Reprinted from the American Journal of Diseases of Children
June 1963, Vol. 105, pp. 663-673

III. The Georgia Epidemic

HENRY R. SHINEFIELD, MD
NEW YORK
MARVIN BORIS, MD
ATLANTA
JOHN C. RIBBLE, MD
NEW YORK
ELLSWORTH F. CALE, MD
ATLANTA
AND
HEINZ F. EICHENWALD, MD
NEW YORK

Definition of Terms.—A glossary of terms used in this publication is included in a previous paper.[1]

Henry R. Shinefield, MD, Assistant Professor of Pediatrics, The New York Hospital-Cornell Medical Center, 525 E 68th St, New York.

From the Department of Pediatrics, The New York Hospital-Cornell Medical Center; The Piedmont Hospital, Atlanta; Communicable Disease Center, Public Health Service, United States Department of Health, Education and Welfare, Atlanta; and the Departments of Preventive Medicine and Pediatrics, Emory University, School of Medicine, Atlanta, Ga. Recipient of Lederle Faculty Award (Dr. Shinefield) Cornell Medical College; Epidemic Intelligence Service Officer, CDC PHS USDHEW, and Instructor, Departments of Preventive Medicine and Pediatrics, Emory University School of Medicine, Atlanta (Dr. Boris); Assistant Professor of Medicine, Cornell University Medical College (Dr. Ribble); Director of Pediatrics Piedmont Hospital, Atlanta (Dr. Cale); Professor of Pediatrics Cornell Medical College (Dr. Eichenwald).

Supported in part by New York Health Research Council Grant U-1231, Nursery Research Fund of New York Hospital, and Grants E-3669, AI-00998, AI-02846 of the National Institutes of Allergy and Infectious Diseases, National Institutes of Health.

In the preceding papers of this series, evidence has been presented which indicates that the 502A strain of *Staphylococcus aureus* is capable of colonizing the cord and nasal mucosa of newborn infants,[1] and that the presence of this organism actively interferes with the subsequent acquisition of other coagulase positive staphylococci, including type 80/81, under epidemic conditions.[2] The present communication presents additional evidence bearing on this point, as well as certain other data on the ecology of staphylococcal infection in newborn infants and their contacts.

During September and October of 1961, an increase in the rate of impetigo among infants discharged from a proprietary Atlanta hospital * was noted by the pediatricians in the area. Preliminary studies were carried out by a group of investigators from the Communicable Disease Center between Nov 19, 1961, and Jan 9, 1962, to determine the rate of colonization of infants in this

* Piedmont Hospital, Atlanta.

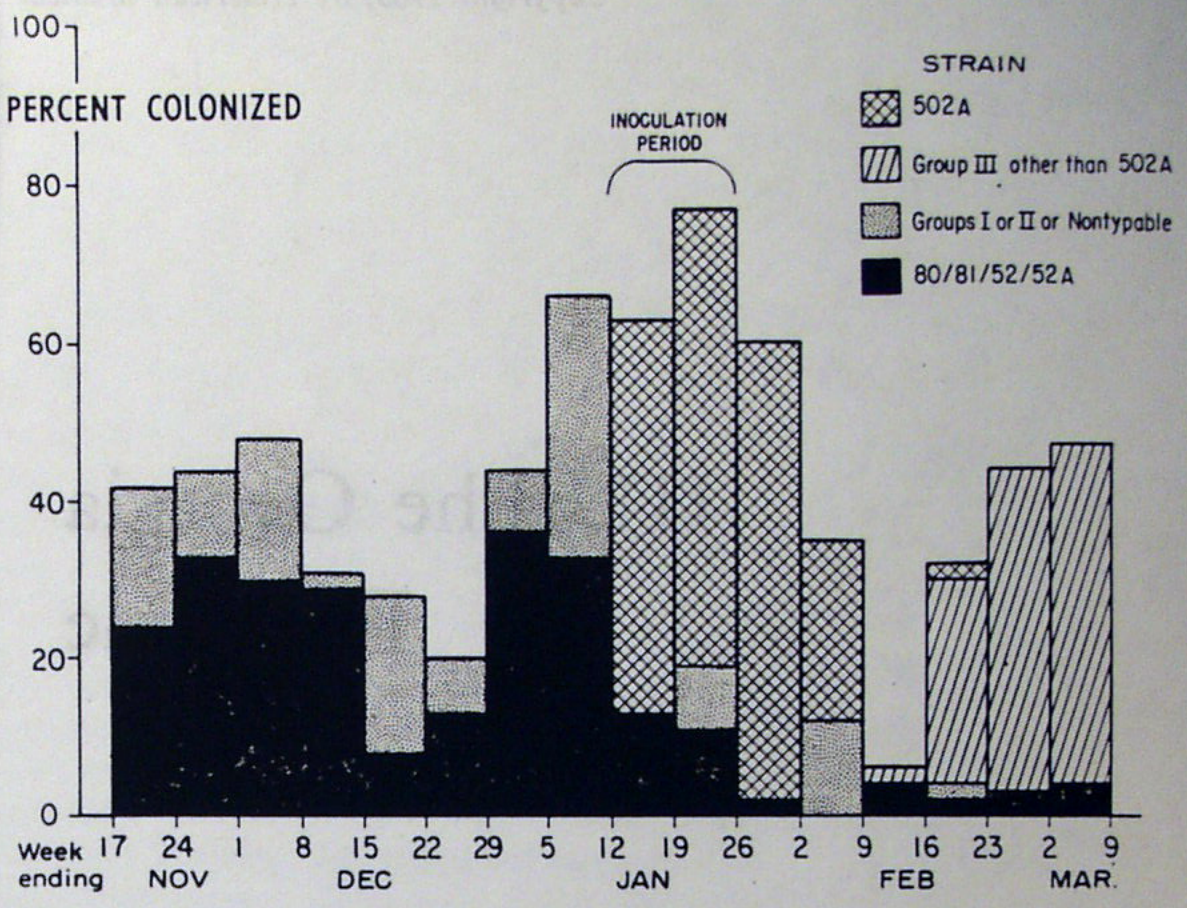

Fig 1.—Newborn nasal staphylococcal colonization.

hospital's nursery, the type of staphylococcus involved, and its pathogenicity as measured by incidence of lesions. These studies consisted of (1) nasal cultures at discharge of all infants born during this period (a total of 337 babies), (2) daily nasal cultures from birth until discharge on 192 infants, and (3) weekly nasal cultures of all nursery personnel.

These investigations demonstrated that at the time of discharge 139 or 40% of the 337 infants carried coagulase positive staphylococci in their nose; 89 of these infants were infected with staphylococcus phage type 52/52A/80/81. Since no umbilical cultures were obtained, it is likely that the proportion of colonized infants is greater than that indicated by these figures, which nevertheless demonstrated a high and continuous acquisition rate of type 52/52A/80/81 (Fig 1). The daily cultures showed that 72% of the babies did not become nasal carriers of staphylococci until the third or fourth day of life. The routes of spread or source of the *Staphylococcus aureus* type 52/52A/80/81 were not established, although personnel carriers possibly played a role since the noses of three of 22 staff members were found to be persistently colonized with this latter organism.

In order to demonstrate that staphylococcus type 52/52A/80/81 was responsible for the majority of lesions, a retrospective telephone survey was performed on a randomly

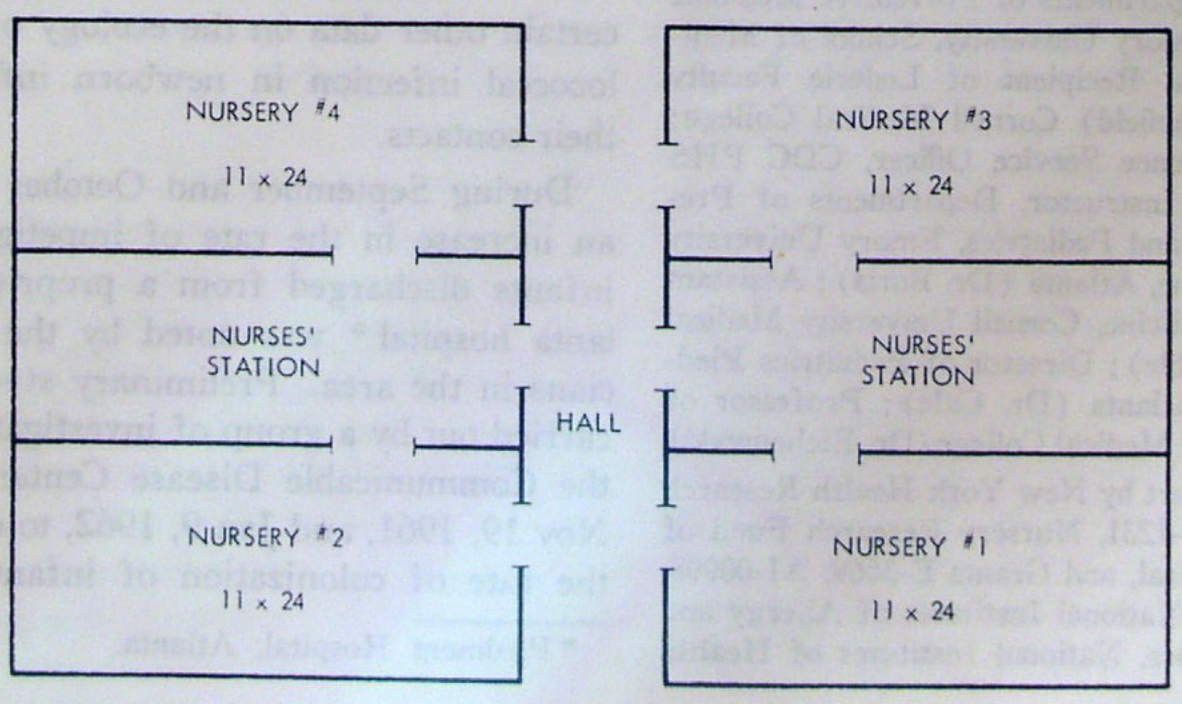

Fig 2.—A simplified floor plan of the nursery unit.

selected sample of 120 of the 337 infants. These data indicated that 14 of 40 type 52/52A/80/81 infected infants (35%) and 6 or 15% of their family contacts developed staphylococcal disease, while the respective figures for babies not colonized with the 52/52A/80/81 strain were 7 (9%) and 1 (1%) for family contacts.

Analysis of these data indicated that an epidemic situation existed which would permit further controlled evaluation of *Staphylococcus aureus* strain 502A. Accordingly on Jan 10, 1962, a study employing artificial colonization with strain 502A was begun.

Methods and Materials

Nursery and Newborn Procedures.—The newborn facilities consisted of a single nursery suite divided into two separate nursery units, separated by a hallway (Fig 2). Each nursery unit was further divided into two subunits (henceforth designated as Rooms *1, 2, 3,* or *4*), each measuring 11 × 24 feet, and separated by a central nurses' station. All full-term newborn infants were transferred directly from the obstetrical suite to the nurseries and assigned to Rooms *1* or *3* ("admitting nurseries"), depending on availability of space and whichever unit happened to be handiest. Premature infants were admitted to Room *4*. After a 3 to 4-day stay in their "admitting nursery" the infants were transferred to room *2* for an additional day or two prior to discharge on the fifth or sixth day of life. The average newborn census during the study was 36 with approximately 12 infants being housed in each of the 3 available rooms. No studies were performed on the premature infants in Room *4*.

Normal admission routine required a complete lotion bath, using a proprietary detergent containing 3% hexachlorophene. The infant was weighed on a communal scale and placed in a Gordon-Armstrong incubator for several hours prior to being transferred to a bassinet. The incubator was routinely cleaned with detergent containing phenol and aired between infants. Babies were transported to their mothers for feedings three to four times daily in common carriers holding four infants. Some babies received local cord medications, consisting of applications of alcohol, or sulfadiazine powder as prescribed by their private pediatricians.

When entering the nursery area nursery personnel donned clean caps and gowns and washed their hands with hexachlorophene containing soap for an unprescribed length of time but practiced no further routine handwashing while handling the infants. Aside from the introduction of disposable umbilical clamps during the second week of the study, no changes were made in admission procedures or nursery techniques during the course of the present investigation nor were the three known personnel carriers of type 52/52A/80/81 removed from regular duty or informed of their colonization status.

Bacteriologic Methods.—Nose and umbilical cultures were obtained daily from all infants. A single dry, sterile swab was inserted into the infant's anterior nares, rotated gently three times and dropped into a tube containing 0.5 ml of trypticase soy broth. Umbilical cultures were obtained by sweeping a dry, sterile swab twice about the base of the umbilical cord and immersing it in a tube containing 0.5 ml of sterile trypticase soy broth. The broth-containing tubes were left at room temperature for approximately four hours and the swabs then streaked on trypticase soy agar. After incubation at 37 C for 48 hours, plates were examined for colony morphology and pigmentation in order to determine the number of colonies to be phage typed. If only one type of colony morphology and color combination was present, a minimum of five colonies was picked from each plate. If two or more types of colonies were noted, three or four of each type were selected for phage typing. Colonies were typed using 22 phages by a standard method. All colonies not yielding a phage pattern were tested for coagulase production by a slide method. Disc antibiotograms were performed on selected strains with disc concentration as follows: penicillin, 2 units; tetracycline, 5 and 30μg; chloramphenicol, 5μg; erythromycin, 2μg; streptomycin, 1μg; novobiocin, 5μg; bacitracin, 10 units. Serologic typing of selected strains was performed by the slide agglutination method using the antibody to the following eight antigens: *a, b, c* polyvalent (c_p),(b)c_1, *h, i, k,* and m(3).

A total of 9,490 cultures were obtained during the nursery and follow-up study; 17,290 colonies were selected for phage typing and further testing.

Artificial Colonization of Infants.—Strain: The staphylococcus used for artificial colonization was the coagulase positive, penicillin-sensitive strain 502A described in detail in an earlier publication of this series.[1,3]

Technique of Inoculation.—Infants born in a two-week period were selected on a random basis for artificial colonization, the remainder served as controls. All inoculations were performed during the first two hours of life. Utilizing a microburette,† 0.0005 ml of a culture containing from 2,000 to 4,000 staphylococci was placed on the mucosa of each nostril and on the umbilical base at the skin junction. Appropriate titrations of the culture were made to determine the number of viable bacteria each infant had received. At 12 hours of age, the

† California Laboratory Equipment Co., Berkeley, Calif.

TABLE 1.—*Per Cent and Sites of Takes* in Infants Inoculated with Strain 502A*

Site	Number Inoculated	Takes	Takes, %
Nose	42	39	93.0
Umbilicus	42	30	71.5

* Take, presence of 502A detected by culture 24 hours after inoculation.

umbilical stumps were reinoculated with an identical dose of the 502A strain.

Follow-Up.—Follow-up epidemiologic data and cultures were obtained on 88 of the 92 infants in the study. Home visits were conducted at three-week intervals by a trained public health nurse. On the occasion of each visit, cultures were obtained from the nose and umbilicus of each infant and from the nares of all household members. Any lesion noted by the nurse at the time of her home visit was also cultured. Since these visits were made during the working day, only relatively few fathers were encountered and because of this, they are omitted from the analysis of data. Additional information was obtained by the nurse using a standardized questionnaire. A household roster was prepared, the method of infant feeding was noted, detailed information about the incidence, duration and specific therapy of any household illness was collected and, when indicated, personal physicians were contacted and hospital records reviewed.

Results

Incidence of Successful Inoculations.—Among the 42 infants in whom artificial colonization was attempted, nasal colonization with strain 502A was achieved in 39 (93%), and umbilical colonization in 30 (71.5%). It is of interest and perhaps of significance that among the 12 infants in whom we failed to establish strain 502A colonization on the umbilicus, eight were noted to have Gram-negative organisms on their cord within the first 24 hours of life.

In the analysis of the data, it was necessary to exclude a number of infants: one artificially colonized baby was noted to have staphylococcus type 52/52A/80/81 and strain 502A in its nose at 24 hours, and two babies had both organisms on their cords on the first day of life. Also excluded were 15 infants, three of whom failed to become nasal carriers of strain 502A and 12 who were unsuccessfully inoculated on the cord.

The Effect of Staphylococcus 502A on Subsequent Nasal Colonization With Other Staphylococci.—The interfering effect of staphylococcus strain 502A on subsequent nasal colonization is clearly demonstrated in Table 2. Of 38 infants artificially colonized with strain 502A, only one picked up a different staphylococcus during his hospital stay, while in a control group nine of 50 infants became nasally colonized with type 52/52A/80/81 and an additional four with other types of coagulase positive staphylococci. This difference in the rate of acquisition of coagulase positive staphylococci other than strain 502A between the control and artificially colonized infants is significant at $P = <0.01$.‡

‡ Statistical analyses were performed using χ^2 with Yates correction term. If numbers totaled less than 50 or contained a zero Fisher's exact test was used.

TABLE 2.—*Nasal Colonization with Coagulase Positive Staphylococci, Other Than 502A in Control and Successfully Inoculated Infants During Hospital Stay and Initial Follow-Up*

	52/52A/80/81		Total Study Coagulase Positive Other Than 52/52A/80/81 or 502A		Total	
Infants	H •	F •	H •	F •	H •	F •
Inoculated takes †	1/38 §	0/35	0/38 §	0/35	1/38 §	0/35
Control	9/50	14/48	4/50	3/48	13/50	17/48
					P = <0.01	

• Infants in category/total number of infants; H, hospital stay; F, follow-up at three weeks.

† Take, presence of 502A detected by culture 24 hours after inoculation.

§ One infant with both 52/52A/80/81 and 502A on first day of life and three unsuccessfully inoculated infants excluded from the analysis of the data.

TABLE 3.—*Spontaneous Colonization of Control Infants with 502A Strain*

Total controls	50
Nasal colonization with 502A	21, 42%
Umbilical colonization with 502A	21, 42%
Total infants colonized with 502A	24, 48%

During the second week of the study, spontaneous colonization with the 502A organisms was noted to be occurring among the controls. The mechanisms of this spontaneous spread are unknown; no personnel carriers were found. Of the entire total of 50 control infants, 21 (42%) became spontaneously colonized in the nose and 21 (42%) at the umbilical site with strain 502A. In all, 24 (48%) infants spontaneously acquired this organism either in the nose, umbilicus or both (Table 3). Coincident with this high rate of spontaneous colonization with type 502A, a fall in the recovery rate of other coagulase positive staphylococci was observed.

Because of the large number of control infants becoming colonized with strain 502A during the second week of the study, the data were analyzed on a weekly basis (Table 4).

During the first week, one of the 23 infants successfully artificially colonized acquired another coagulase positive staphylococcus. During the same period, among the 29 control infants, 11 acquired a coagulase positive strain other than 502A in their nose. This difference in the number of infants colonized is significant at $P = <0.004$.

During the second week, colonization with a coagulase positive strain other than 502A

TABLE 4.—*Nasal Colonization with Coagulase Positive Staphylococci Other Than 502A by Week of Study*

	1st Wk		2nd Wk	
Infants	H *	F *	H *	F *
Inoculated takes †	1/23 ‡	0/22	0/15 ‡	0/13
Control	11/29	16/27	2/21	1/21

* Infants in category/total number of infants; H, hospital stay; F, follow-up at three weeks.

† Take, presence of 502A detected by culture 24 hours after inoculation.

‡ One infant colonized with both 502A and 52/52A/80/81 on day one of life excluded and three unsuccessfully inoculated infants excluded from the analysis of the data.

was limited to two control infants; no baby in the inoculated "take" group became infected by other types of coagulase positive staphylococci.

The Effect of Strain 502A on Subsequent Umbilical Colonization With Other Staphylococci.—In the 28 inoculated "take" infants, no other coagulase positive strains were isolated from the umbilicus during the hospital stay or at the time of follow-up at three weeks (Table 5). Thirteen of the 50 control babies were colonized during the hospital stay with either type 52/52A/80/81 or another coagulase positive staphylococcus, other than strain 502A. The difference in the two groups is significant at $P = 0.002$.

Umbilical colonization data were also analyzed separately for each week (Table 6). During the first week, none of the 16 successful artificially colonized infants acquired a staphylococcal strain other than 502A, while in the control group, 11 of 29 infants acquired *Staphylococcus aureus*. Two con-

TABLE 5.—*Umbilical Colonization With Coagulase Positive Staphylococci, Other Than 502A, in Control and Successfully Inoculated Infants During Hospital Stay and Initial Follow-Up*

	52/52A/80/81		Total Study Coagulase Positive Not 52/52A/80/81 or 502A		Total	
Infants	H †	F *	H *	F *	H *	F *
Inoculated takes †	0/28 ‡	0/28	0/28 ‡	0/28	0/28 ‡	0/28
Control	8/50	0/48	5/50	3/48	13/50	3/48
					P = <.002	

* Infants in category/total number of infants; H, hospital stay; F, follow-up at three weeks.

† Take, presence of 502A detected by culture 24 hours after inoculation.

‡ Two infants colonized with 52/52A/80/81 and 502A on day one of life and 12 no take infants excluded.

TABLE 6.—*Incidence of Umbilical Colonization with Coagulase Positive Staphylococci Other Than 502A by Week of Study*

Infants	1st Wk H *	1st Wk F *	2nd Wk H *	2nd Wk F *
Inoculated takes †	0/16 ‡	0/16	0/12 ‡	0/12
Control	11/29	0/27	2/21	3/21
	$P = <0.003$			

* Infants in category/total number of infants; H, hospital stay; F, follow-up at three weeks.

† Take, presence of 502A detected by culture at 24 hours after inoculation.

‡ Two infants colonized with both 502A and 52/52A/80/81 on day one of life and 12 no take infants excluded.

trol infants were colonized by a strain other than 502A during the second week of the study.

The Relationship of Staphylococcal Disease to Type of Staphylococcus in the Nose.—During the 24 week follow-up period, 17 lesions were recorded in the study infants or their families (Table 7). Of the 17 lesions, 8 were present at the time of a home visit and were cultured. Among the 14 infants who had become nasal carriers of staphylococcus type 52/52A/80/81 while in the nursery, lesions were observed in 10 babies or in a family contact. One baby who developed impetigo was known to have been nasally colonized with both strain 502A and type 80/81, and both organisms were isolated from a culture of the lesion. Among the 54 infants who had only strain 502A on their nasal mucosa throughout their hospital stay or at the time of the initial follow-up visit, two cases of conjunctivitis were observed. From one of these strain 502A was recovered and no staphylococcus was present in the other. One of the mothers of an infant colonized with strain 502A developed mastitis, although she had never breast fed her baby. The lesion did not suppurate, and no discharge from the nipple was noted. At the time of the follow-up visit, no lesion was apparent, and therefore no culture was obtained from this site. No coagulase positive staphylococci were recovered from the mother's nose.

Three additional lesions occurred in infants not colonized either with type 52/52A/80/81 or strain 502A. One was observed in an infant colonized with a nontypable coagulase positive staphylococcus at discharge and two were noted in babies from whom no coagulase positive staphylococci were recovered.

There is a difference at a significance level of $P = <0.0005$ when the incidence of lesions in the type 52/52A/80/81 colonized group is compared to the incidence of lesion found in the other infants. In infants colonized with various staphylococci other than 52/52A/80/81 the incidence of lesions was low and of the same order as was found in infants whose nasal mucosa was free of detectable coagulase positive staphylococci.

TABLE 7.—*Correlation of Type of Nasal Colonization with Staphylococci With Subsequent Lesions*

Lesions	52/52A/80/81	Nasal Colonization Status: 52/52A/80/81 + NT or 502A	502A	Other Coag. + Staph	Noncoag. + Staph
Infants					
Impetigo	6 (3) *	1 † (1)			
Vaginitis				1	
Conjunctivitis	1 (1)		2 (1)		2
Omphalitis	1				
Family					
Maternal mastitis	1 (1)		1 ‡		
Maternal abscess	1 (1)				
Lesions/index family	10/14	1/5 §	3/54	1/4	2/11

* Parentheses indicate organism recovered by culture.

† Infant with both 52/52A/80/81 and 502A cultured from lesion.

‡ Mother not colonized with coagulase positive staphylococci, lesion not cultured.

§ Four infants with 52/52A/80/81 and 502A; one infant with 52/52A/80/81 and NT.

TABLE 8.—*Types of Lesions Observed in Inoculated and Control Infants and Their Family Contacts*

	Inoculated Infants	Control Infants
Infants		
Impetigo	1 *	6
Vaginitis	0	1
Conjunctivitis	1	4
Omphalitis	0	1
Family		
Maternal mastitis	1 †	1
Maternal breast abscess	0	1
Lesions/index family	3/40	14/48

* Infant with 52/52A/80/81 and 502A in nares and lesion.
† Mother uncolonized, lesion not cultured.

The incidence of lesions in the entire inoculated group of infants, irrespective of successful "takes" has been compared to the entire group of control infants, some of whom were spontaneously colonized with strain 502A (Table 8). In the families of the 40 inoculated infants, 3 lesions occurred: 1 case of conjunctivitis, 1 case of maternal mastitis (described above), and 1 infant with impetigo. As noted previously, this latter infant harbored both strain 502A and type 52/52A/80/81 in his nose. One minor lesion (conjunctivitis) could therefore be associated with strain 502A. In the 48 families of uninoculated control infants, a total of 14 lesions occurred. Difference in the inoculated and control groups is significant at $P=0.03$.

Staphylococcal Colonization in the Nursery After Cessation of Artificial Colonization.—Spontaneous colonization with the 502A staphylococcal strain which first became apparent during the second week of the study continued for an additional two weeks after artificial colonization had been stopped (Fig 1). As spontaneous colonization with strain 502A diminished, another phage group III staphylococcus appeared and became the predominant strain colonizing the newborns. As long as these other staphylococci were widely prevalent among the infants, a very low level of type 52/52A/80/81 colonization was noted. Bacteriologic surveillance of the nursery in the succeeding six-month period indicated that the incidence of colonization by staphylococci belonging to the 52/52A/80/81 complex remained at levels below 4%.

Persistence of Nasal Colonization with Coagulase Positive Staphylococci.—In the 21 spontaneously colonized infants, the rate of strain 502A colonization gradually fell from 90% at discharge to 79% and 63% at the 15 and 24 week follow-up period respectively (Fig 3, Table 9). The rate of persistence of strain 502A in the infants artificially colonized fell from 90% at discharge to 47% at the 15-week follow-up and to 31% at the 24-week visit. A striking difference in the duration of colonization was noted in infants nasally colonized with type 52/52A/80/81. Of the 18 infants colonized with this organism at discharge, only three were still colonized at 15 weeks (18%). The five infants who harbored other coagulase positive staphylococci comprise too small a group for valid conclusions.

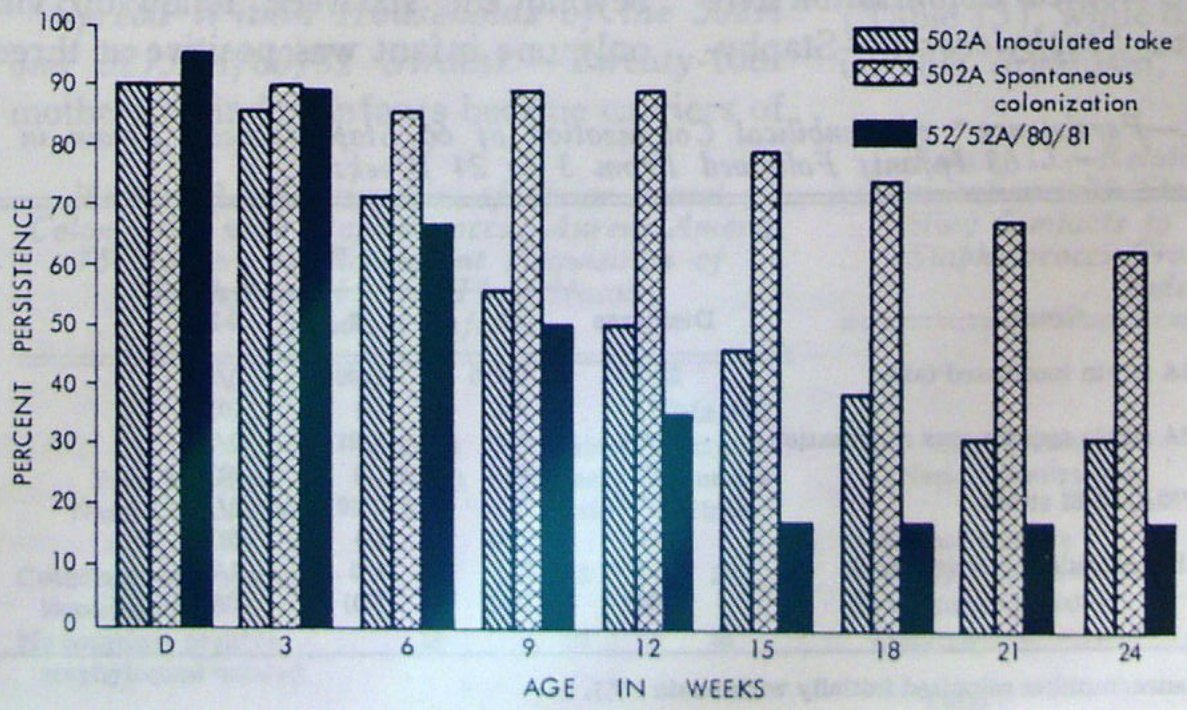

Fig 3.—Comparison of persistence of nasal colonization of the different groups of coagulase positive staphylococci.

TABLE 9.—*Persistence* of Nasal Colonization of 84 Staphylococcal Strains in 77 Infants Followed From 3 to 24 Weeks*

Group	Discharge	Age, Wk 3	6	9	12	15	18	21	24
502A strain inoculated takes	35/39 (90)	31/36 (86)	26/36 (72)	20/36 (56)	18/36 (50)	17/36 (47)	14/36 (39)	11/36 (31)	11/36 (31)
502A strain spontaneous colonization	19/21 (90)	19/21 (90)	18/21 (86)	17/19 (89)	17/19 (89)	15/19 (79)	14/19 (74)	13/19 (68)	12/19 (63)
52/52A/80/81 strain	18/19 (95)	16/18 (89)	12/18 (67)	9/18 (50)	6/17 (35)	3/17 (18)	3/17 (18)	3/17 (18)	3/17 (18)
Other coagulase positive staphylococci	5/5 (100)	4/5 (80)	3/5 (60)	3/5 (60)	2/5 (40)	2/5 (40)	2/5 (40)	2/5 (40)	1/5 (20)

* Number with persistence/number colonized initially with strain (%).

The difference in the persistence rate at 15 weeks observed in infants artificially or spontaneously colonized with strain 502A is significant at a level of $P=0.05$. Difference in staphylococcal persistence in the type 52/52A/80/81 group compared to both strain 502A groups is significant at $P=0.01$.

Persistence of Umbilical Colonization with Coagulase Positive Staphylococci.—Staphylococci were lost from the umbilical site more rapidly in infants colonized with type 52/52A/80/81 than in infants colonized either spontaneously or artificially with strain 502A (Fig 4, Table 10). Of the 10 infants colonized with type 52/52A/80/81 at discharge, no recovery of this organism was possible beyond the six-week follow-up visit, and only one infant was positive at three weeks

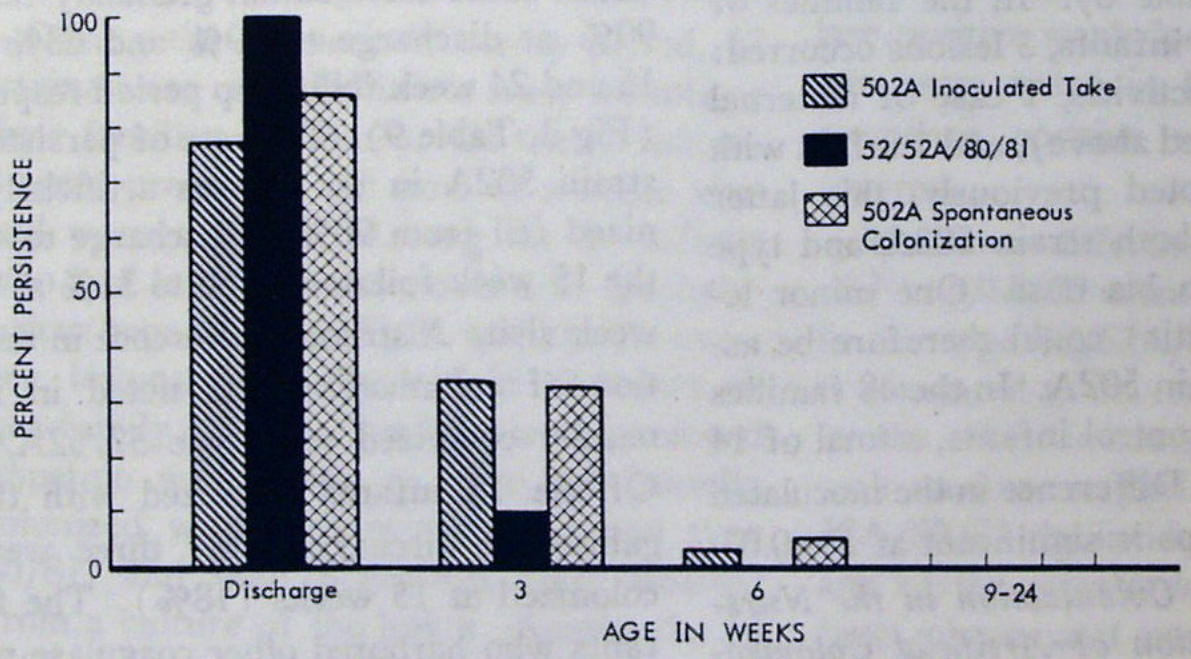

Fig 4.—Comparison of persistence of umbilical colonization of the different groups of coagulase positive staphylococci.

TABLE 10.—*Persistence* of Umbilical Colonization of 66 Staphylococcal Strain in 63 Infants Followed From 3 to 24 Weeks*

Group	Discharge	Age, Wk 3	6	9-24
502A strain inoculated take	23/30 (77)	10/30 (30)	1/30 (3)	0/30 (0)
502A strain spontaneous colonization	18/21 (86)	7/21 (33)	1/21 (5)	0/21 (0)
52/52A/80/81 strain	10/10 (100)	1/10 (10)	0/10 (0)	0/10 (0)
Other coagulase positive staph	5/5 (100)	2/5 (40)	1/5 (20)	0/5 (0)

* Number with persistence/number colonized initially with strain (%).

TABLE 11.—*Nasal Carrier Status at Time of Initial Follow-Up Among Infants With No Coagulase Positive Staphylococci Isolated From Nose or Umbilicus During Nursery Stay*

Infants With No Coagulase Positive Staphylococcus Isolated in Nursery	Follow-Up Nasal Culture at 3 Weeks			
	502A *	52/52A/80/81 *	Coag. + Staph Other Than 502 and 52/52A/80/81	Other †
17	7, 41%	4, 24%	1	5

* Identical to nursery strain by phage type, antibiotic sensitivity pattern and serology.
† Coagulase negative staphylococci or nonstaphylococcal organisms.

of age. No differences within the spontaneously colonized or artificially colonized strain 502A group could be detected. One third of the members of both groups, which totaled 50 infants, were still colonized at the umbilical site at three weeks of age, and only one in each group was positive at six weeks.

Subsequent Nasal Colonization in Infants Who Were Uncolonized Throughout the Nursery Stay.—Despite daily cultures for a minimum of five days, coagulase positive staphylococci were not isolated from either the nasal mucosa or umbilical stump in 17 of the 50 control infants. Coagulase positive staphylococci were isolated from the nasal mucosa in 12 of the 17 infants at the initial three week follow-up (Table 11). Seven isolated were identified as strain 502A, four were type 52/52A/80/81 strains, one was type 3A, and five infants had no detectable coagulase positive staphylococci at any of the follow-up visits.

Spread Within Households of the 502A and 52/52A/80/81 Strains.—Twenty-four mothers of index infants became carriers of nursery strains of staphylococci acquired from their infants (Table 12). Colonization occurred in 15 of 58 mothers exposed to their 502A colonized babies. Similarly, 7 of 19 mothers exposed to type 52/52A/80/81 index babies became colonized with this latter organism. Two of five mothers acquired a coagulase positive staphylococcus other than strain 502A or type 52/52A/80/81 from their infants. It is of interest that only two of the 22 mothers (9%) who carried a coagulase positive staphylococcal strain prior to exposure acquired a nursery strain while 22 of 53 mothers (41%) who did not carry coagulase positive staphylococci nasally picked up the nursery strain. These differences are significant at a level of $P=0.02$.

A similar relationship was found among the siblings of index infants. All 13 siblings who acquired a staphylococcus from the index baby had no pre-existing coagulase positive staphylococcus on the nasal mucosa (Table 13), while of the 59 who did not pick up this organism, 20 had previously been

TABLE 12.—*Relationship of Prior Nasal Colonization with Staphylococcus Aureus Among 75 Mothers to Subsequent Acquisition of Staphylococci From Their Nasally Colonized Infants*

Prior Maternal Nasal Colonization	Total No. at Risk	Acquired Nursery Strain	Did Not Acquire Nursery Strain
Coagulase positive staphylococci isolated	22	2	20
No coagulase positive staphylococci isolated	53	22	31
Total	75	24	51

TABLE 13.—*Relationship of Prior Nasal Colonization with Staphylococcus Aureus Among Sibling Contacts to Subsequent Acquisition of Staphylococci From 77 Nasally Colonized Index Babies* *

Prior Sibling Nasal Colonization	Total No. at Risk	Acquired Nursery Strain	Did Not Acquire Nursery Strain
Coagulase positive Staphylococci isolated	20	0	20
No coagulase positive Staphylococci isolated	52	13	39
Total	72	13	59

* Represents 75 families (two sets of twins).

found to harbor coagulase positive staphylococci. These differences are significant at $P=0.01$.

Subsequent Recolonization in Infants Losing the 502A Strain.—Of the 58 infants with strain 502A on the nasal mucosa, 30 lost the organism at some time during the 24-week follow-up. Twenty-one babies did not reacquire coagulase positive staphylococci, while eight acquired an organism with a phage pattern similar to one isolated from a household member, and one acquired a staphylococcus not related to any strain present in the household.

Comment

These data lend additional support to earlier findings which indicated that the presence of coagulase positive staphylococci interfered with colonization by other coagulase positive strains of staphylococci both on the nasal mucosa and at the umbilical site of newborn infants.[1,2] Although only one minor change was made in nursery routines (disposable cord clamps substituted for Zeigler clamps), the rate of type 52/52A/80/81 colonization declined, and it could be demonstrated that a highly significant degree of protection against type 52/52A/80/81 colonization as well as staphylococcal disease could be obtained by artificially colonizing the infant's noses and cord stumps.

It is of interest that strain 502A proved capable of spontaneous and rapid spread once it had been firmly established in the population, emphasizing the ease with which staphylococci can be acquired by newborns. When this organism had become the predominant nursery strain, colonization with other staphylococci, including type 52/52A/80/81 diminished.

The proportion of successful attempts at artificial colonization on the nasal mucosa is similar to that shown in our previous studies. However, the rate of successful artificial colonization on the umbilicus is slightly below that observed earlier. It is possible that the frequent presence of pseudomonas and proteus on the cord on the first day was responsible for some or all of these failures. These Gram-negative bacteria were apparently acquired by the baby from the Ziegler cord clamps, which had been soaked in benzalkonium solutions. The solutions as well as the clamps were found to be contaminated with proteus and pseudomonas. Disposable cord clamps were substituted for the Ziegler clamps during the latter part of the study, and Gram-negative colonization of the cords with these particular organisms diminished.

The incidence of lesions has been carefully investigated because of the obvious importance of knowing the rate and type of lesions which may accompany staphylococcus strain 502A infection. In the present study, only one lesion, a case of conjunctivitis, was found to be associated with the presence of strain 502A. An etiologic relationship of the organism to the conjunctivitis is not clearly established since two cases of conjunctivitis were found to occur in infants who were not colonized with coagulase positive staphylococci. In any event, the rate of disease following strain 502A infection was very low, and perhaps nonexistent, in contradistinction to the amount of illness observed in type 52/52A/80/81 colonized babies and their contacts.

The fact that family contacts not harboring coagulase positive staphylococci in their nasopharynx were more likely to acquire staphylococci from the index babies is in accord with our previous observations,[2] and those made in adults by other investigators.[4,5]

Facts are not available to explain why infants colonized with the penicillin-resistant type 52/52A/80/81 staphylococcus lose this more rapidly than the penicillin-sensitive 502A strain. Similar differences between penicillin-sensitive and penicillin-resistant staphylococci have been observed among adults by Dowling, Lepper, and Jackson.[6] Of similar interest is the tendency for spontaneously colonized infants to retain strain 502A for longer periods of time than babies artificially colonized with the same organism. It was not possible for us to implicate varying degrees of exposure or previous anti-

biotic therapy as factors responsible for the differences in persistence rates. Local and systemic immunologic and cellular factors that might be responsible for these differences need to be investigated.

Summary

During an outbreak of staphylococcus type 52/52A/80/81 infection and disease in a nursery, interference between staphylococcal strains has been demonstrated to occur in newborn infants at both the nasal and umbilical sites. Artificial colonization with strain 502A offered a high degree of protection against subsequent acquisition of other staphylococcal types.

Striking diifferences in disease rates were demonstrated to occur among infants colonized with type 52/52A/80/81 and strain 502A. While staphylococcus type 52/52A/80/81 produces a high incidence of disease among infants and their family contacts, this was not observed with strain 502A colonized babies.

Staphylococcus strain 502A proved capable of spontaneous and rapid spread once it was firmly established in the nursery population. The routes of dissemination have not been identified but are probably similar to those followed by type 52/52A/80/81.

Of the 17 infants who were discharged with no detectable staphylococcal colonization of nasal or umbilical sites, 11 (65%) were found to be infected with nursery strains at the time of the initial follow-up visit.

The presence of coagulase positive staphylococci in the nose of family contacts of either strain 502A or type 52/52A/80/81 infected infants offered considerable protection against colonization by organisms derived from the infant.

Nasal colonization persisted longest among infants spontaneously colonized with strain 502A and was significantly longer than that observed with babies infected with type 80/81. By six weeks of age the rate of umbilical colonization with all staphylococcal strains was very low.

We would like to acknowledge gratefully the technical assistance of Mrs. Mildred M. Galton, Mr. Emmett B. Shotts, Miss Anita P. King, Mrs. Gladys H. Reynolds, and Mrs. Oreila C. Dickson, RN, Epidemiology Branch of Communicable Disease Center, Atlanta.

The cooperation of the following is also gratefully acknowledged: Thomas F. Sellers, Jr., MD, Professor of Preventive Medicine, Emory University School of Medicine, and Philip S. Brachman, MD, Epidemiology Branch, Communicable Disease Center, Atlanta.

We are particularly indebted to the entire Administrative, Medical and Nursing Staff of the Piedmont Hospital, Atlanta, for their full cooperation during the study.

REFERENCES

1. Shinefield, H. R.; Ribble, J. C.; Boris, M.; and Eichenwald, H. F.: Bacterial Interference: Its Effect on Nursery-Acquired Infection with Staphylococcus Aureus; I. Preliminary Observations on Artificial Colonization of Newborns, Amer J Dis Child, this issue, p 646.

2. Shinefield, H. R.; Sutherland, J. M.; Ribble, J. C.; and Eichenwald, H. F.: Bacterial Interference: Its Effect on Nursery-Acquired Infection with Staphylococcus Aureus; II. The Ohio Epidemic, Amer J Dis Child, this issue, p 655.

3. Cohen, J. O.; Smith, P. B.; Shotts, E. B.; Boris, M.; and Updyke, E. L.: Bacterial Interference: Its Effect on Nursery-Acquired Infection With Staphylococcus Aureus; VI. Detection of Implanted Staphylococcus Aureus Strain, Amer J Dis Child, this issue, p 689.

4. Rountree, P. M., and Barbour, R. G. H.: Nasal Carrier Rates of Staphylococcus Pyogenes in Hospital Nurses, J Path Bact 63:313, 1951.

5. Clarke, S. K. R.: Nasal Carriage of Staphylococcus Aureus, J Path Bact 73:253, 1957.

6. Dowling, H. F.; Lepper, M. H.; Jackson, G. G.: Observations on the Epidemiological Spread of Antibiotic Resistant Staphylococci with Measurements of the Changes in Sensitivity to Penicillin and Aureomycin, Amer J Public Health 43:860, 1953.