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Association of Slime with Pathogenicity of Coagulase-Negative Staphylococci Causing Nosocomial Septicemia

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To assess the role of slime in the pathogenesis of nosocomial bloodstream infections caused by coagulase-negative staphylococci, we compared the characteristics of 27 nosocomial bloodstream isolates with those of 27 skin isolates from non-hospital personnel. Of 27 bloodstream isolates, 14 were judged to be significant by a clinical index, and 13 were contaminants. Slime production was observed in 13 of 14 significant isolates but in only 3 of 13 contaminants ($P = 0.0003$) and 4 of 27 skin isolates ($P = 0.0001$). The 14 pathogens were identified as *Staphylococcus epidermidis*. Only 7 of 13 contaminants and 9 of 27 skin isolates belonged to the same species ($P < 0.006$). Slime-producing strains of *S. epidermidis* represented 13 of 14 pathogens but only 2 of 13 contaminants ($P < 0.0003$). Neither adherence to Teflon catheters nor phagocytosis and killing of coagulase-negative staphylococci by polymorphonuclear leukocytes was significantly influenced by slime production. Nevertheless, the identity of the organism and the slime production test predicted the clinical significance of blood isolates of coagulase-negative staphylococci with an overall accuracy of 89%.

Primary bloodstream infections, those unrelated to a distal anatomic site, represent 20 to 45% of endemic and 80% of epidemic nosocomial bloodstream infections (26, 27). Recently, gram-positive organisms, especially coagulase-negative staphylococci, have emerged as important pathogens in catheter-related bloodstream infections in our institution (R. I. Stillman, L. G. Donowitz, and R. P. Wenzel, Program Abstr. 23rd Intersci. Conf. Antimicrob. Agents Chemother., abstr. no. 933, 1983) as well as in others (4, 12, 15, 24, 28, 34–36). With electron microscopy studies, the catheter has been shown to be heavily colonized with bacteria embedded in a mucoid substance referred to as slime (5, 22).

Slime production has been shown to play a major role in the pathogenesis of infections caused by *Pseudomonas aeruginosa* (20), *Escherichia coli* (13, 29), *Staphylococcus aureus* (18, 37), and others (8–10). The role of slime in infections caused by coagulase-negative staphylococci has also been suggested in animal models (6; L. M. Baddour, G. D. Christensen, A. L. Bisno, W. A. Simpson, M. G. Hester, and E. H. Beachey, 24th ICAAC, abstr. no. 328, 1984) and in clinical studies (3, 5). In a study by Christensen et al. (5), 60% of clinically significant bloodstream isolates of coagulase-negative staphylococci produced slime, as did 37% of contaminants. Their results showed a statistically significant, although not striking, association between slime production and clinical disease. However, hospital strains were not compared with strains carried on the skin of healthy subjects.

To assess the relationship between slime and pathogenicity, we evaluated slime production by isolates of coagulase-negative staphylococci. They were obtained from blood cultures of hospitalized patients with proven sepsis, from blood culture contaminants, and from the hands of non-hospital personnel. We also studied the effect of slime on bacterial adherence to catheters and on the bactericidal activity of polymorphonuclear leukocytes (PMNL).

MATERIALS AND METHODS

Isolation and identification of organisms. We collected 27 coagulase-negative staphylococcal isolates from consecutive blood cultures obtained from 27 patients in different locations at the University of Virginia Hospital. We obtained 27 skin isolates of coagulase-negative staphylococci from the hands of 11 non-hospital personnel by using cotton swabs. All isolates were gram-positive, catalase-positive, coagulase-negative cocci. All were oxidase negative as determined by the 6% tetramethylphenylenediamine dimethyl sulfoxide oxidase reagent, thus excluding micrococci (11). Species identification and biotyping were performed with the Staph-Ident system (19) (Analytab Products, Plainview, N.Y.). American Type Culture Collection strains of *Staphylococcus epidermidis* (ATCC 14990), *S. aureus* (ATCC 25923), *Staphylococcus sciuri* (ATCC 29060), and *Staphylococcus simulans* (ATCC 27851) were used as control organisms. Duplicate isolates from the same subject were excluded if they had the same biotype and slime production test results. The clinical significance of the bloodstream isolates was determined with a grading score by using the following criteria: (i) organism growing in more than one blood culture bottle or in more than one blood culture set; (ii) blood culture positive within the first 3 days; (iii) another site (i.e., catheter) growing the same organism, as determined by species, biotype (using Staph-Ident), and the slime test result; (iv) inflammatory signs at site of intravascular catheter; (v) fever (temperature of >38°C for more than 24 h); (vi) significant decrease in blood pressure (systolic pressure, less than 100 mm Hg); (vii) increase in creatinine value by at least 20% or significant decrease in urine output, or both; (viii) significant increase in leukocyte count over base-line level; (ix) belief of physician that patient is septic and entry of this on chart; and (x) rapid improvement after specific therapy or follow-up consistent with true infection. From these data, a clinical index score was calculated which represented the percentage of fulfilled criteria. A clinical index score of >50%

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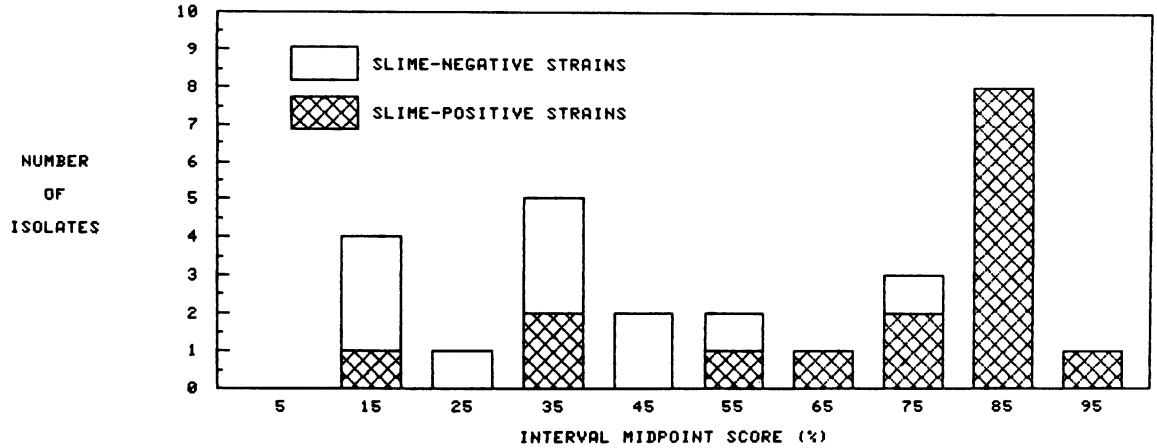

FIG. 1. Distribution of clinical index scores of patients with coagulase-negative staphylococcal bloodstream isolates. Distributions were determined by chart review and expressed as the percentage of fulfilled criteria. Clinical index scores were grouped in intervals. Each bar represents the midpoint score of the corresponding interval. Two distinct distributions of clinical index scores can be observed, one with a mode of 35%, the other with a mode of 85%.

on criteria which could be evaluated was considered to represent a true infection.

Slime production test. Slime production was assessed as described by Christensen et al. (5). We transferred 4 colonies from fresh 5% sheep blood agar plates to 10 ml of tryptic soy broth (Difco Laboratories, Detroit, Mich.) contained in 15-ml plastic conical tubes (Becton Dickinson Labware, Oxnard, Calif.). After 18 to 24 h of incubation at 37°C in ambient air, the culture broth was poured gently, and the tubes were examined for the presence of a film on the inside walls. The absence of a film or the mere presence of a ring at the liquid-air interface was interpreted as a negative result. Positive results were recorded as 1+ if the film covered only the cone of the tube and 2+ if it covered the entire inner surface of the tube. All isolates were coded before we conducted the test so that the interpreter was unaware of the origin of the isolates. In addition, each test was interpreted by two different observers. A minor discrepancy was defined as a disagreement between the two observers on the intensity of a positive result; a major discrepancy was defined as that in which one observer recorded a negative result and the other recorded a positive result. One minor discrepancy occurred, but no major discrepancies occurred between the two observers in 54 tests.

Adherence test. We evaluated the adherence of our clinical isolates to Teflon catheters by the method described by Sheth et al. (32). Segments of 5 cm each of a sterile catheter were cut with a scalpel. Organisms were grown in tryptic soy broth for 4 h at 37°C without shaking, centrifuged at 2,000 × *g* for 10 min, and washed twice in 0.01 M phosphate-buffered saline, pH 7.2. After the organisms were resuspended in phosphate-buffered saline, the final turbidity was adjusted to one-half of McFarland standard 1.0. A dilution (1:100) of this suspension was prepared by transferring 0.1 ml of it to 9.9 ml of phosphate-buffered saline, yielding a final inoculum of approximately 5×10^5 CFU/ml as determined by plate counts. The catheter segments were immersed in the suspension for 30 min at 37°C. They were then removed, rinsed with sterile distilled water, and rolled over the surface of a 5% sheep blood agar plate. We counted the colonies growing and recorded the number after overnight incubation of the plates at 37°C. Each test was done in duplicate, and the mean of both counts was used for statistical analysis.

Phagocytic killing of PMNL. The bactericidal activity of PMNL was tested against five slime-producing, clinically significant organisms and five slime-negative contaminants. PMNL were obtained from the same donor in all experiments by centrifugation after dextran sedimentation (30). Phagocytosis and intracellular killing by PMNL were quantitated by previously described methods (7). The organisms were mixed with PMNL in a ratio of 1:1 at a final concentration of 1×10^6 to 5×10^6 cells per ml. Phagocytosis and bactericidal activity of PMNL were assessed at 0, 15, 30, 60, 120, and 180 min. A strain of *S. aureus* Wood 46 served as a control organism. In addition, slime production was retested concomitantly for each strain.

Statistical analysis. Rates were compared by the exact test of Fisher. Student's *t* test and Mann-Whitney test were used to compare means.

RESULTS

Clinical significance of blood isolates. The clinical index scores obtained by chart review show a bimodal distribution (Fig. 1). One group of patients had a distribution of clinical scores with a mode of 35% and a mean of 29%; another group of patients had a mode of 85% and a mean clinical score of 80%. The probability of obtaining such a distribution by chance alone is less than 0.0001. A score of >50% was used to distinguish one population (pathogens; $n = 14$) from the other (contaminants; $n = 13$).

Slime production. Pathogenicity was much more likely to be associated with slime-producing strains than with slime-negative organisms (odds ratio, 43.3) (Table 1). Furthermore, the proportion of slime producers among clinically significant strains was much higher than it was among contaminants and skin isolates (13/14 versus 4/27; $P = 0.0001$) (Fig. 1 and Table 1).

The species identity also correlated with the clinical significance of the isolates. *S. epidermidis* was found more frequently among pathogenic organisms than it was among contaminants (14/14 versus 7/13; $P = 0.006$) or skin isolates (14/14 versus 9/27; $P < 0.0001$). Slime production was associated with the identity of the organism. *S. epidermidis* was also more common among slime producers than it was among slime-negative organisms (15/16 versus 6/11; $P =$

TABLE 1. Characteristics of bloodstream and skin isolates of coagulase-negative staphylococci

Strain or characteristic	No. of bloodstream isolates		
	Pathogens (n = 14)	Contaminants (n = 13)	Skin isolates (n = 27)
Slime positive	13	3[a]	4[b]
S. epidermidis	14	7[c]	9[d]
Slime-positive *S. epidermidis*	13	2[d]	2[d]

[a] $P = 0.003$ (pathogens versus contaminants).
[b] $P = 0.0001$ (pathogens versus skin isolates).
[c] $P = 0.006$ (pathogens versus contaminants).
[d] $P < 0.0001$.

TABLE 3. Effect of slime on adherence of coagulase-negative staphylococci to polyvinyl chloride catheters

Slime production	Mean adherence (CFU)[a] of:		
	Group 1 (n = 10)[b]	Group 2 (n = 10)[b]	Overall (n = 20)
+	71	29	25
−	28[c]	7[d]	9[e]

[a] Number of colonies adhering to a 5-cm catheter segment, mean of duplicate tests (see the text for details).
[b] Groups 1 and 2 consisted of five clinically significant slime-positive and five slime-negative contaminants each. Their results are presented separately because the tests were performed on different days.
[c] $P = 0.14$.
[d] $P = 0.53$.
[e] $P = 0.24$.

0.027), and produced slime more frequently than did other species (odds ratio, 12.5).

To determine the relative contribution of each factor to the determination of the pathogenicity of the organism, we categorized the clinical isolates into four groups according to their identity and their ability to produce slime. Although the numbers in some categories were small, the distribution of pathogenic isolates was markedly different from that of contaminants. Slime-producing *S. epidermidis* strains were 13 of 14 pathogens but only 2 of 13 contaminants ($P < 0.0001$).

Both slime production and the species of the organism appeared to be important factors in the determination of pathogenicity; 13 of 15 slime-positive *S. epidermidis* strains, but only 1 of 6 slime-negative *S. epidermidis* strains, were clinically significant ($P = 0.0006$). The effect of slime production on the pathogenicity of other species could not be evaluated, since only one isolate belonged in this category.

Based on the preceding results, we estimated the accuracy of the slime production test and the species of the organism in predicting the clinical signficance of bloodstream isolates (Table 2). Although the species of the organism was a sensitive predictor, it lacked specificity and thus had a poor positive predictive value of only 67%. The slime production test was also a sensitive determinant of pathogenicity. It was more specific and thus had a better positive predictive value than did the species of the organism. When both the results of the slime production test and the species of the organism were combined, specificity was increased to 85% without significantly affecting the sensitivity (93%), thus improving the overall predictive value (87%).

Adherence to Teflon catheters. Slime-positive organisms adhered to Teflon in higher numbers on the average than did slime-negative organisms, but the difference was not statistically significant because of wide variations in the counts obtained with this technique (Table 3).

TABLE 2. Accuracy of slime production test and species identity in predicting clinical significance of coagulase-negative staphylococcal bloodstream isolates

Predictor	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Slime positive	93	77	81	91
S. epidermidis	100	46	67	100
Slime-positive *S. epidermidis*	93	85	87	92

Phagocytic killing by PMNL. No difference between slime-positive and slime-negative organisms was observed in the killing curves (Fig. 2).

DISCUSSION

Infections caused by coagulase-negative staphylococci have occurred in association with implantable medical devices such as ventriculoperitoneal shunts, prosthetic heart valves, vascular grafts, and hip prostheses (17, 21, 33). Previous reports have suggested that slime has a role in the pathogenesis of coagulase-negative staphylococcal infections of Holter shunts (3), surgical sutures (18), and intravenous catheters (5). Coagulase-negative staphylococci have been shown by electron microscopy to form microcolonies on the catheter surface in vitro (5, 23, 31) and in vivo (22). It has also been suggested that the organisms can multiply on the catheter surface even in the absence of nutrients in the surrounding medium (31).

In an earlier study of catheter-related sepsis, the association between slime and clinical disease, though present, was not striking (5). In that study, only 22 of 35 suspected pathogens (63%) produced slime, whereas in our study 13 of 14 (91%) produced slime. However, in the former study, patients had an average of two strains per infection, one of which may have been a contaminant, thus affecting the overall percentage of slime producers among true pathogens. Recent reports indicate a similarly high correlation (81%) between slime production and clinical disease (D. S. Davenport, R. M. Massanari, M. A. Pfaller, M. Bale, and W. J. Hierholzer, 24th ICAAC, abstr. no. 452, 1984). The lack of slime production among random skin isolates from non-hospital personnel lends further support to the hypothesis that slime production may be a characteristic specific to nosocomial pathogenic strains of coagulase-negative staphylococci.

S. epidermidis was more prevalent among pathogens than it was among contaminant strains of coagulase-negative staphylococci or among skin isolates of non-hospital personnel. This finding confirms that of a recent study (J. Ramos-Jimenez, S. B. Greenberg, and T. R. Cate, 24th ICAAC, abstr. no. 471, 1984). A high frequency of slime production among *S. epidermidis* strains may underlie this finding (1, 3). Conversely, slime-negative *S. epidermidis* strains were less likely to be pathogenic than slime-positive strains of that species. Both the species of the organism and its ability to produce slime seem to be important in determining pathogenicity, but we could not assess the single effect of slime because of the low number of isolates tested.

It has been suggested that slime may promote adherence

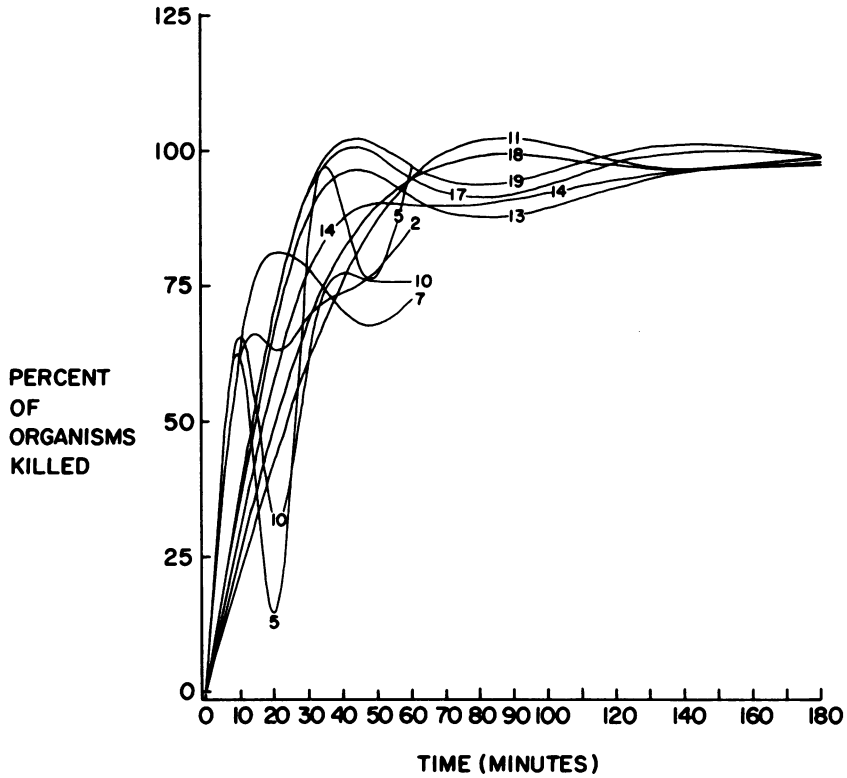

FIG. 2. Bactericidal activity of PMNL against bloodstream isolates of coagulase-negative staphylococci. Strains 7, 10, 17, and 19 are slime-producing pathogens. Strains 2, 5, 11, 13, and 14 are non-slime-producing contaminants.

(5, 31). However, we could not show a significant correlation between adherence to Teflon catheters and slime production. Nevertheless, the wide variations observed with this method suggest that a more reliable technique should be used to assess this question more accurately (2, 16, 25). By the use of sonication to release adherent organisms, it was recently shown that a mucoid strain of *S. epidermidis* adhered better to polyvinyl chloride than did a non-mucoid strain of *Staphylococcus hominis* (D. M. Forman, R. J. Sherertz, R. Johnson, L. C. Koo, and S. O. Heard, 24th ICAAC, abstr. no. 369, 1984). The organisms differed, however, by more than one factor (species and slime production in that case). The type of catheter material should also be taken into account when comparing adherence of organisms (16, 32).

No difference in phagocytic killing was observed between slime-positive and slime-negative organisms. Peters et al., using high concentrations of purified slime, inhibited lymphocytic response to polyclonal activators (14). However, inhibition occurred only when the lymphocytes were incubated with slime for at least 2 days, probably too long for this mechanism to be relevant in vivo. In a more recent study, slime was shown to inhibit PMNL chemotaxis and degranulation (G. M. Johnson, W. E. Regelmann, E. D. Gray, and P. G. Quie, 24th ICAAC, abstr. no. 55, 1984). It is possible that in our study, before incubation with PMNL, slime was washed off or its concentration was reduced below a critical level. Alternatively, slime-producing organisms may escape phagocytosis only in the presence of a foreign body (6, 38, 39). These hypotheses need further assessment.

Our results indicate that knowledge of the species of the organism and its ability to produce slime may assist the clinician in evaluating the clinical significance of a coagulase-negative staphylococcal isolate growing from a blood culture. The predictive values were obtained from data on bloodstream isolates. Any extrapolation to catheter isolates should be made with caution, since the organisms colonizing catheters may be different from those causing septicemia. The stability of slime production in vitro also needs to be reassessed. Although Christensen et al. previously reported that it was a stable parameter (5), we noted that some strains lost that slime-producing ability after repetitive subculturing. Finally, the whole concept of slime-mediated virulence must be reviewed in the light of a possible protective effect conferred by tissue and serum proteins which have been shown to inhibit slime-mediated adherence to catheters (2, 18).

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LITERATURE CITED

1. **Baird-Parker, A. C.** 1965. The classification of staphylococci and micrococci from world wide sources. J. Gen. Microbiol. **38**:363–387.
2. **Barrett, S.** 1983. Staphylococcal infection of plastic inserts; a method to measure staphylococcal adhesion. Br. J. Clin. Pract. **25**:81–85.
3. **Bayston, R., and S. R. Penny.** 1972. Excessive production of mucoid substance in *Staphylococcus* SIIA: a possible factor in colonization of Holter shunts. Dev. Med. Child Neurol. **14**(27): 25–28.
4. **Christensen, G. D., A. L. Bisno, J. T. Parisi, B. McLaughlin,**

M. G. Hester, and R. W. Luther. 1982. Nosocomial septicemia due to multiply antibiotic-resistant *Staphylococcus epidermidis*. Ann. Intern. Med. **96**:1–10.
5. **Christensen, G. D., W. A. Simpson, A. L. Bisno, and E. H. Beachey.** 1982. Adherence of slime-producing strains of *Staphylococcus epidermidis* to smooth surfaces. Infect. Immun. **37**: 318–326.
6. **Christensen, G. D., W. A. Simpson, A. L. Bisno, and E. H. Beachey.** 1983. Experimental foreign body infections in mice challenged with slime-producing *Staphylococcus epidermidis*. Infect. Immun. **40**:407–410.
7. **Cohn, Z. A., and S. I. Morse.** 1959. Interactions between rabbit polymorphonuclear leukocytes and staphylococci. J. Exp. Med. **110**:419–443.
8. **Duguid, J. P., E. S. Anderson, and I. Campbell.** 1966. Fimbriae and adhesive properties in Salmonellae. J. Pathol. Bacteriol. **92**:107–138.
9. **Duguid, J. P., and R. R. Gillies.** 1957. Fimbriae and adhesive properties in dysentery bacilli. J. Pathol. Bacteriol. **74**:397–411.
10. **Ellen, R. P., and R. J. Gibbons.** 1972. M protein-associated adherence of *Streptococcus pyogenes* to epithelial surfaces: prerequisite for virulence. Infect. Immun. **5**:826–830.
11. **Faller, A., and K. Schleifer.** 1981. Modified oxidase and benzidine tests for separation of staphylococci from micrococci. J. Clin. Microbiol. **13**:1031–1035.
12. **Forse, R. A., C. Dixon, K. Bernard, L. Martinez, A. Peter, H. McLean, and J. L. Meakins.** 1979. *Staphylococcus epidermidis*: an important pathogen. Surgery (St. Louis) **86**:507–514.
13. **Fowler, J. E., and T. A. Stamey.** 1977. Studies of introital colonization in women with recurrent urinary infections. VII. Role of bacterial adherence. J. Urol. **117**:472–476.
14. **Gray, E. D., G. Peters, M. Verstegen, and W. E. Regelmann.** 1984. Effect of extracellular slime substance from *Staphylococcus epidermidis* on the human cellular immune response. Lancet **i**:365–367.
15. **Grieble, H. G., S. L. Krause, S. A. Pappas, and M. B. Dicostanzo.** 1981. The prevalence of high-level methicillin resistance in multiply resistant hospital staphylococci. Medicine (Baltimore) **60**:62–69.
16. **Hogt, A. H., J. Dankert, J. A. DeVries, and J. Feijen.** 1983. Adhesion of coagulase-negative staphylococci to biomaterials. J. Gen. Microbiol. **129**:2959–2968.
17. **Karchmer, A. W., G. L. Archer, and W. E. Dismukes.** 1983. *Staphylococcus epidermidis* causing prosthetic valve endocarditis: microbiologic and clinical observations as guides to therapy. Ann. Intern. Med. **98**:447–455.
18. **Katz, S., M. Izhar, and D. Mirelman.** 1981. Bacterial adherence to surgical sutures. Ann. Surg. **194**:35–41.
19. **Kloos, W. E., and J. F. Wolfshohl.** 1982. Identification of *Staphylococcus* species with the API STAPH-IDENT system. J. Clin. Microbiol. **16**:509–516.
20. **Laharrague, P. F., J. X. Corberand, G. Fillola, B. J. Gleizes, A. M. Fontanilles, and E. Gyrard.** 1984. In vitro effect of the slime of *Pseudomonas aeruginosa* on the function of human polymorphonuclear neutrophils. Infect. Immun. **44**:760–762.
21. **Liekweg, W. G., and L. J. Greenfield.** 1977. Vascular prosthetic infections: collected experience and results of treatment. Surgery (St. Louis) **81**:335–342.
22. **Locci, R., G. Peters, and G. Pulverer.** 1981. Microbial colonization of prosthetic devices. I. Microphotographical characteristics of intravenous catheters as detected by scanning electron microscopy. Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. Abt. I Orig. Reihe B **173**:285–292.
23. **Locci, R., G. Peters, and G. Pulverer.** 1981. Microbial colonization of prosthetic devices. III. Adhesion of staphylococci to lumina of intravenous catheters perfused with bacterial suspension. Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. Abt. I Orig. Reihe B **173**:300–307.
24. **Lowder, J. N., H. M. Lazarus, and R. H. Herzig.** 1982. Bacteremias and fungemias in oncologic patients with central venous catheters: changing spectrum of infection. Arch. Intern. Med. **142**:1456–1459.
25. **Mackowiak, P. A., and M. Marling-Cason.** 1984. A comparative analysis of *in vitro* assays of bacterial adherence. J. Microbiol. Methods **2**:147–158.
26. **Maki, D. G.** 1981. Nosocomial bacteremia: an epidemiologic overview, p. 183–196. *In* R. E. Dixon (ed.), Nosocomial infections. Yorke Medical Books, New York.
27. **Maki, D. G.** 1981. Epidemic nosocomial bacteremias, p. 371–512. *In* R. P. Wenzel (ed.), Handbook of hospital acquired infections. CRC Press, Inc., Boca Raton, Fla.
28. **Malmvall, B. E., K. Alesting, O. Dottori, and S. Seeberg.** 1980. Septicemia in patients with central venous catheters: an evaluation of a method including weekly exchange of catheter. Acta Chir. Scand. **146**:155–159.
29. **McNeish, A. S., P. Turner, J. Fleming, and N. Evans.** 1975. Mucosal adherence of human enteropathogenic *Escherichia coli*. Lancet **ii**:946–948.
30. **Minor, A., and L. Burnett.** 1948. A method for obtaining living leukocytes from human peripheral blood by acceleration of erythrocyte sedimentation. Blood **3**:799–802.
31. **Peters, G., R. Locci, and G. Pulverer.** 1982. Adherence and growth of coagulase-negative staphylococci on surfaces of intravenous catheters. J. Infect. Dis. **146**:479–482.
32. **Sheth, N. K., H. D. Rose, T. R. Franson, F. L. A. Buckmore, and P. G. Sohnle.** 1983. *In vitro* quantitative adherence to intravascular catheters. J. Surg. Res. **34**:213–218.
33. **Shurtleff, D. B., E. L. Foltz, R. D. Weeks, and J. Losser.** 1974. Therapy of *Staphylococcus epidermidis* infections associated with cerebrospinal shunts. Pediatrics **53**:55–62.
34. **Sitges-Serra, A., P. Puig, E. Jaurrieta, J. Garau, A. Alastrue, and A. Sitges-Creus.** 1980. Catheter sepsis due to *Staphylococcus epidermidis* during parenteral nutrition. Surg. Gynecol. Obstet. **151**:481–483.
35. **Wade, J. C., S. C. Schimpff, K. A. Newman, and P. H. Wiernik.** 1982. *Staphylococcus epidermidis*: an increasing cause of infection in patients with granulocytopenia. Ann. Intern. Med. **97**:503–508.
36. **Winston, D. J., D. V. Dudnick, M. Chapin, W. G. Ho, R. P. Gale, and W. J. Martin.** 1983. Coagulase-negative staphylococcal bacteremia in patients receiving immunosuppressive therapy. Arch. Intern. Med. **143**:32–36.
37. **Yoshida, K., and R. D. Ekstedt.** 1968. Relation of mucoid growth of *Staphylococcus aureus* to clumping factor reaction, morphology in serum-soft agar, and virulence. J. Bacteriol. **96**:902–908.
38. **Zimmerli, W., P. D. Leuw, and F. A. Waldvogel.** 1985. Pathogenesis of foreign body infection: evidence for a local granulocyte defect. J. Clin. Invest. **73**:1191–1200.
39. **Zimmerli, W., F. A. Waldvogel, P. Vaudaux, and U. E. Nydegger.** 1982. Pathogenesis of foreign body infection: description and characteristics of an animal model. J. Infect. Dis. **146**: 487–497.