

Recurrent Staphylococcal Infection in Families

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• This controlled double-blind study examined the efficacy of a single large inoculum of *Staphylococcus aureus* 502A in interrupting intrafamilial spread of recurrent staphylococcal abscesses. Forty families were enrolled in the study and 32 completed six months of follow-up care. All participants were first treated with oral oxacillin sodium or dicloxacillin sodium, twice daily hexachlorophene showers, and bacitracin given nasally for two weeks. Some then received nasal inoculation of 10^8 to 10^9 organisms of *S aureus* 502A while others were given only sterile broth. Fifteen of 17 families or 29 of 36 individuals who received 502A remained free of recurrence for six months of observation, while only four of 15 control families or 18 of 34 members had no recurrences ($P < .005$). After six months after colonization, 83% of the treatment group retained the 502A organism.

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Intact skin and mucous membranes with their normal bacterial microflora constitute the host's primary defense against invasion by microbial agents. Any alteration of this basic barrier may result in covert or overt infectious processes. Furuncles and subcutaneous abscesses probably represent the most commonly encountered forms of infection and account for as many as one in every 50 visits to hospital emergency facilities.¹ Moreover, skin infections tend to be recurrent in many patients and often spread to other family members. Medical intervention is most appropriately directed toward eradication of the offending organism and, for recurrent infections, toward strengthening the patient's resistance to infection.

Previous studies have demonstrated that artificial colonization with the 502A strain of *Staphylococcus aureus* interferes with subsequent colonization by more virulent strains of *S aureus* in neonates² and adults.³⁻⁶

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Protection against recurrent intrafamilial furunculosis by repeated inoculation of *Staphylococcus* 502A has also been reported.⁷ This controlled study was designed to examine the efficacy of a single large inoculum of 502A in curtailing staphylococcal infection in families having a history of recurrent furunculosis.

MATERIALS AND METHODS

Clinical Data

Criteria for inclusion in the study included the following: (1) five or more deep furuncles among family members in the previous three months, (2) nasal carriage of *S aureus* in more than one family member, and (3) negative history for penicillin allergy in all family members.

Forty qualified families were randomly allotted into a 502A or control nasal inoculation group after the nature of the procedures was explained and informed consent was obtained. Nasal cultures were first obtained in all participants who were then treated with oral oxacillin sodium suspension (50 mg/kg/24 hr, with a maximum of 1 g for children) or dicloxacillin sodium tablets (2 g daily for adults), twice daily hexachlorophene showers, and twice daily bacitracin given nasally for 14 days. Furuncles present were incised and drained. Nasal cultures were obtained two days after this course of therapy and again two weeks and six months after nasal application of 502A or control material. Nasal inoculation was carried out two days after the completion of antibiotic, shower, and nasal bacitracin therapy.

During the six-month observation period, any study subject manifesting a staphylococcal skin infection that was larger than 10 mm or caused pain was considered a treatment failure. The entire family then repeated the sequence of antibiotics administered for systemic and local effect and hexachlorophene showers for 14 days followed by nasal inoculation of *S aureus* 502A.

Bacteriologic Data

Nasal cultures were obtained from all participating subjects with a sterile cotton swab that was incubated at 37 °C in trypticase soy broth (TSB) for two hours prior to streaking on sheep blood agar plates. After 24 to 48 hours' incubation, representative coagulase-positive colonies were selected for antibiotic sensitivity testing and phage typing. Abscesses and other systemic foci of infection were cultured in a similar manner before and during the observation period.

The *S aureus* 502A strain used in this study has been previously characterized.⁸ A

stock slant was originally streaked on trypticase soy agar plates and multiple colonies were inoculated into a suspension of sheep RBC. One-milliliter aliquot parts were then frozen at -20 °C until used; control sheep cells were maintained in a similar fashion. Twenty-four to 36 hours prior to nasal treatment, a culture tube was thawed, an equal volume of TSB was added, and the broth culture was incubated at 37 °C. Colony counts of 502A material yielded 10^8 to 10^9 organisms per milliliter.

The sheep cell-TSB broth was inoculated into the anterior nares using a sterile cotton swab with the subject "sniffing" the material back to the posterior part of the nasopharynx. This method of colonization was employed only once during the study unless recurrent infection indicated treatment failure.

RESULTS

Thirty-two families, 17 treated and 15 control families including 70 individuals, 36 treated and 34 control subjects, completed six months of follow-up care. A systemic staphylococcal illness preceded entry into the study for two families; one family member had septic arthritis and another had staphylococcal pneumonia. Only two isolated strains in the 32 families were sensitive to penicillin and no predominant phage group was identified in this series. In the treatment group, 22 of 36 (61%) family members originally carried the offending staphylococcal strain, while 25 of 34 (74%) of the control group demonstrated nasal colonization. All cultures were negative for *S aureus* prior to nasal inoculation of 502A or control broth. Nasal colonization data during the course of this study are presented in Table 1.

Clinical efficacy data are presented in Table 2. It can be seen that nasal inoculation of 502A significantly prevented subsequent episodes of staphylococcal infection. Of the seven patients who were treatment failures in the group inoculated with 502A, none had 502A in their anterior nares at the time of recurrence. Nasal cultures in the control group revealed the same phage type of *S aureus* as that recovered from the furuncle in nine of 16 treatment failures. The procedure was tolerated well by all participants and no untoward side effects were observed in this study.

COMMENT

This study demonstrates the efficacy of a single nasal inoculum of *S aureus* 502A for interrupting bacterial colonization with more virulent organisms and for preventing subsequent overt infection. This confirms other reports that use similar approaches referred to as "artificial colonization"² or "bacterial interfer-

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Table 1.—Staphylococcal Nasal Colonization During Study Period

Time Culture Obtained	502A-Colonized Group, No. (%) ^a		Control Group, No. (%)	
	Non-502A <i>Staphylococcus</i>	502A <i>Staphylococcus</i>	Non-502A <i>Staphylococcus</i>	502A <i>Staphylococcus</i>
Initially	22/36 (61) ^a	...	25/34 (74)	...
Prior to nasal inoculation	0/36 (0)	...	0/34 (0)	...
2 wk after inoculation	0/36 (0)	34/36 (94)	4/31 (13)	...
6 mo after inoculation	2/29 (7)	24/29 (83)	4/18 (22)	...

^aTreatment failures not included in these data.

Table 2.—Clinical Efficacy of *Staphylococcus* 502A Colonization

	Families ^a		Individuals [†]	
	Total No.	Treatment Failures, No.	Total No.	Treatment Failures, No.
502A-Colonized	17	2	36	7
Control	15	11	34	16

^a*P* < .005

[†]*P* < .05

ence."³⁻⁵ Essentially, the mechanism is, in part, restoration of the host's primary immune barrier against infection, ie, noninvasive bacterial microflora. Certainly colonization with virulent *S aureus* strains on other skin surfaces (perineum, axilla) or mucous membrane areas could account for treatment failures. However, this study demonstrates the importance of nasal colonization as a focus for subsequent dissemination of bacteria.

The methods in this protocol differ from previous ones in that the 502A broth was given as a single inoculum following long-term freezer storage of the bacterium. Thus, practical application was achieved for use of this technique in most outpatient facilities. The only equipment requirements are a standard freezer compartment and a small 37 °C incubator. Aliquot parts of inoculated sheep cells may be readily prepared in a microbiologic laboratory and sent to clinical facilities for storage and subsequent use.

The initial treatment of cutaneous abscesses often involves incision and drainage with the necessity for antibiotics given for systemic effect remaining debatable; the aerobe most prevalent in recovery from cutaneous abscesses is *S aureus*. A recent report demonstrated that there is no apparent therapeutic benefit following routine Gram's stains or cultures of such infections and antimicrobial therapy.¹ However, no study to date has adequately evaluated recurrence or extension of abscesses with and without antibiotic therapy following initial Gram's stain and culture identification of organisms. In practice, the disease process is usually considered too trivial for an expensive laboratory evaluation and treatment approach.

Differences in virulence of *S aureus*

strains account for occasionally greater potential for more serious infection. This study did not suggest that these phage types were more resistant to colonization with 502A as a therapeutic approach.

Systemic spread of *S aureus* from a subcutaneous focus is rare in the nonimmunologically compromised host. However, experience with two individuals in the current series suggests that colonization with virulent *Staphylococcus* sp is related to systemic disease. One study patient had septic arthritis and another had pneumonia with the strain phage types that were also recovered from the nasal flora and, in the former case, from a concomitant cutaneous abscess. It is the appreciation of such systemic spread that supports initial treatment with antibiotics, and this therapy is still a common practice among physicians.

Skin and mucous membrane infections caused by *S aureus* 502A following therapeutic colonization have been reported.^{1,5,8,9} These lesions, however, have not been of serious consequence. Potentially greater risk might be anticipated in the host with compromised immunologic responses. Therefore, in patients who have histories compatible with abnormal host defenses, particularly granulocyte phagocytic responses, a more thorough immunologic evaluation should be provided. We have treated one patient with hypergammaglobulinemia E and cyclic chemotactic dysfunction by 502A colonization and considerable therapeutic benefit has been obtained. Therapeutic colonization with selected benign microflora is currently being employed for patients who have undergone bone marrow transplantation,¹⁰ and this approach to treatment

has also been suggested in a number of other clinical circumstances.^{8,11-14}

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