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in children of women who were shown repeatedly not to be nasal carriers suggests the possibility that the genital sites in these women may serve as the reservoir for spread to others. The transmission of toxin-producing organisms in families also suggests that persons in close contact with patients with toxic shock syndrome may be at some risk of acquiring the disease. To date, no one has reported such an association.

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Vaginal Colonization with *Staphylococcus aureus* in Healthy Women

A Review of Four Studies

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Four studies assessed the frequency of vaginal *Staphylococcus aureus* colonization in healthy women and associated risk factors. An association was found between *S. aureus* vaginal colonization and colonization at the labia minora and the anterior nares. Significant risk factors associated with an increased risk of vaginal *S. aureus* in at least one study were a history of genital herpes simplex infection, insertion of tampons without an applicator, and the use of Rely (Procter & Gamble) tampons. The use of systemic antibiotics within 2 weeks of the vaginal culture decreased the risk of recovery of *S. aureus*. The overall frequency of vaginal *S. aureus* in the 808 women in the four studies was 9.2%.

BECAUSE toxic shock syndrome is associated with the presence of *Staphylococcus aureus* in the vagina, and because little is known concerning the risks for this organism in the vagina, four studies were done in healthy women to define demographic, historical, and behavioral risk factors.

Methods

In study 1, swabs were obtained from 71 menstruating women who visited family planning clinics or a private gynecologist, as previously described (1). Swabs taken from the vagina, vaginal introitus (labia minora), and anterior nares were placed in Carey-Blair transport media before isolation of *S. aureus* was

attempted.

In study 2, women who attended DeKalb County Venereal Disease Clinic, Atlanta, Georgia, were cultured for *S. aureus* during a 3-week period in August 1980. A single swab was obtained from the vagina and plated directly on mannitol-salt agar for selective isolation of *S. aureus*.

Study 3 included 545 female volunteers: 89 employees of the Centers for Disease Control, 218 women attending venereal disease clinics in Columbus, Ohio, and Atlanta, Georgia, and 238 women attending private gynecology clinics in Atlanta, Georgia. Swabs were obtained from the anterior nares, labia minora, and vagina. Vaginal swabs were plated directly on mannitol-salt agar and swabs from the other two sites were placed in Carey-Blair transport media. Cultures from the labia and the nares were processed for all women with positive vaginal cultures and for a systematic sample of 54 women with negative vaginal cultures.

In Study 4, swabs were obtained from the vagina and anterior nares from 127 women workers in a facility that manufactured tampons and placed in Carey-Blair transport media.

All swabs placed in Carey-Blair media from Studies 1 and 4 and a sample of those from Study 3 were subsequently plated on mannitol-salt agar. Isolates from all four studies were identified as *S. aureus*, as previously described (1). All viable staphylococcal isolates were phage typed and tested for the ability to produce pyrogenic exotoxin C (3, 4). All women cultured were asked to complete a self-administered questionnaire. Statistical comparisons were made only for individual studies, using the chi-squared analysis and Fisher's exact tests.

Results

As shown in Table 1, vaginal cultures for *S. aureus* were obtained from 808 women in the four studies. Colonization rates were 9.9%, 15.4%, 8.1%, and 10.2%, respectively. A total of 74 vaginal *S. aureus* isolates were

► From the Venereal Disease Control Division, Center for Prevention Services; Bacterial Diseases Division, Center for Infectious Diseases; and Family Planning Division, Center for Health Promotion and Education; Centers for Disease Control; Atlanta, Georgia.

Some of the findings in these studies previously have been reported (*N Engl J Med.* 1980;303:1436-42).

Table 1. Populations Cultured for Vaginal *Staphylococcus aureus*

Study Number	Population	Date	Total Women Cultured	Vaginal <i>S. aureus</i> Present
			<i>n</i>	<i>n</i> (%)
1	Family planning clinic and private gynecologist	May, June 1980	71	7(9.9)
2	Venereal disease clinic	August, September 1980	65	10(15.4)
3	Venereal disease clinics, gynecology clinics, CDC* employees	October 1980	545	44(8.1)
4	Tampon factory employees	March 1981	127	13(10.2)
Total, Studies 1-4			808	74(9.2)

* CDC = Centers for Disease Control.

recovered for an overall colonization rate of 9.2%.

Cultures from the labia minora were processed for 169 women, 71 from Study 1, and 98 women from Study 3. The *S. aureus* colonization rate for this site was 9.9%. In Study 1 we found a significant association between colonization of labia minora and vaginal colonization. Of seven women with positive vaginal cultures, four had positive cultures from the labia, whereas only three of 64 women with negative vaginal cultures had positive cultures from the labia ($p = 0.01$, Fisher's exact test). We did not have sufficient data to analyze this association in Study 3 because not all cultures from labia of women who had negative vaginal cultures were processed. We did, however, examine the concordance of phage types in *S. aureus* isolates from women in Studies 1 and 3 who had both positive vaginal cultures and positive cultures from labia. Of the 35 paired isolates, 25 had the same phage type and 10 pairs had different phage types.

Anterior nares cultures were processed for 296 women, 71 in Study 1, 98 in Study 3 and 127 in Study 4. The overall colonization rate of anterior nares was 20.7%. In Study 4, nine of 13 women with positive vaginal cultures also had positive nares cultures, whereas only 19 of 114 women with negative vaginal cultures had positive nares cultures for *S. aureus* ($p < 0.001$, chi-squared analysis). This association was not significant in Study 1 and could not be determined in Study 3 because of insufficient data. There was also concordance of vaginal and nares phage types; overall, 16 of 21 paired isolates had the same phage type.

A history of genital herpes infection, insertion of tampons without using an applicator, and the use of Rely tampons (Procter & Gamble) significantly increased the risk for vaginal *S. aureus* colonization in at least one of the four studies. The use of systemic antibiotics in the 2 weeks before culture significantly decreased this risk.

A significant association between *S. aureus* in the vagina and genital herpes infection was found only in Study 3. For 15 women who had had genital herpes infection in the 6 months before culture, the colonization rate was 27%, compared with 8% among the 339 women who had not had herpes infection ($p = 0.03$). This association was not significant in Study 2, the only other study where information on genital herpes was obtained.

In Study 3 significantly more women who inserted a tampon without using an applicator were colonized with

S. aureus than women who used an applicator. The question asked read as follows, "In the past two months have you ever inserted your tampon without a cardboard or plastic inserter, that is, with your fingers only?" The colonization rate among 105 women who answered "yes" to this question was 16%, significantly higher than the 7% rate among 382 women who answered "no" ($p = 0.005$). This question was not asked in the other three studies.

Studies 1 and 2 were completed before the withdrawal of Rely tampons from the market (22 September 1980). In these studies the *S. aureus* vaginal colonization rate for users of Rely was higher than for users of all other tampon brands. As shown in Table 2, the frequency of vaginal colonization in the two studies was 43% for Rely users, compared with 8% for users of other tampons. In Study 1 the frequencies were 29% and 12%, respectively. In Study 2 the frequency was 57% for Rely users, significantly greater than the 5% in other tampon users ($p < 0.002$). In the other two studies, initiated after the withdrawal of Rely, the use of any single tampon brand did not carry a significantly increased risk for vaginal *S. aureus* colonization. Combining the data from all studies, the *S. aureus* vaginal colonization rate for users of other brands of tampons ranged from 7% to 10% and was 8% for those who did not use tampons.

Toxin testing of isolates from Studies 3 and 4 is incomplete. Of the 25 *S. aureus* strains isolated in Studies 1 and 2, 23 were viable and tested for toxin production. Only three were positive; all were isolated from women who used Rely tampons. Of the 136 women in Studies 1 and 2, 14 were exclusive Rely users, 86 were exclusive users of "other" tampon brands, 17 were users of more than one

Table 2. Association of Rely Tampons with Vaginal Colonization with *Staphylococcus aureus*

Study Number	Brand	Total	Positive for <i>S. aureus</i>
		<i>n</i>	<i>n</i> (%)
1	Rely*	7	2(29)
	Other tampons	43	5(12)
2	Rely	7	4(57)
	Other tampons	43	2 (5)†
Total	Rely	14	6(43)
	Other tampons	86	7 (8)

* Procter & Gamble.

† $p = 0.002$ (Fisher's exact test)

Table 3. Frequency of Vaginal *Staphylococcus aureus* Colonization by Age

Age Group	Number	Percentage Positive for Vaginal <i>S. aureus</i>
yrs		
14-19	100	9.0
20-29	356	9.7
30-39	185	8.2
40-49	72	5.5
50+	95	9.5

brand of tampon, and 19 women did not use tampons. None of the strains from either the exclusive users of "other" tampons or from non-tampon users produced toxin. Two of the toxin-producing strains were vaginal isolates from exclusive Rely users (14.3%) and the third was a labia minora isolate from a woman who used both Rely and o.b. brand (Johnson & Johnson) tampons.

Systemic antibiotic use within the 2 weeks before culture protected against *S. aureus* vaginal colonization. In Study 3, 4% of 153 women who used antibiotics were colonized compared with 11% of 319 women who did not ($p = 0.009$). Antibiotics used included ampicillin, penicillin, tetracycline, and metronidazole. In the other three studies the numbers of antibiotic users were too small for statistical comparison.

No significant relation was found between the presence of vaginal *S. aureus* and age, race, parity, marital status, frequency or pattern of vaginal douching, use of a feminine deodorant product, number of sex partners in the month before culture, sexual intercourse compared with abstinence during the week before culture, sexual intercourse during menstruation, the presence of symptomatic or asymptomatic vaginal infection, any tampon use compared with no tampon use, hand washing before tampon insertion, or contraceptive method used. The frequency of vaginal *S. aureus* by age group is given in Table 3.

Although no single contraceptive method was significantly associated with *S. aureus* vaginal colonization in any one study, the combined data are of interest (Table 4). Rates ranged from 3% in women with hysterectomies and tubal ligations to 18% in those who used diaphragms.

Discussion

There have been few studies of vaginal *S. aureus* colonization in premenopausal, nonpregnant healthy women. Morris and associates (5) reported a 2.7% frequency of vaginal *S. aureus* colonization in women attending a family planning clinic. They found, as did we, no difference in frequency of colonization between women who use tampons and those who did not, and women who used oral contraceptives and those who did not. McCormack and associates (6) studied college students and found an *S. aureus* colonization rate of 2.7%. Sautter and associates (7) reported a 3% colonization rate in nurses from whom cultures were taken several times in 1 month, and Tashjian and colleagues (8) found an 8% vaginal *S. aureus* colonization rate in asymptomatic women attending a medical clinic. Corbishley (9) reported a 17% recovery

rate of vaginal *S. aureus* from women attending a clinic for intrauterine devices (IUD).

In each of our four studies the frequency of vaginal colonization with *S. aureus* was 8.1% or higher, with an overall rate for all four studies of 9.2%. The frequency for women who had cultures taken during a menstrual period (Study 1) was 9.9%. Patients from a venereal disease clinic (Study 2) had a slightly higher frequency of vaginal *S. aureus* colonization (15.4%).

We found an association between the presence of *S. aureus* in the vagina and its presence at two other sites, the labia minora and the anterior nares. These findings raise questions concerning the mode of entry of *S. aureus* into the vagina. The fingers and hands may become contaminated after contact with one of these carriage sites, and insertion of contaminated fingers may be a mode of entry into the vagina for this organism. Supporting this concept is the finding that hygienic and contraceptive practices that require insertion of the fingers into the vagina appear to increase the risk for vaginal *S. aureus* carriage. The highest vaginal *S. aureus* colonization rates, by contraceptive method, were found in users of a diaphragm or an IUD; with these methods the fingers enter the vagina either to insert the diaphragm or to check for the presence of an IUD string. Insertion of tampons with fingers was also significantly associated with an increased risk for vaginal *S. aureus* colonization.

The physiologic conditions in the vagina that contribute to the maintenance and growth of *S. aureus* are unknown. Our studies indicate that the use of oral antibiotics reduces the risk for vaginal carriage of this organism, indicating that these substances change the vaginal environment in a way that is unfavorable for *S. aureus*. However, in two different studies users of o.b. tampons, the most commonly used brand of digitally inserted tampons, did not have an increased risk of toxic shock syndrome when compared with users of tampons with cardboard or plastic inserters (10, 11). This finding suggests that other factors in addition to vaginal *S. aureus* colonization may be important in the pathogenesis of toxic shock syndrome.

A history of genital herpes infection was associated with an increased risk for vaginal *S. aureus* colonization, although none of these women had genital lesions at the time of culture. The reason for this association is unknown and the statistical association is relatively weak.

In four different studies women who used Rely tam-

Table 4. Association of Birth Control Method and Vaginal Colonization with *Staphylococcus aureus*

Birth Control Method	Total	Positive for <i>S. aureus</i>
	<i>n</i>	<i>n</i> (%)
None	121	10(8)
Pill	137	14(10)
Diaphragm	45	8(18)
IUD	25	4(16)
Condom + foam	36	2(6)
Other*	63	2(3)
Unknown	241	19(3)

* Other includes hysterectomy, tubal ligation, vasectomy, rhythm.

pons had an elevated relative risk of developing toxic shock syndrome (10-13). It is not known, however, how Rely use contributed to this risk. Of special interest, therefore, is the finding in one of our studies of an association between an increased risk for vaginal *S. aureus* colonization and the use of Rely tampons. One possible explanation for the increased risk of toxic shock syndrome in Rely users is that Rely tampons increased the risk of vaginal *S. aureus* colonization. Our data support this hypothesis.

The signs and symptoms of toxic shock syndrome may be caused by a toxin or toxins produced by *S. aureus* (1). A pyrogenic exotoxin C has been identified in all tested strains of *S. aureus* isolated from patients with toxic shock syndrome (4). The exact role this toxin plays in the syndrome has not been established. We found that only three of 23 strains of *S. aureus* from healthy women produced this toxin. All three isolates were cultured from the genital tract of women who at least occasionally used Rely tampons; two of the women used Rely exclusively. Therefore, our data also support the hypothesis that Rely use increased the risk of carriage of toxin-producing strains of *S. aureus*. Because Rely tampons are no longer marketed, further clinical studies to elucidate the relation of Rely use and vaginal *S. aureus* will not be possible.

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