Control of Staphylococcal Carriers in Three Hospitals

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ALTHOUGH controversy surrounds the importance of the carrier of pathogenic staphylococci in initiating and perpetuating nursery and hospital epidemics (*1*, *2*), few deny that patient welfare is served best if the carrier is eliminated (*3–6*). The carrier state may be remedied. The obvious advantages of eliminating the carrier state engendered a study to determine means of feasibly and successfully divesting these carriers of pathogens. Treatment of persons who are staphylococcal carriers does not preclude the use and enforcement of conventional aseptic measures.

Materials and Methods

Carriers were detected during screening initiated to investigate staphylococcal outbreaks in nurseries at three institutions. The detection program was extended to medical students, new employees, personnel in noncritical areas, and families of some persistent carriers. The highest positive yields were from the external nares (*7*) and, unless the person had gross lesions or physical problems at other sites, most specimens cultured in this study were taken from the nares. Other areas sampled during the early phase of the study included hair, hands, wrists, armpits, and throat.

Sterile cotton-tipped applicators were inserted approximately 2 centimeters into both nares, rotated, and inoculated immediately onto staphylococcus medium No. 110 (*8*). Both the nasal fossae and vestibule were sampled by this method.

All representative staphylococcal colonies were tested for the presence of free and bound coagulase (*9*). If the morphology of the isolate was homogeneous, only one sample was taken; if two or more colonies showed different characteristics, each representative colony was studied. All coagulase-positive organisms were tested for antibiotic sensitivity by the impregnated disk technique using 15 antibiotics. Only organisms isolated from patients in the nursery and nursery personnel were phage typed. Phage typing was performed by the Texas State Department of Health.

Of the 224 carriers treated in this study, approximately half were actively engaged in patient care; the other half were selected from nonpatient areas. A control group of 60 carriers, whose duties were in nonpatient or noncritical areas, were not treated. At monthly intervals specimens were obtained from the control group and cultured to determine how many spontaneously became noninfective. Persons who received antibiotic or chemotherapeutic drugs for any cause were eliminated from this group.

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The therapy used on the carriers included systemic and intranasal chemotherapeutic and antibiotic agents (see table). As the testing progressed, it became evident that spray agents had practical advantages when both efficacy and convenience were considered. These agents were employed both with and without vasoconstrictors, topical anesthetics, wetting agents, and steroids. A preparation was used until it irritated the nasal mucosa or was ineffective in eliminating the carrier state.

Each person was instructed to spray three times daily for 4 days. Three days after the person stopped spraying, a specimen was obtained and cultured. The course was repeated if the culture was still positive for staphylococcus. Participants were encouraged but not coerced to follow this regimen.

Specimens were obtained and cultured at monthly intervals on successfully treated persons in an effort to ascertain the long-term protection afforded by the topical treatment. Treatment of noncarriers should be avoided because disruption of their normal flora may predispose them to pathogens (*10*).

Results

Specimens from approximately 2,000 persons were cultured during the study. The absolute carrier rate for this sample was 24 percent. Preclinical medical students showed the lowest staphylococcal carrier rate, 6 percent, while 63 percent of the nursery personnel were infected during the height of an epidemic.

The carrier rate almost always correlated with the degree of exposure to infected patients. For example, fewer than 10 percent of postpartum mothers normally harbored *Staphylococcus aureus*. However, when an epidemic existed in a nursery, more than 70 percent of postpartum mothers yielded positive specimens. Slightly less than 12 percent of new employees harbored pathogenic staphylococci. Practically all cultures of specimens from mothers were performed 12 to 36 hours after delivery. Quantitation of growth proved valueless because of the numerous variables associated with sampling. Although the sampling method lacked quantitative accuracy, it was qualitatively reliable.

Only 18 persons were found to have more than one strain of *S. aureus*. All but one of these persons were stationed in patient areas and in every instance one of the strains proved to be an epidemic variety of *S. aureus* prevalent in the nursery area at the time of study.

Almost all recurrences to the carrier state in nonpatient areas involved the original staphylococcus strain. This was confirmed by studying the morphological and antibiotic sensitivity patterns of organisms obtained by periodic sampling. Approximately half of the persons in patient areas contracted a staphylococcus different from the organisms endemic to the patient environment. Persons harboring one strain (70/44A/29) contracted another (52/81/80) when the strain prevalent in the nursery changed.

Of the various nasal-spray mixtures tried, most were found to be too noxious to the nasal mucosa for continuous use. The nitrofurans and quaternary compounds were highly effective in eliminating the carrier state in a small number of persons, but their usefulness was limited

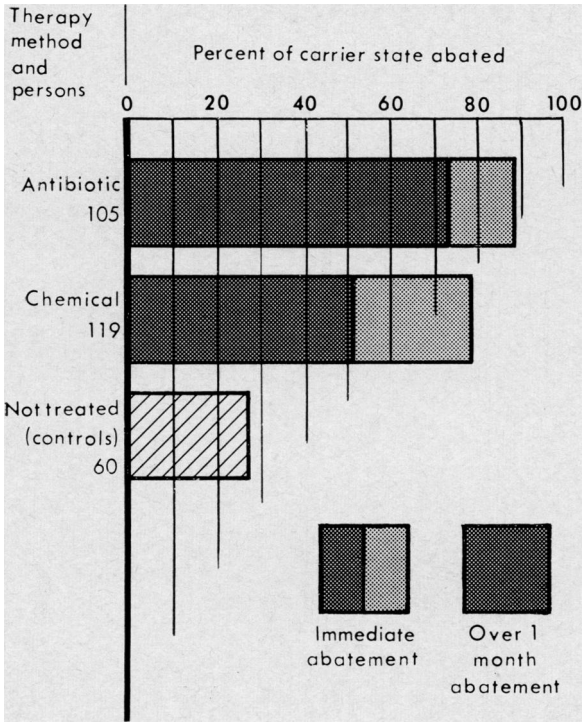
Chemotherapeutic and antibiotic agents tested against staphylococci in carriers among hospital staff

Drug [1]	Number of carriers [2]	Carrier state immediately suppressed (percent)	Percent with side effects
Group 1			
Clorpactin (2 types)	75	78	10
Furacin	3	100	100
Neomycin	10	70	0
Polymyxin B	15	13	6
Zepharin	5	20	40
Staph phage (nonspecific)	5	0	0
Sulfa cream	8	25	0
Lysozyme	2	0	0
Triclobisonium (triburon)	8	12	100
Specific antibiotic	9	56	0
Group 2			
Gramicidin, neomycin, polymyxin B, hydrocortisone	105	89	3

[1] Except for the specific antibiotics, which were taken orally, all drugs were applied topically.

[2] The numbers of carriers in group 1 total more than 119 because several persons were tested with 1 or more drugs.

Comparison of abatement of carrier state in persons who received chemical agents, or antibiotic spray, or were not treated



because they were extremely irritating. Nascent chloride agents were only moderately irritating, but they were not sufficiently potent to eradicate the more tenacious strains of staphylococci.

Because the number of persons treated with certain chemotherapeutic agents was statistically too small to evaluate, all who received medications other than topical antibiotics were classified with those who were given "chemical agents." Of 119 persons in group 1, 79 percent were immediately relieved of their carrier state (see table). Approximately half of this group were still free of *S. aureus* after 1 month.

Some mixtures of topical antibiotics were harmless to the mucous membrane and at the same time were highly effective in eliminating staphylococci from the nasopharnyx. The optimal mixture finally selected on the basis of maximum therapeutic efficacy with minimum side effects contained gramicidin, 0.05 mg. per cc.; neomycin, 0.6 mg. per cc.; and polymyxin B, 2,000 μ per cc. Hydrocortisone, 0.2 mg. per cc.; hydroxyamphetimine, 5 mg. per cc.; and phenylephrine, 1.25 mg. per cc., augmented the action of the active ingredients.

The staphylococcal carrier state was eliminated in 89 percent of 105 persons (group 2) treated with the antibiotic spray. Seventy-three percent of this group remained free of pathogenic staphylococci for 30 days or longer (see chart). Normal flora will develop within a 4-day period in former carriers, provided reexposure to pathogenic organisms is prevented. The chi-square value of 89 percent over the 79 percent rate of eliminating the carrier state by using chemical agents is significant at the 0.1 level; both, when compared to the 27 percent spontaneous cure rate, are significant at the 0.01 level.

Approximately 15 percent of the persons given antibiotic nasal sprays had failed to respond to chemotherapeutic agents, and they were stationed in areas where exposure to reinfection was inevitable. In addition, all persons whose carrier state was not abated by other means were treated with antibiotic sprays.

An estimated 25 percent of those successfully treated by antibiotic nasal spray harbored the more tenacious phage types 53/77/83A and 52/80/81. These strains did not disappear spontaneously.

The rate of disappearance of the carrier state from among the 60 untreated carriers was 27 percent. In general, the spontaneous disappearances were limited to those phage types which were nonepidemic or nontypable. Rarely did the epidemic strains 20/44A/29, 6/47/70/44A, 42/80/81, or 53/77/83A disappear without therapy, and rarely would a carrier spontaneously become negative for staphylococci while stationed in a contaminated area.

Three patients reacted unfavorably to the antibiotic spray. Side effects observed were nausea, dry nasal membranes, and external nasal irritation. These persons had not been previously exposed to the spray ingredients, but all had pronounced histories of allergy. No adverse long-term effects were seen. There was no evidence of increased resistance by staphylococci to the three antibiotics contained in the spray.

Some people with long-standing pharyngeal or paranasal disease required as many as six

courses of therapy before cultures negative for staphylococci were obtained. Phage type 52/80/81 was the most difficult to eradicate.

Persons on inadequate diets seemed particularly susceptible to *S. aureus* and were somewhat resistant to therapy. Some of these people responded to treatment when their diets were supplemented with therapeutic vitamins A and C.

Concurrently during this study, other measures were being conducted to control the nursery epidemics. These included rigorous isolation measures, prophylactic systemic antibiotic protection, hexachlorophene baths, and installation of germicidal lights. Doubtlessly, these parallel efforts significantly limited cross-infection and indirectly improved clearance rates.

Although prophylactic treatment temporarily reduced the incidence of the carrier state among infants and mothers, the rate remained high among nursery personnel. Subsequent treatment of personnel with antibiotic nasal spray was associated with a decrease in personnel carrier rate and coincidentally a lower rate among infants and mothers. The staphylococci isolated subsequently were nontypable or nonepidemic.

Discussion

Several investigators consider hospital personnel the active reservoir of staphylococcal infection (*5,6,11,12*), and the number of carriers is frequently so large that their removal—even temporarily—from patient areas is impractical (*13*). The 89 percent efficacy of topical antibiotic therapy suggests that this is a rational approach to protection of patients, hospital personnel, and their families.

It may be reasoned that as a result of sprays or other therapy, organisms are not eradicated but merely suppressed, and that recurrences are a regrowth rather than a reinfection. Studies by Eichenwald and co-workers (*10*) and by us indicate that colonization can occur rapidly if only a few organisms are present.

Although it would be impossible to prove, and unsound to claim, that spray therapy eradicates "all" staphylococci present in the nasopharnygeal region, it may be theorized that the pathological flora is so suppressed that normal defensive measures supplemented by rapid nonpathogenic colonization effect complete elimination of the staphylococci. Topical antibiotic intranasal spray is not the only approach to control of the carrier state, but it appears to have certain advantages over other means that have been suggested or attempted (*2,10,14–18*).

Although our background clinical conditions varied, our technical conditions were constant, well controlled, and recorded in depth. The 11 percent failure rate may be attributed to (*a*) participants' failure to spray adequately, (*b*) reinfection before specimens were obtained for culture in routine followup, (*c*) advanced nasopharnygeal disease which prevented adequate penetration of the antibiotics, and (*d*) organisms which had unusual resistance to antibiotic therapy.

In several instances the families of intractable carriers were examined and other carriers were identified. Apparently some participants were being reinfected in a heavily contaminated home environment. When the carrier state of his immediate contacts was eliminated, the hospital employee who was a carrier usually would respond to therapy. Although it is a staggering undertaking to investigate and eliminate staphylococci from the families of infected personnel, it may prove necessary when the carrier state cannot otherwise be eliminated from hospital employees. Disposition of the truly intractable carrier presents a problem and should be decided by responsible hospital committees at the local level.

Prolonged use of antibiotics against resistant organisms may increase risk of more persistent growth or development of a more resistant strain (*19*). Topical antibiotics used in this study have not given rise to resistant strains. Even resistant staphylococci succumb to highly concentrated topical antibiotics (*20*), and highly concentrated antibiotics may be used safely in topical therapy.

Conclusions

The use of antibiotic nasal spray may successfully neutralize the staphylococcal carrier state. A combination of gramicidin, neomycin, and polymyxin B with hydrocortisone and two vasoconstricting agents appeared to have value on the basis of therapeutic efficacy with mini-

mum side effects. This spray is apparently safe, reliable, inoffensive, and easily administered.

We recognize that many of our observations can be completely unrelated to our therapeutic effort. We hope the reader will compare the data we have presented with his own or reported figures and act accordingly.

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