JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1992, p. 2975–2979
0095-1137/92/112975-05$02.00/0

Vol. 30, No. 11

Colonization of the Female Genital Tract with *Staphylococcus saprophyticus*

MARK E. RUPP,[1]†* DAVID E. SOPER,[2] AND GORDON L. ARCHER[1]

Department of Internal Medicine[1] and Department of Obstetrics and Gynecology,[2] Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia 23298

Received 11 June 1992/Accepted 17 August 1992

The prevalence of colonization by *Staphylococcus saprophyticus* of the urogenital tracts of 276 women from an outpatient gynecology practice was determined by using selective and enrichment culture techniques. Nineteen subjects (6.9%) were found to be colonized by *S. saprophyticus*. The rectum was the most frequent site of colonization and was responsible for 40% of the isolates; this was followed in decreasing order by the urethra, urine, and cervix. Women colonized by *S. saprophyticus* were more likely to have experienced a urinary tract infection in the previous 12 months ($P = 0.058$; odds ratio, 2.844; 95% confidence interval, 1.054 to 7.671). Patients colonized by *S. saprophyticus* tended to have had their menstrual periods more recently ($P = 0.066$), experienced sexual intercourse more recently ($P = 0.168$), and had a recent or concurrent diagnosis of vaginal candidiasis ($P = 0.111$; odds ratio, 2.393; 95% confidence interval, 0.877 to 6.528). A seasonal variation in colonization was observed, with colonization most likely occurring during the summer and fall. Follow-up for an average of 6.75 months failed to document any colonized woman progressing to symptomatic urinary tract infection. In addition, 21 women colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci were identified and characterized.

Staphylococcus saprophyticus, a coagulase-negative staphylococcus, is an important uropathogen. Investigators in the United States and Europe have demonstrated that *S. saprophyticus* is second only to *Escherichia coli* as a causative agent of urinary tract infection (UTI) in young healthy women (1, 4, 6, 20). *S. saprophyticus* causes up to 42% of UTIs in this population (20). Infection with this organism frequently involves the upper urinary tract, as demonstrated by the antibody-coated bacteria test, and impaired renal concentrating capacity (6, 9). Recurrence of infection is not unusual (2, 6). Non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci have occasionally been implicated as causative agents of UTIs (8, 12, 15). However, little is known about the prevalence or sites of colonization by these staphylococcal species.

Although it is accepted that UTI secondary to gram-negative enteric bacillus infection is preceded by periurethral colonization from a fecal reservoir (18), the pathogenesis of *S. saprophyticus* UTI is less clear. Some investigators have been unable to isolate *S. saprophyticus* from mucosal sites or have recovered it in a small minority of patients (1, 10, 14, 17, 20). Others have stated that colonization of the periurethral membranes correlates well with infection (4, 6). Several studies have suggested a causal role for sexual intercourse (3, 4), which has been disputed by others (1). In addition, a seasonal variation in the occurrence of *S. saprophyticus* UTI has been noted but remains unexplained (20).

Therefore, we conducted a cross-sectional survey to identify women whose urogenital tracts were colonized by *S. saprophyticus* and to follow them longitudinally in order to discern factors associated with colonization and the development of UTI. In addition, women colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci were identified and analyzed.

(This study was presented in part at the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, Ill., 29 September to 2 October 1991 [16a].)

MATERIALS AND METHODS

Study design and culture method. The study was designed as a prospective survey. Women presenting for routine gynecologic care were enrolled into the study over the course of 12 months from an office-based gynecologic practice. Although randomization was not formalized, nonenrollment was a random event based on a number of factors such as nursing schedule, clinic patient load, and vacation schedules. Pregnant women were excluded. Demographic, clinical, and behavioral data were collected by direct patient interview by one of the investigators. Data obtained included age, race, history of UTI, menstrual history, sexual history, method of contraception, antibiotic use, and urogenital symptoms. Signs and symptoms screened for included the following: dysuria, urinary frequency, hematuria, abdominal or pelvic pain, and fever. Urinalysis was performed by using urine dipsticks (Chemstrip 9 urine test strips; Boehringer Mannheim Diagnostics, Indianapolis, Ind.). Abnormal urinalysis was defined as any one or more of the following: positive leukocyte esterase, positive nitrite, pH ≥ 7, protein ≥ 30 mg/dl, glucose ≥ 0.05 g/dl, positive ketones, urobilinogen ≥ 1 mg/dl, positive bilirubin, or positive blood.

Samples from the urethra, cervix, rectum, and urine of each patient were cultured by using selective and enrichment media. Samples from the sites were obtained for culture by using sterile cotton-tipped swabs which were immediately inoculated onto selective agar and into enrichment broth. The broth cultures were incubated at 37°C for 24 h and were then subcultured onto selective agar. The selective plates were incubated for 24 h at 37°C. This was done to maximize the recovery of small numbers of *S. saprophyticus*. Voided

* Corresponding author.
† Present address: Division of Infectious Diseases, University of Nebraska Medical Center, 600 South 42nd Street, Omaha, NE 68198-5400.

urine was obtained by the clean-catch midstream method. Undiluted urine (0.1 ml) was used for inoculation for quantitative culture. All patients who were colonized by *S. saprophyticus* were followed, primarily by telephone, for the development of acute UTI.

Recent and concurrent gynecologic diagnoses were obtained by chart review. The 10 most frequent diagnoses, consisting of human papillomavirus infection, herpes simplex virus infection, vaginal candidiasis, cervical dysplasia, infertility, endometriosis, dysfunctional uterine bleeding, uterine fibroids, bacterial vaginosis, and a normal examination, were cataloged and analyzed.

Media. Selective media consisted of brain heart infusion agar (Difco Laboratories, Detroit, Mich.) containing 5 μg of novobiocin per ml and 25 μg of nalidixic acid per ml (antibiotics were from Sigma Chemical Company, St. Louis, Mo.). Enrichment media consisted of brain heart infusion broth containing the same selective antibiotics.

Bacteria. Bacterial isolates were Gram stained and tested for production of catalase and coagulase (13). Coagulase-negative staphylococci were identified to the species level as described by Kloos and Schleifer (5). Briefly, coagulase-negative staphylococci that were resistant to 5 μg of novobiocin per ml were classified as *S. saprophyticus* if they were urease positive; produced acid aerobically from maltose, sucrose, and trehalose; and did not produce acid from xylose. Urease production was tested by screening the isolates on urease agar (Urea Agar Base; Difco Laboratories).

Statistical analysis. Because of the small sample size in certain categories of measurement, Fisher's exact test (21) was used to determine whether there was an overall association between the quantitative variables and colonization by *S. saprophyticus*. Because of the large range of values for variables such as age, last menstrual period, and last sexual intercourse, the nonparametric Wilcoxon test (21) was used to determine whether there was a significant difference between the colonized and noncolonized subjects. To further assess the degree of association, the odds ratio (OR) and its 95% confidence interval (95% CI) were calculated in 2-by-2 tables (21).

RESULTS

Colonization. A total of 257 women were studied during the 12-month study period. Nineteen women (6.9%) whose urogenital tracts were colonized by *S. saprophyticus* and 21 women (7.6%) whose urogenital tracts were colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci were identified. Three women (1%) were found to be experiencing symptomatic infections caused by *S. saprophyticus*. One woman had a UTI, while two women had urethritis (urinary frequency with positive urethral cultures for *S. saprophyticus* and negative urine cultures). A total of 235 noncolonized, noninfected women were identified and served as the control group.

Use of both selective and enrichment techniques allowed for the maximum recovery of *S. saprophyticus*. The enrichment technique resulted in the recovery of 38% of isolates that would have been missed if only selective medium had been used. Likewise, 35% of the isolates were recovered only on the selective medium.

The rectum was the most frequent site of colonization, where 12 of 30 (40%) of the isolates were found; this was followed in decreasing order by the urethra, 9 of 30 (30%); urine, 6 of 30 (20%); and cervix, 3 of 30 (10%). Only three subjects were colonized at more than one anatomic site.

Table 1 summarizes the demographic and clinical data and compares the subjects colonized by *S. saprophyticus* with the control group. The two groups were evenly matched with regard to age and race. Women colonized by *S. saprophyticus* had experienced more recent UTIs than had the noncolonized women, defined as UTI occurring in the previous 12 months ($P = 0.058$; OR, 2.844; 95% CI, 1.054 to 7.671), but their lifetime incidences of UTIs were similar (47.4 versus 58.3%). The last menstrual period tended to be more recent in women colonized by *S. saprophyticus*, 8.5 days compared with 14 days ($P = 0.066$), as did the last episode of sexual intercourse, 3.5 days compared with 7 days ($P = 0.168$). There was little difference in the proportions of women in either group who used various forms of birth control ($P = 0.269$). Essentially equal proportions of women in the colonized and noncolonized groups had abnormal urinalyses, 68.4 versus 65.5% ($P > 0.999$; OR, 1.140; 95% CI, 0.418 to 3.110); used antibiotics in the 2 weeks prior to the study, 5.3 versus 7.2% ($P > 0.999$; OR, 0.712; 95% CI, 0.090 to 5.664); and had related urogenital symptoms, 10.5 versus 12.3% ($P > 0.999$; OR, 0.836; 95% CI, 0.184 to 3.806). A larger proportion of women colonized by *S. saprophyticus* had a recent or concurrent diagnosis of vaginal candidiasis, 31.6 versus 16.2% ($P = 0.111$; OR, 2.393; 95% CI, 0.856 to 6.687). The proportions of subjects experiencing the other nine concurrent diagnoses were quite similar. The three most common diagnoses, excluding a normal examination, consisted of human papillomavirus infection, cervical dysplasia, and vaginal candidiasis. The data for these three diagnoses are given in Table 1; the data for the other diagnoses are not shown.

Progression to symptomatic UTI and persistence of colonization. All patients identified as being colonized by *S. saprophyticus* were followed for the development of acute UTI. The average follow-up period was 6.75 months (range, 5 to 9 months), resulting in 128.25 patient-months. None of the colonized women developed a symptomatic UTI. Samples from 4 of the 19 women colonized by *S. saprophyticus* were recultured up to four times during the 12-month study period. None of the women received antibiotics. Two became culture negative, while two remained persistently positive. All three of the acutely infected women were followed, and samples from the women were recultured. None of the women received antibiotics. Two became culture negative and one remained culture positive for samples from the rectal site. All became asymptomatic.

Seasonal variation. A marked seasonal variation was observed in the colonization of women with *S. saprophyticus* (Fig. 1). Approximately two-thirds of the colonized subjects were identified during the months of August and September. Because of logistical problems, only two women were enrolled during July; thus, the study was extended for an additional month to include August.

Non-*S. saprophyticus* novobiocin-resistant, coagulase-negative staphylococci. A total of 21 women who were colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci were identified. The species identified and the number of women colonized were as follows: *S. kloosii* ($n = 8$), *S. cohnii* ($n = 12$), and *S. xylosus* ($n = 1$). Table 2 summarizes the comparison between women colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci and the control group. The two groups were evenly matched with regard to demographic variables. Interestingly, there appeared to be an inverse

TABLE 1. Comparison of demographic, behavioral, and clinical data between women colonized by *S. saprophyticus* and noncolonized women

Parameter	*S. saprophyticus*:		Comment
	Colonized	Noncolonized	
No. of women	19	235	
Median age (yr) [Q1, Q3][a]	29 (25, 36)	31 (24, 38)	$P = 0.544$
Race (no. [%])			$P = 0.592$; OR, 1.317; 95% CI, 0.474–3.661
White	12 (63.2)	166 (70.6)	
Black	6 (31.6)	63 (26.8)	
Other	1 (5.2)	6 (2.6)	
History of UTI (no. [%])			
Lifetime	9 (47.4)	137 (58.3)	
<1 yr	7 (36.8)	40 (17)	$P = 0.058$; OR, 2.844; 95% CI, 1.054–7.671
Last menstrual period (days)	8.5	14	$P = 0.066$
Last sexual intercourse (days)	3.5	7	$P = 0.168$
Birth control (no. [%])			$P = 0.269$
None	5 (26.3)	85 (36.2)	
Oral contraceptive	9 (47.4)	76 (32.3)	
Condom	0	26 (11.1)	
Diaphragm	1 (5.2)	6 (2.6)	
Other or not reported	4 (21.1)	42 (17.9)	
Abnormal urinalysis (no. [%])	13 (68.4)	154 (65.5)	$P > 0.999$; OR, 1.140; 95% CI, 0.418–3.110
Antibiotic use (no. [%])	1 (5.3)	17 (7.2)	$P > 0.999$; OR, 0.712; 95% CI, 0.090–5.664
Urogenital symptoms (no. [%])	2 (10.5)	29 (12.3)	$P > 0.999$; OR, 0.836; 95% CI, 0.184–3.806
Concurrent diagnosis (no. [%])			
Human papillomavirus	4 (21.1)	48 (20.4)	$P > 0.999$; OR, 1.039; 95% CI, 0.330–3.273
Cervical dysplasia	3 (15.8)	30 (12.8)	$P = 0.721$; OR, 1.281; 95% CI, 0.352–4.660
Vaginal candidiasis	6 (31.6)	38 (16.2)	$P = 0.111$; OR, 2.393; 95% CI, 0.856–6.687

[a] Q1, 25% quartile; Q3, 75% quartile.

relationship between colonization with non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci and a recent or concurrent diagnosis of vaginal candidiasis, 0 versus 16.2% ($P = 0.030$; OR, 0.099; 95% CI, 0.006 to 1.666). There were no other significant differences or identifiable trends between the colonized and control groups in relationship to any of the parameters examined.

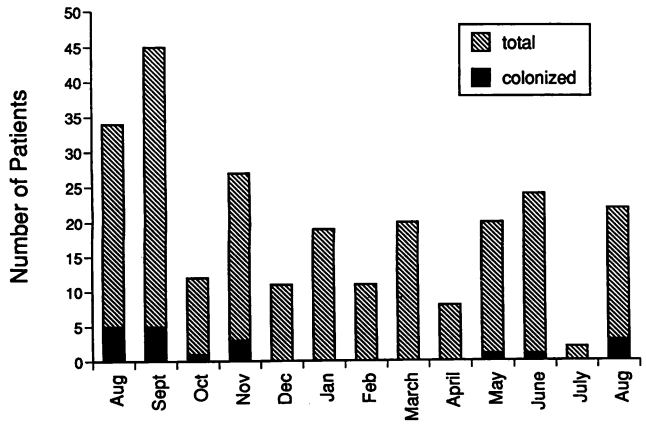

FIG. 1. Seasonal variation of colonization by *S. saprophyticus*.

DISCUSSION

S. saprophyticus has been demonstrated by others to be the second most common cause of UTI in young females (2, 4, 6, 20). Despite this clinical importance, relatively little is known about the pathogenesis of these infections or the virulence determinants of this organism. Previous studies examining colonization by *S. saprophyticus* and the pathogenesis of UTIs primarily concerned themselves with the study of women presenting with acute UTI (4, 6). Other investigators have performed culture surveys without attempting to longitudinally follow colonized patients or discern the factors related to colonization (16, 19).

Our longitudinal study identified several patient characteristics associated with *S. saprophyticus* colonization. Although the sample size was small, thus limiting the ability to discern significance, we found several associations that approached significance. First, patients colonized by *S. saprophyticus* were more likely than noncolonized patients to have experienced a UTI in the preceding year (OR, 2.844; 95% CI, 1.054 to 7.671). Unfortunately, data were not available to determine whether these episodes of sympto-

TABLE 2. Comparison of demographic, behavioral, and clinical data between women colonized by non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci and noncolonized women

Parameter	Non-*S. saprophyticus*, coagulase-negative staphylococci:		Comment
	Colonized	Noncolonized	
No. of women	20	235	
Median age (yr [Q1, Q3])[a]	28 (20, 38)	31 (24, 38)	$P = 0.544$
Race (no. [%])			$P = 0.129$; OR, 2.075; 95% CI, 0.832–5.172
White	12 (57.1)	166 (70.6)	
Black	9 (42.9)	63 (26.8)	
Other	0	6 (2.6)	
History of UTI (no. [%])			
Lifetime	9 (42.9)	137 (58.3)	
<1 yr	3 (14.3)	40 (17)	$P = 0.774$; OR, 0.716; 95% CI, 0.202–2.538
Last menstrual period (days)	14	14	$P = 0.446$
Last sexual intercourse (days)	6	7	$P = 0.504$
Birth control (no. [%])			$P = 0.874$
None	7 (33.3)	85 (36.2)	
Oral contraceptive	7 (33.3)	76 (32.3)	
Condom	2 (9.5)	26 (11.1)	
Diaphragm	1 (4.8)	6 (2.6)	
Other or not reported	4 (19)	42 (17.9)	
Abnormal urinalysis (no. [%])	134 (66.7)	154 (65.5)	$P > 0.999$; OR, 1.046; 95% CI, 0.406–2.695
Antibiotic use (no. [%])	3 (14.3)	17 (7.2)	$P = 0.177$; OR, 2.422; 95% CI, 0.641–9.154
Urogenital symptoms (no. [%])	2 (9.5)	29 (12.3)	$P > 0.999$; OR, 0.740; 95% CI, 0.164–3.345
Concurrent diagnosis (no. [%])			
Human papillomavirus	4 (19)	48 (20.4)	$P > 0.999$; OR, 0.907; 95% CI, 0.292–2.820
Cervical dysplasia	4 (19)	30 (12.8)	$P = 0.493$; OR, 1.655; 95% CI, 0.521–5.219
Vaginal candidiasis	0	38 (16.2)	$P = 0.030$; OR, 0.099; 95% CI, 0.006–1.666

[a] Q1, 25% quartile; Q3, 75% quartile.

matic UTI were due to *S. saprophyticus*. Second, UTI caused by *E. coli* is associated with sexual intercourse and diaphragm use (7, 19). We examined these factors in relation to colonization by *S. saprophyticus* and found that although there was no association between the method of birth control and colonization, women colonized by *S. saprophyticus* tended to have had more recent sexual intercourse ($P = 0.168$). In this light, it is interesting that Hovelius et al. (3) noted *S. saprophyticus* to be a cause of urethritis in a group of men attending a venereal disease clinic. Third, an association ($P = 0.066$) was observed between menstruation and colonization by *S. saprophyticus*, in that women colonized by *S. saprophyticus* had more recently experienced their menstrual period (8.5 versus 14 days). Thus, colonization may be related to hormonal effects or some other factor that is regulated by the menstrual cycle. Fourth, colonized women experienced vaginal candidiasis with greater frequency than did women in the noncolonized control group ($P = 0.111$; OR, 2.393; 95% CI, 0.856 to 6.687). The colonized women did not have conditions known to increase the incidence of vaginal candidiasis, such as antibiotic use, diabetes mellitus, or steroid therapy; serologic testing for antibodies to the human immunodeficiency virus was not performed. Vaginal candidiasis may cause or reflect alterations in the vaginal microenvironment and, thus, may relate to an increased propensity for colonization by *S. saprophyticus*. Further study of these factors in relation to *S. saprophyticus* colonization and UTI seems warranted.

The study population was slightly older in this survey (overall median age, 29 years; 25% quartile, 25 years; 75% quartile, 36 years) than were the college-aged women studied in previous surveys from the United States (4, 6), and this may explain the low incidence of *S. saprophyticus* UTI and colonization in our study compared with those in the previous studies. However, Wallmark et al. (20) found that among 787 Scandinavian women outpatients with UTIs of all causes ranging in age from childhood to 65 years, women in the age group from 26 to 35 years experienced 26% of the UTIs caused by *S. saprophyticus* and *S. saprophyticus* caused 34% of the total number of UTIs in women in this age group. In contrast, we observed only one patient with an acute UTI caused by *S. saprophyticus*, and in the cohort of women who were colonized by this organism, who are presumably at high risk for the development of symptomatic UTI, none developed a UTI. The disparity between our observations and those in the Scandinavian study may indicate differences in the host population or pathogen. A geographic or racial difference in the prevalence of colonization and UTI may exist, or alternatively, there may be differences in the regulation or expression of virulence determinants by *S. saprophyticus* from these distinct geographic regions. Also, a selection bias in our study cannot be excluded because of the association of the outpatient practice with an inner-city university hospital. This may explain the relatively high percentage of patients with recent or concurrent diagnoses of human

papillomavirus infection, cervical dysplasia, and vaginal candidiasis.

The seasonal predilection for *S. saprophyticus* UTI during the summer and fall that has been previously noted can be extended to include colonization. Approximately two-thirds of the colonized patients were identified during the months of August and September. The reason for this seasonal variation remains obscure.

The rectum was the most frequent site of colonization. This observation favors the theory that the pathogenesis of *S. saprophyticus* UTI is similar to that of UTIs caused by gram-negative enteric organisms. Namely, the bowel serves as a reservoir from which urogenital colonization occurs, which precedes development of symptomatic UTI. However, colonization does not invariably proceed to infection. In fact, in our study population, colonization of the urogenital tract was not observed to be followed by symptomatic UTI over the ensuing 6 months.

Low numbers of *S. saprophyticus* recovered from the urine (10^2 to 10^3 CFU/ml) do not necessarily indicate infection. Six women with low numbers of *S. saprophyticus* in their urine were identified. None had urogenital symptoms, and none developed an acute UTI during the period of observation. Some investigators (2, 20) have espoused the treatment of all patients in whom small numbers of *S. saprophyticus* have been recovered from the urine because of this organism's proven ability to cause symptomatic infection when recovered at numbers as low as 10^3 CFU/ml. However, this recommendation may result in some patients being subjected to unnecessary, costly, and potentially toxic antibiotic therapy, since some patients with *S. saprophyticus* in their urine exhibit no symptoms, do not develop symptomatic UTI, and spontaneously clear their urine of this organism. Our results would support the treatment only of symptomatic women or those with persistent bacteriuria.

Clinical microbiology laboratories routinely classify all coagulase-negative staphylococci that are novobiocin resistant as *S. saprophyticus* (11). A uropathogenic role for non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci has not been demonstrated. Results of our study demonstrate that small numbers of non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci may be recovered from the urine and genital tracts of some patients even though they do not exhibit symptoms of UTI. We found that the number of these patients is equal to or greater than the number of patients colonized by *S. saprophyticus*. In order to avoid unnecessary treatment of these patients, our results support more frequent determination to the species level of the coagulase-negative staphylococci recovered from the urinary tract.

In conclusion, a small percentage of healthy women are colonized by *S. saprophyticus*. These colonized women are significantly more likely to have experienced a recent UTI. In addition, they tend to have had more recent menstruation, sexual intercourse, and vaginal candidiasis than did noncolonized women. The colonized women rarely progress to the development of symptomatic UTIs. A pathogenic role for non-*S. saprophyticus*, novobiocin-resistant, coagulase-negative staphylococci remains unproven.

ACKNOWLEDGMENTS

We thank L. Johnston, C. Josenberger, M. Turick, and E. Weller for assistance.

This study was supported in part by the National Institutes of Health (grants F32 AI 08416 and AI 21772).

REFERENCES

1. **Gillespie, W. A., M. A. Sellin, P. Gill, M. Stephens, L. A. Tuckwell, and A. L. Hilton.** 1978. Urinary tract infection in young women, with special reference to *Staphylococcus saprophyticus*. J. Clin. Pathol. **31**:348–350.
2. **Hovelius, B., P. A. Mardh, and P. Bygren.** 1979. Urinary tract infections caused by *Staphylococcus saprophyticus*: recurrences and complications. J. Urol. **122**:645–647.
3. **Hovelius, B., I. Thelim, and P. A. Mardh.** 1979. *Staphylococcus saprophyticus* in the aetiology of nongonococcal urethritis. Br. J. Vener. Dis. **55**:369–474.
4. **Jordan, P. A., A. Iravani, G. A. Richard, and H. Baer.** 1980. Urinary tract infection caused by *Staphylococcus saprophyticus*. J. Infect. Dis. **142**:510–515.
5. **Kloos, W. E., and K. H. Schleifer.** 1975. Simplified scheme for routine identification of human *Staphylococcus* species. J. Clin. Microbiol. **1**:82–88.
6. **Latham, R. H., K. Running, and W. E. Stamm.** 1983. Urinary tract infections in young adult women caused by *Staphylococcus saprophyticus*. JAMA **250**:3063–3066.
7. **Leibovici, L., G. Alpert, A. Laor, O. Kalter-Leibovici, and Y. L. Danon.** 1987. Urinary tract infections and sexual activity in young women. Arch. Intern. Med. **147**:345–347.
8. **Leighton, P. M., and J. A. Little.** 1986. Identification of coagulase-negative staphylococci isolated from urinary tract infections. Am. J. Clin. Pathol. **85**:92–95.
9. **Mabeck, C. E.** 1969. Significance of coagulase negative staphylococcal bacteriuria. Lancet **ii**:1150–1152.
10. **Marrie, T. J., C. Kwan, M. A. Noble, A. West, and L. Duffield.** 1982. *Staphylococcus saprophyticus* as a cause of urinary tract infections. J. Clin. Microbiol. **16**:427–431.
11. **McTaggart, L. A., and T. S. J. Elliott.** 1989. Is resistance to novobiocin a reliable test for confirmation of the identification of *Staphylococcus saprophyticus*? J. Med. Microbiol. **30**:253–266.
12. **Nicolle, L. E., S. A. Hoban, and G. K. M. Harding.** 1983. Characterization of coagulase-negative staphylococci from urinary tract specimens. J. Clin. Microbiol. **17**:267–271.
13. **Paik, G.** 1980. Reagents, stains, and miscellaneous test procedures, p. 1000–1024. *In* E. H. Lennette, A. Balows, W. J. Hausler, Jr., and J. P. Truant (ed.), Manual of clinical microbiology, 3rd ed. American Society for Microbiology, Washington, D.C.
14. **Pead, L., J. Crump, and R. Maskell.** 1977. Staphylococci as urinary pathogens. J. Clin. Pathol. **30**:427–431.
15. **Rimland, D., and W. Alexander.** 1989. Absence of factors associated with significant urinary tract infections caused by coagulase-negative staphylococci. Diagn. Micobiol. Infect. Dis. **12**:123–127.
16. **Ringertz, O., and J. Torssander.** 1986. Prevalence of *Staphylococcus saprophyticus* in patients in a venereal disease clinic. Eur. J. Clin. Microbiol. **5**:358–361.

16a. **Rupp, M. E., D. E. Soper, and G. L. Archer.** 1991. Program Abstr. 31st Intersci. Conf. Antimicrob. Agents Chemother., abstr. 1261.

17. **Sellin, M., D. I. Cooke, W. A. Gillespie, and D. G. H. Sylvester.** 1975. Micrococcal urinary tract infection in young women. Lancet **ii**:570–572.
18. **Sobel, J. D., and D. Kaye.** 1990. Urinary tract infections, p. 582–611. *In* G. L. Mandell, R. G. Douglas, Jr., and J. E. Bennett (ed.), Principles and practice of infectious diseases, 3rd ed. Churchill Livingstone, New York.
19. **Strom, B. L., M. Collins, S. L. West, J. Kreisberg, and S. Weller.** 1987. Sexual activity, contraceptive use, and other risk factors for symptomatic and asymptomatic bacteriuria. Ann. Intern. Med. **107**:816–823.
20. **Wallmark, G., I. Arremark, and B. Telander.** 1978. *Staphylococcus saprophyticus*: a frequent cause of acute urinary tract infection among female outpatients. J. Infect. Dis. **138**:791–797.
21. **Woolson, R. F.** 1987. Statistical methods for the analysis of biomedical data. *In* W. A. Shewhart and S. S. Wilks (ed.), Wiley series in probability and mathematical statistics. John Wiley & Sons, Inc., New York.