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Use of a Chlorhexidine Dressing to Reduce Microbial Colonization of Epidural Catheters

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We performed a prospective randomized controlled trial to assess the efficacy of a chlorhexidine dressing in reducing the microbial flora at the insertion site of epidural catheters. These catheters were used for acute pain management and were dressed either by a standardized method or with a CHX/urethane sponge composite. Microbial colonization of the catheter developed in 9 of 31 controls (29.0%) and 1 of 26 (3.8%) catheters with the CHX dressing ($P < 0.05$). The CHX dressing caused no adverse effects. The data suggest that delivery of antiseptic to the catheter wound site reduces catheter colonization with a possible reduction in the risk of epidural catheter-related infection. (Key words: Anesthetic Techniques, Epidural: Infection, catheter. Antiseptic: chlorhexidine.)

FOREIGN BODIES, including catheters, compromise defense mechanisms of the host against infection. Many factors are involved in the evolution of such infections, and include foreign-body-related tissue damage, impairment of local host defenses, and the ability of microorganisms to adhere to implant materials and establish a microenvironment resistant to antimicrobial agents.[1]

The use of epidural catheters to infuse analgesic agents for pain management has become an increasingly popular treatment modality. Epidural abscess is a recognized complication of the use of such catheters.[2,3] Though rare, epidural abscess can rapidly progress to meningitis, paralysis or death. With surgical and antibiotic treatment, the mortality rate was reduced to 13% during the 1980s.[4] Because of the risk of infection, percutaneous catheters are in many cases discontinued or moved to a new site prior to indication of malfunction or evidence of catheter-related infection. Unnecessary catheter removal may pose additional risk, discomfort, and expense to the patient who requires continual vascular access or epidural pain management.

Staphylococcus epidermidis—the organism most frequently isolated from infections associated with medical devices—and other microbes colonizing the skin can be transported by capillary action along the wound tract of a percutaneously inserted catheter.[5] Organisms colonizing the skin at the insertion site are responsible for most episodes of central venous catheter related bacteremias.[6–8] The chain of events leading to infection might be broken by reducing the microbial population at the catheter wound site.

Although suppression of skin flora with an appropriate antiseptic is an essential step prior to any procedure that breaks the integument, the suppressed microflora can rapidly grow back and invade the compromised skin site. Agents applied to the skin undergo drug decay, inactivation by tissue fluids, and loss from desquamation. Therefore, it might prove beneficial to apply a wound dressing which continually delivers antiseptic to provide ongoing protection against invasion from extrinsic organisms on the skin.

Chlorhexidine (CHX) gluconate is an antimicrobial agent used for disinfecting skin surfaces. It has been used widely as a surgical scrub, hand wash, and skin disinfectant. Its safety and efficacy are supported by over 25 yr of clinical experience and extensive laboratory testing on volunteers.§[9]

We present the results of a clinical trial to evaluate the efficacy of a CHX patch in preventing expansion of skin flora at the site of epidural catheter insertion.

Materials and Methods

The dressing consisted of a urethane composite material to which CHX gluconate (Lonza Inc., Fair Lawn, NJ) was chemically bound. The dressing was held in place by a clear urethane film with an acrylic adhesive. The dressing matrix is spongelike, adheres well to skin, and is able to absorb eight times its weight in water. The semipermeable matrix is nonocclusive and has a greater water vapor transmission rate than does intact skin.

In Vitro Analysis of Chlorhexidine Gluconate Dressing

Kinetic Studies of CHX Drug Delivery

Weighed discs of the CHX dressing were placed in 0.9% saline (1 g dressing per 1 l saline). After mixing at

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§ OTC Antimicrobial products and drug and cosmetic products, Report of the FDA OTC Antimicrobial Panel, Sept. 13, 1974. Federal Register 39:179, Part 2.

room temperature on a rotary shaker for 24 h, an aliquot of the saline was analyzed for CHX to determine the amount of drug released from the dressing. CHX was assayed by measuring the absorbance spectrophotometrically at 254 nm and comparing the results to those obtained from a standard curve of known concentrations of CHX. The dressing was transferred to fresh saline and the analysis repeated for a total of 7 sequential days.

Bioassay of CHX Dressing

Discs (6-mm) of the dressing were placed on Mueller-Hinton agar plates seeded with *S. epidermidis* (American Type Culture Collection [ATCC] #12228). Bacterial susceptibility to CHX was determined with the use of standard clinical test procedures that rely on the principles of agar diffusion.[10] After overnight incubation at 35° C, zones of bacterial growth inhibition were measured with calipers and the test discs transferred to freshly inoculated plates. Serial transfer was continued for a total of 10 days, and zone diameters were compared to control discs containing known CHX concentrations. Cellulose discs were spiked with 100 and 25 μg CHX in order to compare drug delivery kinetics from the CHX dressing matrix with those of cellulose.

Dressing Assessment on Nonwounded Skin Sites

After institutional approval and the informed consent of volunteers had been obtained, test and control patches were applied on nonwounded skin sites, either the volar portion of the forearm or on the trunk. Thirty volunteers wore six to eight patches for periods ranging from 1 to 5 days. The control patches were made from the urethan matrix without CHX. The following variables for each site were evaluated:

1. Skin irritation: Patients were questioned daily concerning patch comfort and the presence of burning or itching. Upon removal of the patch, erythema—if present—was documented.

2. Level of skin colonization: Skin sites beneath the patches from 15 volunteers were cultured by placing a sterile cylinder over the patch site, introducing 1 ml phosphate buffered saline (pH = 7.0) and scrubbing the site with a Teflon bar for 1 min. The saline was recovered and the residual CHX neutralized by diluting 1:10 with 10% Tween 80/3% Lecithin. An aliquot then was cultured to blood and eosin–methylene blue (EMB) agars.

3. CHX concentration at skin site: The remaining 15 patients had their scrub-site recovery solutions analyzed for CHX concentration by bioassay or high-performance liquid chromatography (HPLC).[11] The bioassay was done by adding 20 μl of the wash recovery solution to cellulose discs and applying the discs to seeded agar plates, as described above.

Dressing Assessment at Epidural Sites

With institutional approval and informed consent, epidural catheters were inserted in the operating room by the authors (J.M.S. or J.K.G.). Masks and sterile gloves were worn during placement. All patients received epidural medications (morphine sulfate, fentanyl, or hydromorphone) for acute pain management after thoracic, abdominal, or orthopedic surgery. After cutaneous antisepsis with povidone-iodine, a Concord/Portex (Keene, NH) epidural catheter was inserted *via* an L3-to-L5 interspace by standard lumbar insertion technique using the loss of resistance method.

The control dressing consisted of a sterile catheter support pad placed at the insertion site. The exposed length of the catheter was directed cephalad along the spine and over the shoulder, where it was secured with tape to the chest wall. The entire length of the catheter was taped to prevent dislodgement. The CHX test dressing was placed under the support pad and the catheter secured as described above. Catheters were left in place as long as clinically indicated. No insertion-site care was performed, and catheter sites were inspected only at the time of catheter removal.

There were two separate study populations. 1) A pilot study with 17 patients was done to determine the amount of catheter and site colonization with the control dressing. 2) The pilot study was followed by a randomized, controlled clinical trial comprised of 57 patients. Use of the control or CHX dressing was determined by random number.

Microbiologic Methods

Skin at the Insertion Site

The skin at the site of catheter insertion was cultured immediately after catheter removal by pressing a blood agar contact-plate to the skin. Initial studies using Lecithin/Tween 80 incorporated into the agar to neutralize CHX transferred from the skin did not show an increase in recovery of microorganisms. Therefore these additives were not used in the clinical study.

Catheter Wound Tract

A mini-tip swab (Marion Scientific) was inserted into the catheter wound tract, rotated, and placed in transport media until culture. The swab was then streaked onto blood agar and EMB plates.

Catheters

Catheters were removed, with care to avoid touching the adjacent skin, and were placed in a sterile tube for

transport. The 5-cm portion of the distal catheter tip was amputated, placed in 1 ml T-Soy broth and vortexed for 1 min prior to plating 100 μl aliquots to blood agar and EMB.

Catheter Hubs and Lumen

Catheter segments and hubs were flushed with broth, and 100-μl aliquots were cultured to determine the level of intraluminal and hub colonization. Consistently negative results during the pilot study led to the abandonment of this method for the clinical study.

All culture plates were incubated aerobically at 35° C. Colony counts were performed at 48 h. All isolates were identified by standard microbiologic methods.[12] Staphylococcus biotypes were determined with a commercial kit (Staphident, Analytab Products, Plainview, NY).

A catheter was considered colonized (positive) if the culture results met both of the following criteria:

1. Greater than or equal to 10^3 colonies isolated from the wound tract and catheter tip cultures.
2. Concurrent isolation from the skin culture of those isolates recovered from the catheter or wound track.

This presumes that catheter colonization originates at the insertion site after a critical level of skin colonization has been reached.

Statistical Analysis

Cultures with no growth were scored "0," and positive cultures were scored "1." The mean score for each group was computed and compared using Student's t test for independent observations. A one-tailed test of significance was chosen to test the expectation that the CHX dressing would reduce the number of positive cultures. In addition, a comparison of proportions of positive cultures in both groups was conducted by computing the nonparametric z-score. Statistical significance was defined as $P < 0.05$. Data analysis was performed using the Abstat Statistical Program (Anderson-Bell).

Results

In Vitro Results

The bioassay demonstrated that the CHX dressing delivered drug in a biphasic mode; greater concentrations were delivered from days 1–3 compared to steady-state release approximating zero-order kinetics from days 4–10 (fig. 1). Quantitative analysis of the dressing after 10 days of serial transfer showed a 30% decrease in total drug concentration. In contrast, the spiked cellulose discs displayed a first-order drug release profile, indicative of decreased drug bioavailability as a function of time.

CHX delivery measured by efflux in saline showed increasing amounts of drug released at each time point through 7 days (fig. 2).

Assessment of *In Situ* Dressing on Nonwounded Skin

The CHX dressings were well tolerated and did not cause any adverse skin reactions. Culture results at each test point demonstrated that the CHX dressing reduced the microbial population an average of 2 $\log_{10}$ compared to the nonmedicated control dressing (fig. 3).

Measurement of CHX concentrations from the skin washes of 15 patients showed that the CHX dressing was

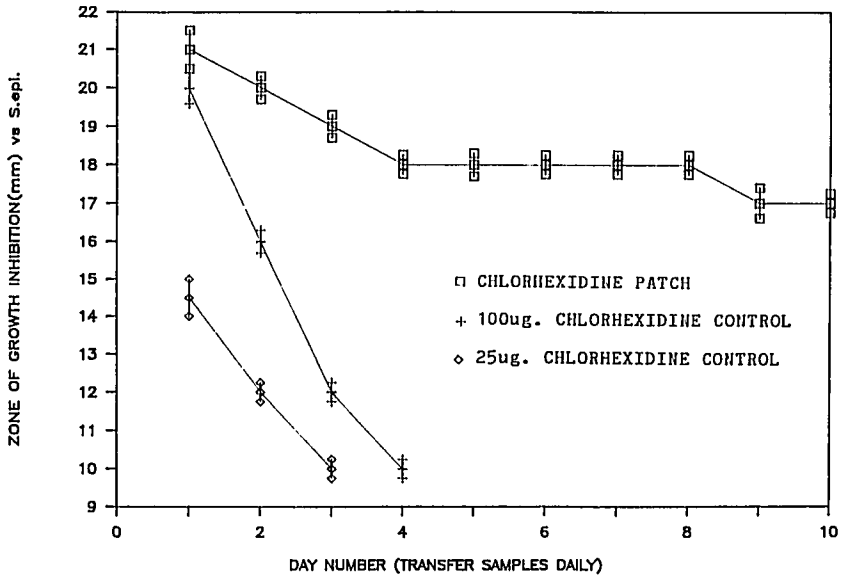

FIG. 1. Zones of inhibition of CHX/dressing and cellulose discs against *S. epidermidis*. Samples removed and placed on freshly seeded plates at daily intervals. One hundred- and 25-μg CHX standards will produce zones of 20 and 14.5 mm, respectively. Data are expressed as mean ± SD.

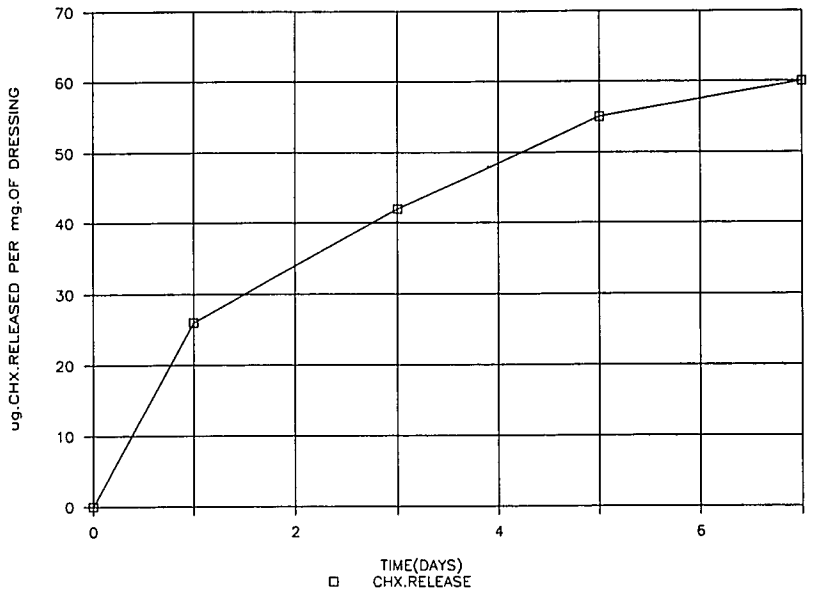

FIG. 2. *In vitro* loss of CHX from dressing in saline: drug efflux as a function of time. Sample transferred daily to fresh solvent. Samples run in triplicate. SD <4%.

able to deliver drug approximating steady-state conditions for 5 days (figure 4). The wide range of drug concentrations recovered reflect the variability in skin-scrub efficiency and individual patient differences.

PILOT STUDY

Of 17 patients, 5 (29.4%) had positive culture results, as previously defined. Similar results obtained from quantitative culture of intravascular catheters have aided in distinguishing contamination from infection.[13] Since all catheters associated with bacteremia had at least 10^3 cfu, catheters with $\geq 10^3$ cfu were considered infected. Catheters were left in place 2–8 days (mean 3.8 days). The average days in place for positive catheters was 4.5 days *vs.* 3.5 days for negative catheters (table 1). All cultures of the catheter hub and lumen were negative. *S. epidermidis* was the predominant isolate from four of the five positive cultures. *Pseudomonas spp.* predominated in one set of cultures. All skin sites were graded as unremarkable, showing slight erythema around the catheter wound site.

CLINICAL STUDY

Of 31 control catheter cultures, 9 were colonized (29.0%). The test group had 1 of 26 positive cultures (3.8%). The difference was statistically significant ($P = 0.006$). *S. epidermidis* was the predominant isolate from all colonized catheters or wound tracts. Control popula-

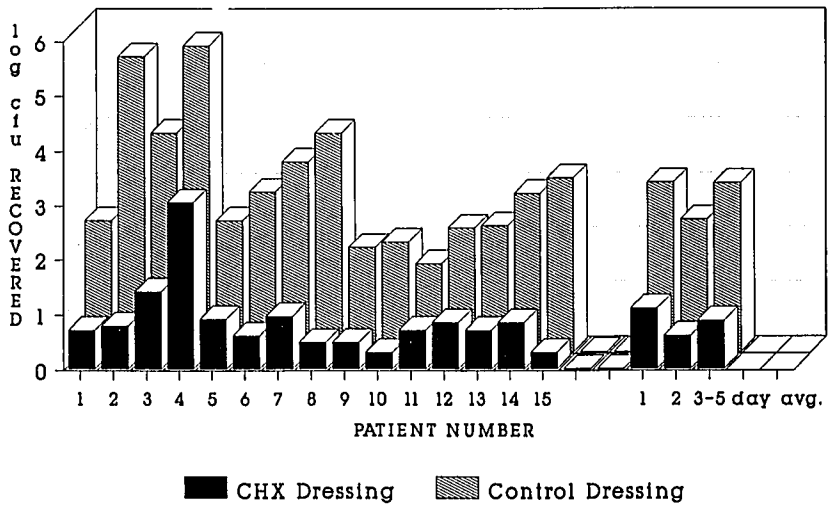

FIG. 3. Skin culture results. Number of organisms recovered from nonwounded skin sites under control and CHX dressings. Data shown are from cultures taken after dressing was in place for 3–5 days on each of 15 patients. At right are 1-, 2-, and 3–5-day averages.

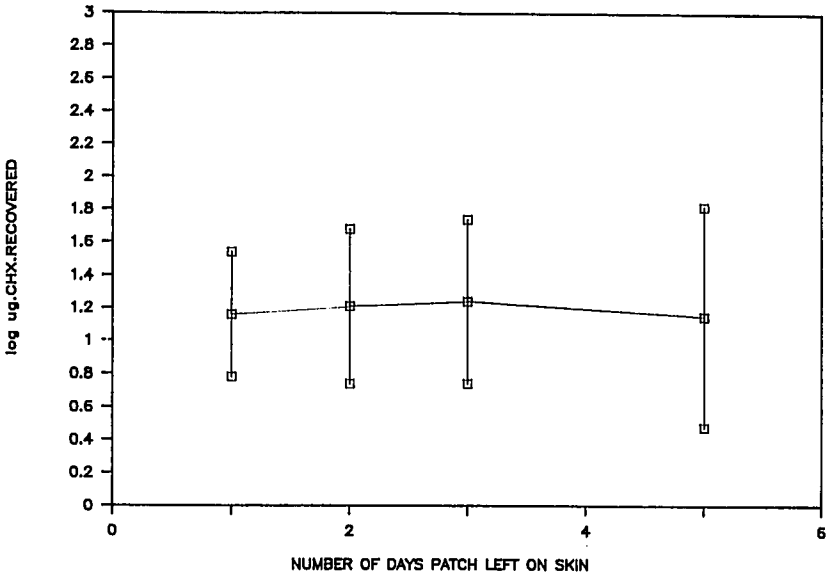

FIG. 4. Quantitative analysis of CHX concentrations recovered from skin washes of nonwounded sites: analysis of skin-scrub solutions. Bioassay data are expressed as mean ± SD. n = 15.

tion catheters were in place an average of 3.7 days *vs.* 3.6 days for the test catheters. Skin site evaluation showed no significant difference in inflammation between the two dressing regimens. The CHX dressings were well tolerated and did not cause any adverse skin reactions. The CHX dressings absorbed blood and exudate from the catheter tract, and thus prevented the accumulation of potential growth substrates for microorganisms.

Discussion

Although percutaneous devices are mainstays of modern health care delivery, these devices disrupt the primary barrier to infection, the intact epithelium. Most device-related infections result when a critical microbial inoculum, overwhelming local host defenses, is reached.[14] The presence of a foreign device reduces the number of organisms necessary to initiate infection. It is well established that infections caused by implants are resistant to antimicrobial therapy. Phagocytic functions of resident neutrophils are deficient in the presence of a foreign body, and effective treatment often necessitates removal of the device.[1,15]

S. epidermidis and other coagulase-negative Staphylococci are the organisms most frequently isolated from infections of indwelling foreign devices.[15] Because of their

TABLE 1. Catheter Site Colonization Associated with Epidural Catheters

Parameter	Controls (n = 48)		Chlorhexidine Dressing (n = 26)
	Pilot (n = 17)	Clinical (n = 31)	
Number of colonized catheters	5 (29.4%)	9 (29.0%)	1 (3.8%)
Days *in situ*			
Mean ± SD (range)	3.8 ± 1.3 (2–8)	3.7 ± 1.3 (2–8)	3.6 ± 1.2 (2–8)
Colonized catheters (mean)	4.5	4.3	3.0 (n = 1)
Noncolonized catheters (mean)	3.5	3.4	3.6

Isolates from Colonized Catheters and Catheter Sites

Organism	Controls (n = 14)	CHX Dressing (n = 1)
S. epidermidis	12	1
S. hominis	2	
S. hæmolyticus	1	
Enterococci	1	
Pseudomonas sp.	1	
Bacillus sp.	1	
Candida sp.	1	
Diptheroids	3	

prevalence on the skin, increased resistance to most antibiotics, and ability to adhere to biomaterials, *S. epidermidis* strains have become significant nosocomial pathogens.[16] By adhering to catheter polymers and producing biofilms (slime), these strains are able to avoid host defense factors and antibiotics.[17] This virulence mechanism is best overcome by efforts to prevent bacterial colonization of catheters.

CHX is a broad-spectrum antimicrobial agent of low toxicity. Dermal absorption has been shown to be absent or negligible.[9] Additionally, CHX has a low skin irritancy and sensitization potential. The optimum *p*H range of CHX activity is 5.5–7.0, which corresponds to skin *p*H. CHX disrupts microbial cell membranes and thereby leads to the loss or precipitation of cell contents. Minimum inhibitory concentrations of CHX for Staphylococci are <10 μg/ml.[9] Although isolated instances of plasmid-mediated resistance to CHX have been reported, the majority of studies and clinical experience have not shown an association between resistance to antibiotics and concomitant resistance to CHX.[18]

CHX is for external use only. It has a strong affinity for the skin, and thus demonstrates persistence, an important attribute for skin antiseptics.[19] Unlike the alcohols and iodophors, the activity of CHX is not significantly affected by blood or other organic material.[20] The iodophors lack persistence and demonstrate a propensity for skin irritation and allergic reactions in sensitive individuals. In a large, prospective clinical trial, 2% CHX was found superior to both povidone-iodine and 70% alcohol for cutaneous disinfection of catheter sites.¶

Results with the CHX dressing we studied suggest that continuing delivery of antiseptic to the catheter insertion site is a promising advance for the prevention of catheter-related infection. In the randomized clinical trial, patients had catheters in place for similar time periods. Catheters with CHX dressings were less than one seventh as likely to become colonized. There were no reported or observed adverse effects from the dressing. The dressing aided in securing the catheter and absorbed wound tract drainage. Although it was not possible to visualize the insertion site with the dressing in place, assessment of the site was possible by palpation. The semi-permeable nature of the matrix allowed fluid transport. Underneath occlusive dressings or tape, bacterial growth may be enhanced as a result of the moist microenvironment favorable to microbial proliferation.

Epidural abscess is a recognized complication of epidural anesthesia. The increased use of epidural catheters, together with the tendency to leave catheters in place for longer periods, may lead to an increase in catheter-related infections. Previous studies have demonstrated the potential for contamination of epidural catheters.[21,22] Recently, a case of bacterial meningitis was reported after epidural anesthesia.[23] Upon removal of the catheter 48 h after insertion, cellulitis and tenderness at the insertion site was found. The patient subsequently developed meningitis confirmed by diagnostic lumbar puncture.

Greater numbers of critically ill, immunocompromised patients have epidural catheters inserted for pain management with the accompanying risk of infection. We conclude that the use of a CHX dressing can reduce the level of colonization at epidural catheter sites and thus possibly reduce the risk of epidural catheter-related infection.

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References

1. Dougherty SH: Pathobiology of infection in prosthetic devices. Rev Infect Dis 10:1102–1117, 1988
2. Baker AS, Ojemann RG, Swartz MN, Richardson EP: Spinal epidural abscess. N Engl J Med 293:463–468, 1975
3. North JB, Brophy BP: Epidural abscess: A hazard of spinal epidural anaesthesia. Aust NZ J Surg 49:484–485, 1979
4. Danner RL, Hartman BJ: Update of spinal epidural abscess: 35 cases and review of the literature. Rev Infect Dis 9:265–274, 1987
5. Cooper GL, Schiller A, Hopkins CC: Possible role of capillary action in pathogenesis of experimental catheter-associated dermal tunnel infections. J Clin Microbiol 26:8–12, 1988
6. Maki DG: Infections associated with intravenous lines, Current Topics in Clinical Infectious Disease. Edited by Swartz M, Remington J. New York, McGraw-Hill, 1982, pp 309–363
7. Bjornson HS, Colley R, Bower RH: Association between microorganism growth at the catheter site and colonization of the catheter in patients receiving total parenteral nutrition. Surgery 92:720–727, 1982
8. Maki DG, Cobb L, Garman JK, Shapiro JM: An attachable silver-impregnated cuff for prevention of infection with central venous catheters: A prospective randomized multicenter trial. Am J Med 85:307–314, 1988
9. Gardner JF, Gray KG: Chlorhexidine, Disinfection, Sterilization and Preservation. Edited by Block SS. Philadelphia, Lea & Febiger, 1983, pp 251–270
10. Barry AL, Thornsberry C: Susceptibility tests, Manual of Clinical Microbiology, 4th edition. Edited by Lennette EH, Balows A, Hausler WJ, Shadomy HJ. Washington, American Society for Microbiology, 1985, pp 978–987
11. Broughham LR, Cheng H, Pittman KA: Sensitive high-performance liquid chromatographic method for the determination of chlorhexidine in human serum and urine. J Chromatogr 383: 365–373, 1986
12. Kloos WE, Smith PB: *Staphylococci*, Manual of Clinical Microbiology, 4th edition. Edited by Lennette EH, Balows A, Hausler WJ, Shadomy HJ. Washington, American Society for Microbiology, 1985, pp 143–153

¶ Maki DG, Alvarado C, Ringer M. Abstract No. 341, Program Abstracts, Twenty-Seventh Interscience Conference on Antimicrobial Agents and Chemotherapy, 1987.

13. Cleri DJ, Corrado ML, Seligman SJ: Quantitative culture of intravenous catheters and other intravascular inserts. J Infect Dis 141:781–786, 1980
14. Christensen GD, Baddour LM, Hasty DL, Simpson WA: Microbial and foreign body factors in the pathogenesis of medical device infections, Infections Associated with Indwelling Medical Device Infections. Edited by Bisno A, Waldvogel F. Washington, American Society for Microbiology, 1989, pp 27–59
15. Johnson GM, Lee DA, Regelmann WE, Gray ED, Peters G: Interference with granulocyte function by *Staphylococcus epidermidis* slime. Infect Immun 2:1266–1268, 1986
16. Hamory BH, Parisi JT: *Staphylococcus epidermidis:* A significant nosocomial pathogen. Am J Infect Control 15:59–74, 1987
17. Ludwicka A, Peters G, Seng PM, Gray ED, Pulverer G: Investigation on extracellular slime substance produced by *Staphylococcus epidermidis.* Zentralbl Bakteriol Hyg [A] 258:256–267, 1984
18. Yamamoto T, Tamura Y, Yokota T: Antiseptic and antibiotic resistance plasmid in *Staphylococcus aureus* that possesses ability to confer chlorhexidine and acrinol resistance. Antimicrob Agents Chemother 32:932–935, 1988
19. Leyden JJ, Stewart R, Kligman AM: Updated methods for evaluating topical antimicrobial agents on human skin. J Invest Derm 72:165–70, 1979
20. Lowbury EJ, Lilly HA: The effect of blood on disinfection of surgeons' hands. Br J Surg 61:19–21, 1974
21. Barreto RS: Bacteriological culture of indwelling epidural catheters. ANESTHESIOLOGY 23:643–646, 1962
22. Hunt JR, Rigor BM, Collins JR: The potential for contamination of continuous epidural catheters. Anesth Analg 56:222–225, 1977.
23. Ready LB, Helfer D: Bacterial meningitis in parturients after epidural anesthesia. ANESTHESIOLOGY 71:988–990, 1989.