintaining central catheters; b) creating a catheter insertion cart to make it easier for providers to obtain all of the materials needed to follow CDC guidelines for sterile central venous catheter insertion; c) asking daily whether central venous catheters can be removed; d) implementing a checklist to ensure adherence to evidence-based guidelines for preventing CR-BSIs; and e) empowering nurses to stop the procedure if evidence-based guidelines are not followed.

Intervention 1: Implementing an Educational Intervention to Increase Provider Awareness of Evidence-Based Infection Control Practices (Introduced: February 1999)

Reducing nosocomial infections has been a major focus at our institution. As part of this effort, HEIC adopted nationally recognized definitions for CR-BSIs in January 1998 and provided feedback of CR-BSI rates to all ICUs. In February 1999, HEIC developed, in collaboration with clinicians, and the hospital's Medical Board passed a vascular access device policy based on the CDC guidelines (www.hopkins-heic.org/prevention/vad.html). The procedures detailed in this policy include the standard requirements for training, vascular access device site selection, insertion, site assessment, dressing change requirements, documentation requirements, appropriate flushing procedures, tubing replacement, and central catheter removal and/or replacement requirements. As part of this policy, in October 2000, all physicians or physician extenders who insert central catheters were required to complete a Web-based training module and successfully complete a ten-question test before they were allowed to insert a central venous catheter in our institution. The Web-based training module (www.hopkins-heic.org) was designed to increase provider awareness of evidence-based infection control practices, including appropriate use of hand hygiene, chlorhexidine skin preparation, full-barrier precautions during central venous catheter insertion, subclavian vein placement as the preferred site, maintaining a sterile field while inserting the catheter, and the care of central catheters once inserted. In 2002, proof of completion of the module was required before physician received credentials. In addition, HEIC staff provided 16 lectures for nurses and five for doctors to reinforce these evidence-based practices. CR-BSI rates were posted in the SICU for providers to see. The vascular access device policy was revised in September of 2002 to incorporate changes from the CDC, Society of Critical Care Medicine, Society of Healthcare Epidemiologists of America, and Infectious Disease Society of America prevention of catheter infection guidelines (9).

Intervention 2: Creating a Central Catheter Insertion Cart (Introduced: June 1999)

We identified that a potential barrier to compliance with the evidence-based practices was that physicians in the study SICU had to go to eight different places to collect the equipment needed to comply with the CDC guidelines. We hypothesized that we could improve compliance by decreasing the number of steps required. To test our hypothesis, we created a central catheter insertion cart that contained the equipment and supplies needed and, thereby, reduced the number of steps required for compliance from eight to one. Our central catheter insertion cart has four drawers with partitions to organize the contents, and the cart can be rolled to the patient's room. To ensure that the central catheter cart is stocked at all times, our support associate stocks the cart every 4 hrs from the ICU supply room and signs off on the checklist located on top of the cart. At our institution, support associates are indirect care providers with a high school diploma, or equivalent degree, who assist nursing staff with a variety of environmental, nutritional, clinical, and transportation services.

Intervention 3: Asking Providers Daily Whether Catheters Can Be Removed (Introduced: June 2001)

One of the most effective strategies for preventing CR-BSIs is to eliminate, or at least reduce, exposure to central venous catheters. The decision regarding the need for a catheter is complex and, therefore, difficult to standardize into a practice guideline. Nonetheless, to reduce exposure to central venous catheters, the ICU team in the study ICU asked daily during patient rounds whether any catheters or tubes could be removed. To ensure that this question was asked, we added it to the rounding form, called the daily goals form, which is used to develop daily care plans for patients in our SICU (13, 14).

Intervention 4: Implementing a Checklist to Be Completed by the Bedside Nurse (Introduced: November 2001)

To help ensure compliance with the evidence-based guidelines for central catheter insertion, we developed a standardized checklist to be completed by the bedside nurse during central venous catheter insertion in the study SICU (Appendix). We pilot tested the checklist in the SICU for 1 wk and interviewed ten SICU nurses, using a convenience sample, regarding the clarity of the form, burden of data collection, and the need for modification. Based on this feedback, we modified the form and provided in-services to the study SICU nursing staff.

We then implemented the checklist in two phases. During the first phase, we asked SICU nursing staff for 2 wks to observe the physicians during catheter placement and to complete the checklist for each procedure. Physicians were not aware that they were being observed during the first phase. We audited the percentage of central venous catheter insertions that had the checklist completed. We also interviewed ten SICU nurses who had completed the checklist to evaluate their perceptions of the form, the burden, and the average time to complete the form.

Intervention 5: Empowering Nurses to Stop Procedures if Guidelines Were Not Followed (Introduced: December 2001)

During the second phase, we modified the checklist and asked nursing staff to continue to observe the physician during central venous catheter placement. In this phase, we informed the residents that the checklist was being implemented and we empowered SICU nurses to stop the procedure, except in an emergency, if they observed a violation in compliance with the evidence-based guidelines. The nursing staff indicated if the procedure was stopped on the modified checklist. To decrease the burden of data collection, we did not collect data on the nature of the violation. Finally, we discussed with both residents and nurses that the nurse should page the SICU attending physician if the resident, after the nurse identifies a violation, fails to correct the violation.

Control ICU

The only intervention in the control ICU during the study period was the institutional educational intervention to increase provider awareness of evidence-based infection control practices for inserting and maintaining central catheters.

Analysis and Interpretation

We calculated the rate of adherence to evidence-based practices during a 2-wk observation period when the checklist was implemented and the percent of central venous catheter insertions that required nursing intervention for a violation in compliance for 1 month. The rates of CR-BSIs were calculated by dividing the number of infections identified by a risk-adjusted denominator—1,000 catheter days (3, 15). We obtained the denominators from an administrative database, which was validated by the infection control practitioners. Catheter days are calculated by counting every patient with a central catheter at midnight. Only one catheter per patient is included. We followed the rate of CR-BSIs per 1,000 catheter days from January 1,1998, through December 31, 2002, using a control chart (16). A Poisson regression model with a spline was used to model the change in infection rates over time in the control and intervention groups. A knot was included at the first quarter of 1999, i.e., the point at which the intervention was introduced into the SICU. The regression model included six covariates, allowing the intervention and control groups to each have its own intercepts, slopes before the knot, and slopes after the knot. To assess the effect of the intervention, we tested whether the slopes after the knot were equivalent. The group-specific parameters (e.g., slopes) were compared using Student's *t*-tests, with a two-sided α level of 0.05.

Estimated Savings

Estimates of attributable morbidity, mortality, and costs of care for CR-BSIs vary. To estimate the number of CR-BSIs that we may have prevented and the potential savings as a result of our improvement, we used mean published estimates (ranges): 18% (0% to 35%) mortality and extra costs of $45,254 ($34,508–$56,000) per CR-BSI. These estimates are consistent with those cited by the 2002 Guidelines for the Prevention of Intravascular Catheter-Related Infections (9).

RESULTS

During the 2-wk observation period before we implemented the checklist, nursing completed the checklist for 26 procedures: eight (31%) for new central venous access and 18 (69%) for catheter exchanges over a wire. None of the procedures were emergent. Overall, we found that physicians were compliant in all of the evidence-based infection control guidelines during 62% of the observed procedures (Table 1). The SICU nurses interviewed recommended a few minor changes to improve the clarity of the central catheter insertion checklist.

The SICU leadership then empowered nurses to stop the procedure if they observed a violation in compliance with the evidence-based guidelines. During the first month, nursing completed the checklist for 38 procedures: eight (24%) for new central venous access, 30 (79%) for catheter exchanges over a wire, and three (8%) were emergent. A nursing intervention was required in 32% (12/38) of central venous catheter insertions. All providers interviewed reported that the format of the central catheter insertion checklist was easy to understand and could be completed in <3 mins. The SICU nurses also indicated that they found the form helpful in that they were more comfortable intervening if they observed a violation, because they felt that an expectation had been set and as a result, they were less likely to have an uncomfortable encounter with the physician inserting the central venous catheter.

During the study period, 22,785 patient days and 19,905 catheter days were included in the study SICU. In the control ICU, 21,964 patient days and 17,383 catheter days were included.

The CR-BSI rate in the study ICU was 11.3/1,000 catheter days in the first quarter of 1998 and 0/1,000 catheter days in the fourth quarter of 2002. The CR-BSI rate in the control group was 5.7/1,000 catheter days in the first quarter of 1998 and 1.6/1,000 catheter days in the fourth quarter of 2002. The fitted Poisson regression model is shown in Figure 1. Before quarter 5, the slope in the intervention arm equaled 0.046 ($p = .48$) and the slope in the control arm equaled 0.08 ($p = .41$). There were no significant differences found when comparing the intercepts ($p = .11$) and the slopes before quarter 5 ($p = .80$).

Our improvement in performance was sustained. Between January 2003 and April 2004, there were two CR-BSIs in the study SICU or 0.54/1,000 catheter days, and we have not had a CR-BSI in >9 months. The educational intervention, central catheter insertion cart, daily goals form, and checklist are now routinely used in our SICU. As a result of this improvement, we estimate that in our SICU alone, we may have prevented up to 43 CR-BSIs, eight (0–15) deaths, and $1,945,922 ($1,483,844–$2,408,000) in additional costs per year.

Table 1. Baseline surgical intensive care unit compliance with evidence-based infection control guidelines

Guideline	n (%)
Cleaned hands	16 (62)
Sterilized procedure site	26 (100)
Draped patient in sterile fashion	22 (85)
Used hat, mask, and sterile gown	24 (92)
Used sterile gloves	26 (100)
Applied sterile dressing	26 (100)
Compliance with all guidelines	16 (62)

DISCUSSION

In many healthcare settings, evidence-based clinical practice guidelines have been developed but bridging the gap between best evidence and best practice has been a struggle (11). In our SICU, we used five simple and inexpensive interventions to increase compliance with evidence-based infection control practices and dramatically decreased the rate of CR-BSIs in our SICU, whereas the rates in a control ICU were unchanged. Our improvements likely translate into significant reductions in patient morbidity, mortality, and costs of care in our SICU.

There is debate whether CR-BSIs can be eliminated or whether ICUs should strive to achieve a benchmark, such as the National Nosocomial Infections Surveillance 50th percentile for similar patient populations. Although we, and others, believed that zero CR-BSIs should be the goal, we were unsure if we could achieve that performance. In this study, we demonstrated that it is possible to nearly eliminate CR-BSIs; therefore, we should not accept National Nosocomial Infections Surveillance mean values as a measure of success, but rather, we should shift our focus on zero harm. Given the significant morbidity, mortality, and costs associated the CR-BSIs, broad application of this intervention may improve clinical and economic outcomes for hospitalized patients.

There were several important lessons from this initiative that can be incorporated into future efforts to improve ICU care. First, we reduced our rate of CR-BSIs using relatively simple and inexpensive interventions, as opposed to implementing more expensive interventions, such as antibiotic/antiseptic catheters. For interventions to work in the busy world of clinical practice, they should be simple to implement. By changing systems rather than exhorting providers to

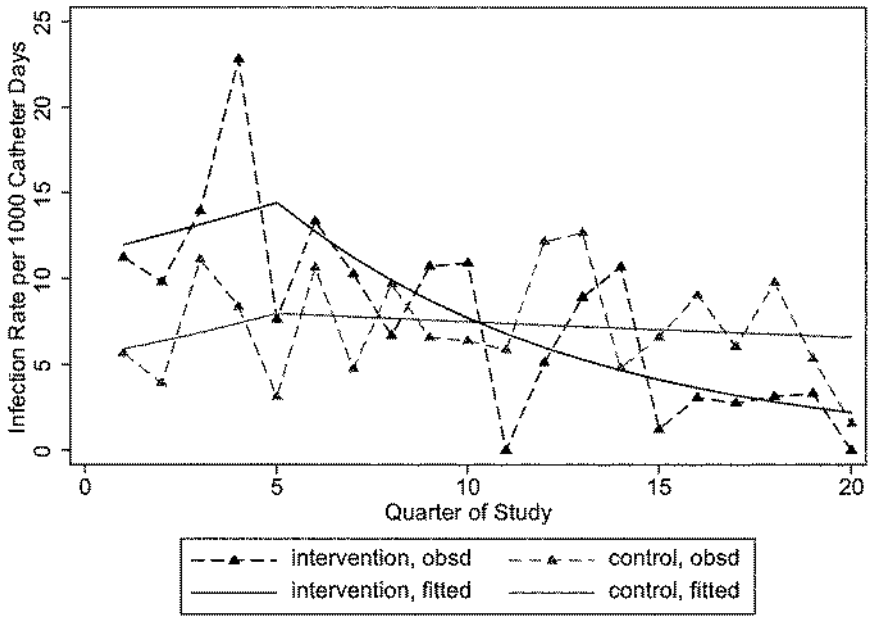


Figure 1. Catheter-related bloodstream infection rates in the surgical intensive care unit (ICU) and control ICU (1998–2002). The rate of catheter-related bloodstream infections per 1,000 catheter days observed in the intervention (*intervention, obsd*) and control (*control, obsd*) groups. A Poisson regression model with a spline was used to model the change in infection rates over time in the intervention (*intervention, fitted*) and control (*control, fitted*) groups. There were no significant differences found when comparing the intercepts ($p = .11$) and the slopes before the knot at quarter 5 ($p = .80$). After quarter 5, the slope in the intervention arm equaled -0.12 ($p < .001$) and the slope in the control arm equaled -0.013 ($p = .56$). *VAD*, vascular access device; *obsd*, observed.

comply with guidelines, we can help ensure that patients receive effective therapies. For example, it was difficult to write a detailed guideline regarding the need for a central venous catheter; there are too many decisions to account for. It is unlikely that detailed guidelines would be practical for complex decisions, such as ICU admission and discharge, extubation, and use of catheters (17). Rather, we simply asked physicians to consider daily whether central catheters could be removed, highlighting the risk of catheters yet allowing physicians to use their clinical judgment.

Second, because each step in a process has an independent probability of failure, care processes that require more steps are more likely to fail than processes that require fewer steps (12). As a result, efforts to improve safety whether in health care or other industries focus on reducing or eliminating steps in a process (18). We found that providers had to go to eight different places within our SICU to gather the supplies needed to comply with the evidence-based infection control practices. As a result, providers often omitted steps, especially when busy. By introducing a central catheter cart, we reduced the complexity by decreasing the number of steps in the process. Given the complexity of ICU care, this concept has broad applicability.

Third, creating independent redundancies, through the use of a checklist, is an effective technique to ensure that patients receive the care processes they should receive. Checklists are used extensively in aviation (18) to create independent redundancies for key steps in a process. With the central catheter insertion checklist, nurses serve as an independent, redundant check to help ensure physician adherence. When the improvement team first introduced the CR-BSI checklist, staff expressed concern. Barriers identified included the following: a) the nurses perception that their job was not to police residents; and b) the residents perception that credibility and authority would be challenged if they were critiqued or corrected by nursing staff. The SICU leadership met with both groups of providers and emphasized our focus on patient safety and teamwork. When presented in this light, residents and nurses understood that they need to work together to ensure patient safety. In addition, HEIC required leaders from hospital administration to support the initiative and provide the SICU with the additional resources required.

Fourth, we must have a culture that supports patient safety. Although efforts to improve interpersonal communication have resulted in improved aviation safety (18, 19), health care lags behind where the culture is still hierarchical (20). Although we did not formally train staff in interpersonal or communication skills, successful implementation of the checklist requires these skills and provides a means to learn teamwork skills experientially. We are observing that the teamwork skills developed through the use of the checklist are spilling over to other areas. In addition, our results highlight the importance of collaboration between hospital level services, such as HEIC, and ICU clinical services.

We recognize several limitations of our study. First, the pre- and post-study design may not have accounted for other confounding factors that may have decreased our CR-BSI rate, independent of our interventions. For example, we did not collect standardized measures of patient acuity to allow comparison of patient severity of illness or patient demographic characteristics over time or to determine whether patients in the study ICU were sicker than patients in the control ICU. The members of our improvement team, which include the SICU codirectors and active SICU nursing staff, are not aware of other changes in practice or changes in our surgical patient population during the study period. In the absence of a new patient product-line, risk adjusted severity of illness tends to change little over time (21) and, therefore, is unlikely to jeopardize the validity of our results.

Second, we do not know the nurses' rate of adherence with completing the checklist following the observation period. Our ICUs do not routinely collect data for the number of central venous catheter insertions or the number of guidewire exchanges. Nonetheless, on average nurses complete 20–30 checklists every 2 wks and there is a relatively constant 15% to 25% violation rate in our SICU, likely reflecting the fact that our residents rotate through our ICU. In addition, we did not collect data about the nature of infection control practice violations following the observation period, whether the catheter was inserted in the operating room or ICU, the duration of catheterization, or antibiotic use during the study period. Although this informa-

Multifaceted interventions that helped to ensure adherence with evidence-based infection control guidelines nearly eliminated catheter-related bloodstream infections in our surgical intensive care unit.

tion would be helpful in guiding future improvement efforts, we accomplished the goal: reducing the CR-BSI rate. Furthermore, the ongoing need for reinforcement of best practice is supported by these findings.

Third, we did not evaluate other evidence-based interventions for reducing CR-BSIs. For example, we discussed the use of antimicrobial-coated catheters and decided to first ensure that we were compliant with simple and inexpensive interventions known to reduce CR-BSI rates before escalating to more expensive interventions. Our strategy is consistent with current guidelines that recommend antimicrobial-coated catheters in adults when the CR-BSI rate remains above the goal set by the individual institution based on benchmark rates after standard procedures have been implemented and then balanced against the concern for emergence of resistant pathogens (9). In addition, some of our interventions may have been more effective than others, and we may have been able to achieve our results without all five interventions or if we implemented the interventions in a different sequence.

Fourth, we evaluated interventions in a surgical ICU at an academic medical center, potentially limiting the ability to generalize. Nonetheless, our interventions were effective and were not burdensome or expensive and, therefore, can be widely applied. Although we did not quantify the impact of our interventions on nursing time in our ICU, the overwhelming impression among nursing staff and the nurse manager (KE) is that the ongoing burden is minimal and the checklist can be completed in <2 mins. In fact, several ICU nurses indicated that the central catheter cart saved them time because they did not have to go to multiple locations to gather supplies. In addition, these interventions have been subsequently implemented in the control ICU with similar results and at other institutions as part of collaborative projects sponsored by VHA, Inc., and the Institute for Healthcare Improvement.

Finally, we assumed that each patient has only one central catheter, and as a result, we may have underestimated our CR-BSI rate, the number of CR-BSIs prevented, and the potential savings. For example, a patient may have two or more central catheters on a single day but would be counted as having one catheter day. In addition, we were not able to account for patients who developed more than one CR-BSI in our statistical analysis. However, the rate of autocorrelation among patients was low (113 patients developed 126 CR-BSIs in the study ICU, and 140 patients developed 167 CR-BSIs in the control ICU) and, therefore, would not be expected to impact upon our results (16). In addition, we do not have the patient level data required to exclude duplicate patients from the denominator (catheter days). Nevertheless, we re-ran our analysis excluding duplicate CR-BSIs from the numerator, and the statistical inference was unchanged.

CONCLUSIONS

Catheter-related bloodstream infections are a preventable cause of morbidity and mortality in critically ill patients. Although debate continues about the extent to which CR-BSIs are preventable, our study demonstrates that they can be nearly eliminated. Our improvement model combined traditional infection control strategies with improvement models designed to ensure provider adherence with evidence-based guidelines. We included interventions that enhanced provider awareness, reduced complexity, created independent redundancies, and empowered nurses to enforce adherence to evidence-based infection control practices to nearly eliminate CR-BSIs in our SICU. These interventions can be implemented in other ICUs and in many acute care sites to reduce nosocomial complications, length of stay, and costs of hospital care.

We acknowledge the tremendous efforts of the ICU team. These improvements would not have been possible without their dedication to improving patient care. We thank Xioayan Song, MD, and Ann Richards in Hospital Epidemiology and Infection Control for providing us with data. The authors would also like to thank Jeanne Kowalski, Assistant Professor, Department of Oncology, Johns Hopkins University for statistical review.

REFERENCES

1. Mermel LA: Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000; 132:391–402
2. Pittet D, Tarara D, Wenzel RP: Nosocomial bloodstream infection in critically ill patients: Excess length of stay, extra costs, and attributable mortality. *JAMA* 1994; 271: 1598–1601
3. CDC: National Nosocomial Infections Surveillance (NNIS) system report, data summary from October 1986–April 1998, issued June 1998. *Am J Infect Control* 1998; 26: 522–533
4. Heiselman D: Nosocomial bloodstream infections in the critically ill. *Ann Intern Med* 1994; 272:1819–1820
5. Goetz AM, Wagener MM, Miller JM, et al: Risk of infection due to central venous catheters: Effect of site of placement and catheter type. *Infect Control Hosp Epidemiol* 1998; 19:842–845
6. Raad II, Hohn DC, Gilbreath BJ, et al: Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. *Infect Control Hosp Epidemiol* 1994; 15(4 Pt 1):231–238
7. Mermel LA, McCormick RD, Springman SR, et al: The pathogenesis and epidemiology of catheter-related infection with pulmonary artery Swan-Ganz catheters: A prospective study utilizing molecular subtyping. *Am J Med* 1991; 91:197S–205S
8. Maki DG, Ringer M, Alvarado CJ: Prospective randomised trial of povidone-iodine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. *Lancet* 1991; 338:339–343
9. O'Grady NP, Alexander M, Dellinger EP, et al: Guidelines for the prevention of intravascular catheter-related infections. *MMWR Recomm Rep* 2002; 51(RR-10):1–29
10. Sherertz RJ, Ely EW, Westbrook DM, et al: Education of physicians-in-training can decrease the risk for vascular catheter infection. *Ann Intern Med* 2000; 132:641–648
11. Cabana MD, Rand CS, Powe NR, et al: Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; 282:1458–1465
12. Reason J: Human Error. Cambidge, Cambridge University Press, 1990
13. Pronovost P, Berenholtz S, Dorman T, et al: Improving communication in the ICU using daily goals. *J Crit Care* 2003; 18: 71–75
14. Berenholtz SM, Milanovich S, Faircloth A, et

al: Improving care for the ventilated patient. *Jt Comm J Qual Saf* 2004; 30:195–204
15. Joint Commission on the Accreditation of Healthcare Organizations (Ed): Joint Commission on the Accreditation Manual for Hospitals. Chicago, IL, 1994, pp 121–140
16. Shewhart W: Statistical Method from the Viewpoint of Quality Control. Washington, DC, U.S. Department of Agriculture, 1945
17. Pronovost PJ, Jenckes M, To M, et al: Reducing failed extubations in the intensive care unit. *Jt Comm J Qual Improv* 2002; 28: 595–604
18. Kohn L, Corrigan J, Donaldson M (Eds): To err is human: Building a safer health system. Washington, DC, Institute of Medicine Report, National Academy Press, 1999
19. Salas E, Fowlkes J, Stout R, et al: Does CRM training enhances teamwork skills in the cockpit? Two evaluation studies. *Hum Factors* 1999; 41:326–343
20. Mayor S: Poor team work is killing patients. *BMJ* 2002; 325:1129
21. Pronovost PJ, Angus DC, Dorman T, et al: Physician staffing patterns and clinical outcomes in critically ill patients: A systematic review. *JAMA* 2002; 288:2151–2162

APPENDIX 1: Central Line Insertion Checklist

Catheter-related Blood Stream Infection
Care Team Checklist

Purpose: To work as a team to decrease patient harm from catheter-related blood stream infections
When: During **all** central venous or central arterial line insertions or re-wires
By whom: Bedside nurse

1. Today's date: ____/____/____ (month / day / year)
2. Procedure: ☐ New line ☐ Rewire
3. Is the procedure: ☐ Elective ☐ Emergent
4.

	Yes	No	Don't know
Before the procedure, did the housestaff:			
Wash hands (chlorhexidine or soap) immediately prior	☐	☐	☐
Sterilize procedure site	☐	☐	☐
Drape entire patient in a sterile fashion	☐	☐	☐
During the procedure, did the housestaff:			
Use sterile gloves	☐	☐	☐
Use hat, mask and sterile gown	☐	☐	☐
Maintain a sterile field	☐	☐	☐
Did all personnel assisting with procedure follow the above precautions	☐	☐	☐
After the procedure:			
Was a sterile dressing applied to the site	☐	☐	☐

Please return completed form to the designated location in your ICU.

reduce the rate of CLA-BSI among children with long-term CVC (PICC or tunneled catheters) may be needed. Strategies we are considering include 1) reducing the frequency of CVC access; 2) modifying the protocol for CVC hub preparation prior to access; and 3) establishing a dedicated catheter-care team.

Vancomycin-Resistant *Enterococcus* (VRE) Primary Bacteremia Associated with Dialysis Catheter Access

*P Ghazarian**
M Fulton
H Goodpasture
Via-Christi Regional Medical Center, Wichita, Kansas

BACKGROUND: From April 1998 to March 2000, nine patients at Via Christi Regional Medical Center (VCRMC) experienced VRE primary bacteremia (PB). Seven of these infections occurred between May 1, 1999, and March 1, 2000. Six were dialysis patients who were cared for by one of the two dialysis providers at VCRMC.

METHODS: Investigation included retrospective chart review of the infected patients, analysis of surveillance data, review of dialysis policies, and direct observations of the dialysis procedures for both providers.

RESULTS: Both providers had similar patient volumes. There was no statistical difference in the VRE colonization rate between the two. The seven strains of VRE were different by pulsed-field gel electrophoresis. The policies for VRE patient care were similar. Observation of the dialysis units found both to be crowded with less-than-optimal facilities for handwashing, storage, and adequate spatial separation of patients. Breaks in technique and variance from stated polices were the same for both providers. The major difference identified was that the dialysis provider with no cases VRE PB used sterile dressings and sterile gloves during the dressing change, whereas the other provider did not.

CONCLUSIONS: The affected provider group implemented sterile dressings and sterile gloves during dressing changes. The incidence of VRE PB disappeared and has not reoccurred in more than 18 months of follow-up. Although we did not perform environmental cultures, VRE is known to contaminate the environment. Touch contamination during dressing changes under less-than-optimal conditions may lead to PB. Using sterile technique may prevent cross-contamination in dialysis setting.

Continuing Evolution of Multidisciplinary Approach to Prevention of Central Line–Associated Bacteremias

*LL Fauerbach**
C Ruse
MA Gross
R Kelly
D Danek
L Larson
J Janelle
Shands Hospital at the University of Florida, Gainesville, Florida

ISSUE: Prevention of central line–associated bacteremias (BSIc) is a major focus for our 570-bed tertiary/transplant center. Historical risk-reduction strategies include: use of antimicrobial impregnated CVL, CVL insertion tray designed to facilitate total barrier technique compliance, and use of 0.5% chlorhexidine gluconate

and 70% alcohol solution (0.5% CHG) for site prep. Our rates increased following market removal of 0.5% CHG. When new 2 % CHG skin prep solution (2% CHG and 70% alcohol) and a CHG–impregnated patch became available, studies to determine impact of these new products were initiated.

PROJECT: BSIc surveillance was performed by infection control professionals according to CDC definitions and reported quarterly. Initially, CVL utilization was 151 patients/per day had at least one CVL. Staff was educated about each new product prior to implementation. The skin prep was first changed to 2% CHG. Subsequently, CHG–impregnated patch was introduced.

RESULTS: During the study, CVL utilization increased to 220 patients/day with a CVL. Introduction of 2% CHG prep plus the CHG patch resulted in an overall 31% reduction in BSIc, of which a 16% reduction was attributable to the CHG patch. This reduction resulted in averting 135 infections and cost aversion of $2.5 million.

LESSONS LEARNED: Implementing new technologies for reducing BSIc must be an ongoing process. The use of 2% CHG skin prep and a CHG-impregnated patch significantly reduced BSIc in our setting. Evaluation and comparison to hospital-specific baseline data is important to determine the impact of the changes on patient safety and cost management.

Skin Health Improvements Associated with Use of Nitrile Exam Gloves with Dermal Therapy Coating

*D Davis**
R Harper
Cardinal Health, McGaw Park, Illinois

DermTech International, San Diego, California

BACKGROUND: The association between irritated, damaged skin on the hands of healthcare workers (HCWs) and increased risk of transmission of healthcare-associated infections has led the Centers for Disease Control and Prevention to recommend the use of products that help maintain skin integrity.

METHOD: Nitrile exam gloves coated with ingredients involved in skin repair, moisturization, and protection of the skin's barrier properties were studied to determine the effect use of these gloves has on the hands of HCWs with compromised skin. Twenty-six HCWs with dry skin wore a nitrile exam glove with a coating comprised of ingredients proven to have beneficial effects on skin health on one hand and an equivalent nitrile exam glove without the coating on the other.

RESULTS: After 12 successive 15-minute wear periods (each time with new gloves), measurements of skin moisture, erythema, transepidermal water loss, and overall skin dryness were taken from both hands of each subject at baseline and following the final wear period. Nitrile exam gloves with dermal therapy coating produced quantifiable improvements in the skin of clinicians with dry, compromised skin. Wearing exam gloves with the dermal therapy coating resulted in a greater improvement in skin moisturization, produced less erythema, reduced skin flaking, and did not increase water loss through the skin.

CONCLUSIONS: Routine use of exam gloves with this dermal therapy coating has the potential to improve clinicians' skin and contribute to a reduction in the number of healthcare-associated infections by reducing scaliness of the skin and improving overall skin wellness.

Comparison between Glutaraldehyde and Ortho-Phthalaldehyde Air Levels during Endoscopic Procedures

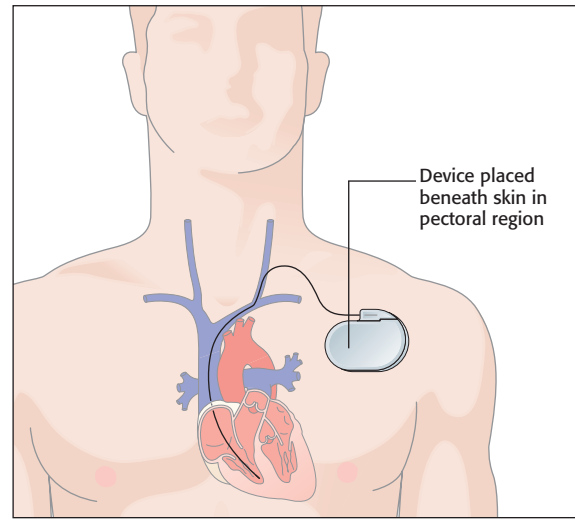
*C Marena**

Cutting surgical-site infection rates for pacemakers and ICDs

BY BETH A.TAYLOR, RN,BC, CVNII

OUR HEART CENTER placed 477 permanent pacemakers or implantable cardioverter-defibrillators (ICDs) in 2003. Out of those surgeries, we received six reports of surgical-site infections. That was six too many. Because I'm the patient-care specialist in the invasive heart lab, my unit director asked me to research the situation and improve our process to prevent infections.

In this article, I'll tell you the steps I took, the evidence-based improvements we made, and the results we achieved.



Getting started

As a first step, my unit director, the technical specialist, our facility's infection control nurse, and I met to review the six infection cases. I compared our infection/complication benchmarks with those of two other facilities, reviewed the literature, and studied recommendations by the Centers for Disease Control and Prevention (CDC) and the Association of periOperative Registered Nurses (AORN). I then compared our facility's policies with recommendations issued by these organizations.

Gathering information

By reviewing the literature, I learned that perhaps 40% to 60% of surgical-site infections are preventable. I also found information about risk factors for surgical-site infections, as follows:

• *Patient risk factors* include advanced age, poor nutritional status, diabetes, smoking, obesity, other infections at a remote body site, colonization with microorganisms, altered immune response, and longer preoperative stay. Some of these factors couldn't be modified on an emergent basis; others could be.

• *Surgical factors* affecting infection risk include duration of surgical hand scrub, scrub technique used on the surgical site, timing and method of preoperative shaving, preoperative skin preparation solution, duration of surgery, antimicrobial prophylaxis, OR ventilation, foreign material in the surgical site (such as a surgical drain), and quality of aseptic technique. We decided to focus on those surgical factors that we could usually modify.

Next, I reviewed all charts in medical records of patients receiving pacemakers or ICDs from January 1 to March 30. I noted the antibiotic used, the dose given, the time it was given compared with the time the incision was made, the procedure used, the length of the surgery, patient age, and whether the patient was diabetic. If the patient was diabetic, I also noted his preoperative blood glucose level.

I learned that to be most effective, the antibiotic must be given within an hour before the incision. When our heart center's data department graphed the antibiotic infused in relation to the time of incision, we learned that this timing was variable in our facility.

I also asked our pharmacists for information about the antibiotics we were using, cefuroxime sodium (Zinacef) and vancomycin. Based on the evidence-based research I reviewed, I believed that we were underdosing our cardiac patients.

Investigating environmental factors

As part of my research, I contacted our hospital's heating and cooling department to discuss the ventilation in our pacemaker/ICD insertion room. I learned that we met all CDC guidelines for proper air exchanges and filter changes.

I also contacted the housekeeping department, which cleans the surgical room between procedures and cleans the walls on weekends. I asked them to send documentation of wall cleaning to my unit director each month. I found that our protocol met AORN recommendations, which call for cleaning the immediate vicinity of the surgery and outward until no debris is visible after each surgery. Walls need to be cleaned between procedures only if they're splattered,

which normally doesn't occur with pacemaker and ICD insertions.

Assembly of experts

I organized a panel of our heart center's experts for a question-and-answer session focused on preventing surgical infections. The panel consisted of two infectious-disease physicians, the nurse who works with them, and our facility's infection control nurse. Also attending were nurses involved in surgical, preoperative, or postoperative care. The panel made several recommendations:

- We needed to improve the timing of the antibiotic administration so infusions would begin less than 1 hour before an incision is made.
- We needed to change our skin preparation solution from povidone-iodine (Betadine) to chlorhexidine gluconate and isopropyl alcohol (ChloraPrep). Although Betadine is clinically acceptable, ChloraPrep has been proven to be much more effective.
- We needed to change our shaving policy. Previously we'd routinely shaved our patients' chests in the preparation area. The AORN recommends not shaving at all because microscopic abrasions increase the infection risk.

We needed to improve the timing of the antibiotic administration so infusions would begin less than 1 hour before an incision is made.

Spreading the word

I compiled packets about the advantages of ChloraPrep and proper antibiotic dosing and distributed them to the cardiac catheterization lab and the cardiovascular surgeons. The cardiac catheterization lab personnel and the surgeons agreed to switch from Betadine to ChloraPrep after reading the literature I'd given them. The surgeons also agreed to adjust the preoperative dose of cefuroxime sodium from 750 mg to 1.5 grams unless renal function is impaired. (We continue to use vancomycin for any patient who's allergic to penicillins or cephalosporins. We have the nurses in the unit start it on call because it takes at least an hour to infuse.)

Hair affairs

Under our new policy, we no longer shave patients before pacemaker or ICD insertion. If hair must be removed, we clip (not shave) with clippers (not a razor) as close to the time of surgery as possible in the preparation area, rather than in the surgical suite. I involved our staff in conducting trials of two different brands of clippers and let them choose which brand to purchase.

Timing is everything

Another significant change involved the timing of prophylactic antibiotics. The optimum time for administering them is within 1 hour of incision. In 2003, we met this standard only 30% to 40% of the time. In 2005, we met this standard 89% of the time.

Our goal is for the surgeon to make the incision within 30 minutes after the antibiotic infusion is complete. We're accomplishing this by giving the antibiotic ourselves in the preparation area instead of having the unit nurse start the antibiotic when the patient is called to surgery.

To educate staff throughout the facility about our improvement efforts, I've made presentations to various clinical and quality control committees. I've also distributed learning packets to all nursing units that care for our pacemaker/ICD patients before and after the insertion procedure. Preventing surgical infections is an ongoing team effort.

Dramatic success

The evidence-based improvements in our heart lab protocols have yielded dramatic results. For 22 months, we had no infections—a zero percent infection rate. At the end of 2005, we had two infections out of 632 pacemaker/ICD surgeries performed. We believe that one of these was due to the patient habitually touching the site and the other one was also unrelated to nursing care.

Because we made several improvements at once (changing the solution preparation, antibiotic dose and timing, and shaving policy), we can't say for sure which were more influential. But we can say that by adhering to key evidence-based standards and protocols, we're protecting our patients from avoidable infections.

SELECTED REFERENCES

Abbott Laboratories. *Best Practices: Guidelines for Prevention of Insertion Site Infection*. Redwood City, Calif., Abbott Laboratories, 2001.

Barnard BM. Fighting surgical site infections. *MPH Infection Control Today*. 75(1):26-32, April 2002.

Centers for Disease Control and Prevention. Guidelines for prevention of surgical site infection, 1999. *Morbidity and Mortality Weekly Report*. 48(15):316, April 23, 1999.

McGarry SA, et al. Surgical site infection due to *Staphylococcus aureus*. *Infection Control and Hospital Epidemiology*. 25(6):461-467, June 2004.

Beth A. Taylor is a patient-care specialist in the invasive heart lab at Aultman Hospital in Canton, Ohio.

SELECTED WEB SITES

Institute for Healthcare Improvement 100,000 Lives Campaign **http://www.ihi.org**

Surgical Care Improvement Project **http://medqic.org/scip/scip_homepage.html**

Last accessed on February 6, 2006.

2% Chlorhexidine Gluconate in 70% Isopropyl Alcohol Donor Arm Scrub Validation

Blood Systems, Inc.
October, 2004
Mona Wilkins, MT(ASCP)HP; Sheryl Kempin, RN; Linda Laukaitis, RN, MGA

Background: In 1994 a large multi center blood collection facility compared the two-step Blood Donor Prep Kit (70% alcohol Sepp® and a 2% iodine tincture Frepp®) to 10% povidone-iodine. Positive skin cultures were lowest using the Blood Donor Prep Kit. As a result of this validation the blood center switched donor arm prep agents.
In 2003 the US Food and Drug Administration (FDA) issued "Options for Arm Preparation", which detailed FDA approved arm preparation procedures. The blood center conducted a Donor Arm Prep validation in 3 facilities comparing two of the four approved arm prep procedures. The objective was to determine the efficiency of 2% chlorhexidine in 70% isopropyl alcohol (ChloraPrep® 1.5 mL Frepp® Applicator) to their current two-step Blood Donor Prep Kit.

Study Design: The validation was divided into two parts. First, a site was selected to do a focused validation that required one specifically trained individual to do side-by-side scrubs and collect skin cultures for colony counts on 40 different volunteers/potential donors. The second part of the validation occurred in two additional sites where several different individuals were trained to do side-by-side scrubs and collect skin cultures for colony counts on 100 different volunteers/potential donors per site.

RESULTS:

Arm Preparation Agent	Site 1 n=40	Site 2* n=100	Site 3 n=100
CHG/IPA	36 no growth 4 growth ≤ 10 CFU	86 no growth 3 growth ≤ 10 CFU 11 growth > 10 CFU	99 no growth 1 growth ≤ 10 CFU
Blood Donor Prep Kit	31 no growth 9 growth ≤ 10 CFU	88 no growth 4 growth ≤ 10 CFU 8 growth > 10 CFU	98 no growth 2 growth ≤ 10 CFU

*Discrepancies in sampling errors and collection area contamination

Conclusion: The 2% chlorhexidine in 70% isopropyl (CHG/IPA) alcohol solution demonstrated efficacy comparable to the Blood Donor Prep Kit. The CHG/IPA prep offers the following advantages; 1) a one-step prep procedure, therefore reducing donor arm preparation time and 2) an alternative prep for donors allergic to iodine.