

## Male Predominance in Persistent Staphylococcal Colonization and Infection of the Newborn

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*The hospital environment has been shown to play a particularly important role in the incidence of neonatal staphylococcal colonization.<sup>1</sup> The infant who becomes colonized with staphylococci within the immediate newborn period is more likely to develop neonatal staphylococcal infection than the uncolonized newborn.<sup>2,6</sup> Consequently, staphylococcal colonization surveillance has become a technique used increasingly to detect and control staphylococcal colonization in the newborn.<sup>4</sup>*

Brown suggested that infants having quantitatively higher colony counts on direct agar-skin contact plates might be at higher risk of developing staphylococcal skin disease.<sup>7</sup>

A prospective birth-cohort study was designed to determine the value of semiquantitative colonization of *S. aureus* as a predictor of eventual staphylococcal pyoderma. This study also was designed to evaluate gender-related differences in staphylococcal colonization and subsequent staphylococcal disease in the newborn.

### Materials and Methods

A birth-cohort of newborn infants born at Tripler Army Medical Center after Oct. 22, 1979, and discharged before April 2, 1980, were included in the study. Only those babies who were admitted to the "well-baby" nursery and routinely discharged from "rooming-in" were included.

Excluded were all infants who were born outside the hospital and later admitted to the "well-baby" nursery and any infants who were first admitted to the "sick-baby" nursery for observation but later transferred to the "well-baby" nursery. Infants who were first admitted to the "well-baby" nursery and later transferred to the "sick-baby" nursery also were excluded.

Cultures were made of 1,343 infants: 591 circumcized males (males-C), 99 uncircumcized males (males-UC), and 653 females by direct agar-skin contact plate (Rodac) technique twice before the infants were discharged from the hospital. Informed consent was obtained from the parents for this study before the infants were admitted to the newborn nursery.

The mean age of infants at the time of culture was one day and 2 days, corresponding to release from the nursery to rooming-in, and discharge to home, respectively.

A culture was taken at 72 hours on all infants not ready for discharge. At the time of the second culture, parents were assigned a return appointment at 10 to 14 days of age (mean time for follow-up culture, 12.5 days). The infants who completed the entire protocol numbered 1,134: 486 males-C, 73 males-UC, and 575 females.

## **Cultures**

Direct application of agar plates to skin is an effective method of detecting skin colonization.<sup>8,11</sup>

Direct-contact plates: The first and second nursery cultures were obtained by the direct agar-skin contact method using Rodac plates containing mannitol salt agar. This selective medium has been shown to enhance the recovery of *S. aureus* by inhibiting gram-negative organisms.<sup>12</sup>

The agar surface of the plate was applied directly to the skin surface just to the right of the umbilicus. The agar surface was pressed down with even pressure and slight rocking motion to ensure even distribution of agar-skin contact. Care was taken not to twist or slip the agar to prevent smudging the culture inocula or the agar surface.

Follow-up swabs: Cultures were obtained from infants returning to the follow-up clinic using dry cotton swabs to sample the skin just to the right of the umbilicus. Swab cultures were plated on blood agar and mannitol salt agar. Any disease lesions detected during this period were cultured by the same swab method. Swabs were used, rather than Rodac plates, since qualitative and not quantitative cultures were desired.

## **Staphylococcal Isolates**

Organisms were identified on plates by colony morphology and confirmed microscopically. Direct-contact plates were counted after 24 hours and 48 hours. Colony counts were recorded as exact numbers up to 99 colonies. Plentiful overgrowth of staphylococcal isolates, precluding exact colony counts, were recorded as "greater than" 99 colonies.

All staphylococcal isolates were tested for catalase, coagulase, and DNAase. All coagulate-positive staphylococci, whether isolated from surveillance skin cultures or disease lesions, were phage-typed by the Department of Health, State of Hawaii,

During the study, the names of the patients were not known to the laboratory. All laboratory evaluations were done by culture numbers and reported to the physician by number.

The follow-up examinations were performed by physicians in the well-baby clinic or by the staff pediatricians when infants had skin infections before their scheduled appointments. The physicians performing these examinations were unaware of previous culture findings.

Statistical significance was determined using the chi-squared distribution with one degree of freedom.

## Results

There was no association between quantitative colony counts of positive nursery cultures and subsequent staphylococcal skin disease.

Results of the first culture established an overall 10.2% colonization rate (10.3% females, 10.1% males-C, and 11.0% males-UC, See Table 1.) Overall colonization rate after the second culture was 17.5% (15.6% females, 20.6% males-C, and 12.3% males-UC). The nursery colonization rate determined by an infant having at least one positive nursery culture was 22.8% (20.9% females, 25.3% males-C, and 20.5% males-UC).

Staphylococcal colonization at follow-up, without overt disease, was 7.4% overall (2.4% females, 13.4% males-C, and 6.8% males-UC). Interestingly, staphylococcal colonization in the nursery did not correlate with colonization at the follow-up examination when infants with overt disease are excluded. (See Table 2.)

TABLE 1.					
Newborn Staphylococcal Colonization and Skin Disease as a Function of Sex of Infant					
Positive Followup Culture w/o Disease	Skin Disease At Followup N	Totals First Nursery Culture	Positive Second Nursery Culture	Positive First or Nursery Culture	Positive Follow-up Culture Disease
Circ. Males	486	49 (10.1%)	100 (20.6%)	123 (25.3%)	
6 (13.4%)	31 (6.4%)				
Uncirc. Males	73	8 (11.0%)	9 (12.3%)	15 (20.5%)	
5 (6.8%)	2 (2.7%)				
Females	575 (100%)	19 (10.3%)	90 (15.7%)	120 (20.9%)	
14 (2.4%)	13 (2.3%)				
Totals:	1,134 (100%)	116 (10.2%)	199 (17.5%)	258 (22.8%)	
84 (7.4%)	46 (4.1%)				

Staphylococcal skin disease was detected in 46(4.1%) infants during follow-up examination, including 13 females (2.3%) and 33 (5.9%) males: 31 (6.4%) males-C and 2 (2.7%) males-UC. (See Table 1.)

<b>TABLE 2.</b>		
<b>Staphylococcal Colonization at Follow-Up, Without Overt Diseases, as a Function of Nursery Colonization</b>		
	<u>Follow-Up Cultures</u>	
	+	-
Nursery Positive 1st or 2nd cult	31	205
Nursery Negative 1st and 2nd cult	53	799

Skin disease occurred in 7.8% (N = 116) of first culture-positive infants (CPI), compared to 3.6% (N = 1,018) of first culture-negative infants (CNI) ( $0.05 < p < 0.1$ ). Disease was noted in 10.1% of second CPI versus 2.8% (N = 935) of second CNI ( $p < 0.005$ ).

Skin disease was documented in 8.5% (N = 258) of first *or* second CPI (defined as the nursery colonization rate) vs. 2.7% (N = 876) of the first *and* second CNI ( $p < 0.005$ ) (Table 3).

### **Results by Gender**

Of the 1,134 (84%) infants who completed the protocol, having a follow-up exam at two weeks of age, 575 were female and 559 were male (486 male-C and 73 male-UC).

Staphylococcal colonization rates during hospitalization (first nursery culture, second nursery culture, and first or second nursery culture positive) were not statistically different among females, males-C, or males-UC ( $p < 0.10$ ).

Males exceeded females for staphylococcal colonization without disease at the follow-up examination ( $p < 0.005$ ), and also for skin disease ( $p < 0.005$ ).

Staphylococcal colonization at followup and skin disease rates among uncircumcized males were more similar to the rates of the females than to their circumcized counterparts.

**Circumcized males had rates of follow-up colonization and skin disease that were twice those of uncircumcized males.** However, these differences were not statistically significant ( $p < 0.10$ ), perhaps due to the relatively small number of males-UC compared to males-C in the study population.

### Phage-Type Results

The *staphylococci* isolated during the study represented 58 different phage types, some nontypable. The most common phage types, in order, were (95), (nontypable), (96), (94/96), and (29). These phage types accounted for 71.4% of nursery isolates and 70.6% of follow-up isolates. Phage type (95) represented 40% of all nursery and 39.4% of all follow-up isolates. Twenty percent of infants with positive follow-up cultures were previously colonized with the identical phage type in the nursery.

### Discussion

Most newborn infants are sterile at birth, unless the delivery is complicated by prolonged rupture of membranes. Colonization of newborn infants by potentia pathogens logically must precede the development of invasive disease.

Most infants become staphylococcal carriers during the first days of life while in the newborn nursery.<sup>2</sup>

	First Culture		Second Culture		First or Second Culture	
	+	-	+	-	+	-
	CPI	CNI	CPI	CNI		
Disease	9	37	20	26	22	24
N=46						
N=1,088						
no	107	981	179	909	236	852
Disease						
Totals	116	1,018	199	935	258	876
N=1,134						

**Generally, the umbilicus and groin are colonized first,** and the nose and neck much less rapidly.<sup>2,13</sup> the primary reservoir of *staphylococci* apparently is the infants themselves,<sup>14</sup> The umbilicus is thought to be the most important reservoir.<sup>15</sup>

The earlier and more widely that an infant becomes colonized with *staphylococci*, the more likely he is to develop infection with *staphylococci* later.

Infants with positive cultures at discharge have had higher rates of disease than those with negative cultures at discharge.<sup>2,5</sup> Our results unequivocally confirm these earlier observations.

It is tempting to suggest that babies differ in their susceptibility to *staphylococci*.<sup>16</sup> **Many investigators have noted that males are particularly prone to both staphylococcal colonization and later development of staphylococcal infection,<sup>3, 4, 6, 17</sup> particularly in the diaper area.<sup>17</sup>** Curran and Al-Salihi described a massive outbreak of Staphylococcal Scalded-Skin Syndrome (SSSS), and remarked that the preponderance of males with generalized exfoliative skin disease suggests that the circumcision wound may provide a site of colonization for staphylococci resulting in an increased incidence of SS in males They did not document male preponderance for bullous impetigo;<sup>18</sup> however, their investigation was retrospective.

Our study prospectively confirms the male predilection for neonatal staphylococcal skin disease. During hospitalization, males and females have similar colonization rates, but males have greater colonization and eventual staphylococcal skin disease thereafter.

This study did not confirm any superiority of quantitative culture over simple qualitative swab methods for predicting eventual staphylococcal skin disease. However, the more selective media resulted in identifying most twice as many infants colonized with *S. aureus* as did a similar smaller study done previously at our institution.<sup>6</sup>

**The increased incidence of staphylococcal colonization and pyoderma in males may be associated with circumcision performed after the first 24 hours of life in the nursery.**

Circumcision is performed on approximately 90% of the male infants born at our hospital.<sup>6</sup> In our study population, 87% of the males were circumcized.

**Circumcision, by its very nature, requires more staff-patient “hands-on” contact. The infants are all lined up and their stomachs lavaged clear in preparation for the procedure. The circumcisions are done daily, as a group, in a small area, using reusable circumcision restraints.**

**Postoperatively, there is also more handling of the diaper area in caring for the fresh, hemorrhagic wound.**

A larger study, involving more infants, is required to validate the hypothesis that circumcision is the culprit responsible for the increased rate of staphylococcal colonization and infection in newborn males. This may be due to the remarkably high rate of neonatal circumcision done in the United States. A much smaller study would be satisfactory if it were performed in Great Britain or one of the developed countries of Europe, where the incidence of noncircumcision is more equal to the rate of circumcision in the U.S.

**Gellis eloquently indicted circumcision, noting that the infant “has enough portals of entry for organisms as it is,” referring to the infant's nose, mouth, conjunctiva, and the cut end of his umbilicus. “It seems totally unnecessary to aid and abet lurking bacteria by adding a raw wound to his genitalia.”<sup>19</sup>**

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