NASAL RESERVOIR AS THE SOURCE OF EXTRANASAL STAPHYLOCOCCI

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Abstract

Nasal administration of oxacillin to nasal carriers of coagulase-positive staphylococci rapidly decreased the frequency of positive nasal cultures and the number of staphylococci isolated from the positive cultures. This therapy was effective both in carriers of penicillin-sensitive staphylococci and in carriers of penicillin-resistant staphylococci. Depression of nasal staphylococci was followed by a rapid reduction of both skin staphylococci and aerial staphylococci. The frequency of positive skin and air samples was roughly proportional to the number of nasal staphylococci isolated at the time the skin and air cultures were obtained. These studies suggest that the nose is the primary focus of multiplication and dissemination of organisms onto the skin and into the air, and that multiplication and dissemination from the skin itself is a minor source of staphylococci in the environment.

Staphylococci are disseminated into the air and on to the skin from heavy nasal carriers of coagulase-positive staphylococci more frequently than they are from either intermediate carriers, light carriers, or noncarriers (White, 1961). In addition, suppression of the number of staphylococci in the anterior nose with nasal administration of methicillin was followed by a rapid reduction in the frequency of positive skin and air samples and in the number of staphylococci isolated in positive samples (Varga and White, 1961).

Oxacillin is also highly resistant to staphylococcal penicillinase, and when administered orally was effective in suppressing staphylococci in nasal carriers (Smith and White, 1963). In the present study, oxacillin was administered intranasally, and was followed by a rapid and marked drop in the frequency of positive skin cultures and in the frequency with which staphylococci could be isolated from air samples.

Materials and Methods

The methods of collecting and enumerating quantitative nasal cultures and of phage-typing staphylococci were those described previously (White, Foster, and Knight, 1959). All staphylococci were coagulase-positive.

Air samples were collected near the beds of patients by use of slit-samplers (Wolf et al., 1959) at the rate of 1 ft^3 of air per min. Only samples from patients without overt staphylococcal infections were included. Since we were attempting to observe conditions as generally present on the ward, no attempts were made to either increase or decrease activity during the period of sampling, but one sampling from each patient was made while the patient was resting quietly in bed and one sampling from each patient was made while the sheets were shaken lightly for 15 sec during the collection period.

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Skin cultures (White, 1961) were made by swabbing an area (3 by 1 in.) on the forearm with a cotton swab moistened with Heart Infusion Broth. The swab was then placed in a culture tube with 3 ml of Heart Infusion Broth and shaken for 5 min in a Kahn shaker. The broth was then enumerated for staphylococci as reported for nasal cultures.

A coagulase-positive staphylococcus from each positive culture was phage-typed (White et al., 1959), and its susceptibility to penicillin G, tetracycline, erythromycin, chloramphenicol, kanamycin, and methicillin was determined by plate dilution methods (Jackson and Finland, 1951). Staphylococci requiring 10 μg or more for inhibition were considered resistant. By these standards, none of the staphylococci was resistant to methicillin or oxacillin.

Selected patients who were nasal carriers were treated either with an ointment containing 5 mg of oxacillin per g of petrolatum and lanolin ointment or with petrolatum and lanolin ointment without oxacillin. A small amount of ointment was applied with the patients' fingers completely around the anterior nares three times per day for 1 to 2 weeks. Patients did not receive any other antimicrobial agent during this study. Skin cultures of forearm and air samples collected with slit-samplers were obtained before therapy and one to three times per week during and after therapy.

Results

A total of 27 nasal carriers of coagulase-positive staphylococci were treated with nasal oxacillin ointment three times a day for 7 to 10 days. Of the 27 patients, 13 were carriers of staphylococci which were resistant to penicillin G, but all staphylococci isolated were susceptible to oxacillin.

Coagulase-positive staphylococci were isolated from all nasal cultures obtained before therapy; the mean log of positive cultures was 4.5 (Table 1). During treatment with topical oxacillin, carrier rates fell from 100% before therapy to 12% by the seventh to tenth day of treatment, and the mean log of positive cultures fell from 4.5 to 2.1. After treatment was discontinued, carrier rates rose to 25% by the seventh to tenth day after treatment, and the mean log of the positive cultures rose from 2.1 to 3.1.

In 13 patients treated with ointment without oxacillin, carrier rates remained between 95 and 100% during therapy, and the mean log of positive cultures varied from 4.8 to 5.4 (Table 2).

Coagulase-positive staphylococci could be isolated from 27% of skin cultures obtained from nasal carriers before topical oxacillin therapy (Table 3). During treatment, coagulase-positive staphylococci were isolated from only 0 to 8% of skin cultures, and no coagulase-positive staphylococci were isolated from 46 skin cultures obtained during the 10 days after therapy.

TABLE 1. *Effect of topical oxacillin on nasal carrier rates for coagulase-positive staphylococci in 27 patients*

Treatment day		No. cultured	Per cent positive	Mean log of positive cultures
Before treatment	-1 to -3	73	100	4.5
During treatment	1 to 3	51	63	4.1
	4 to 6	53	25	2.3
	7 to 10	43	12	2.1
After treatment	1 to 3	24	25	2.5
	4 to 6	24	29	3.3
	7 to 10	36	25	3.1

TABLE 2. *Nasal carrier rates for coagulase-positive staphylococci in 13 placebo patients*

Treatment day		No. cultured	Per cent positive	Mean log of positive cultures
Before treatment	-1 to -3	28	100	5.1
During treatment	1 to 3	22	100	4.8
	4 to 6	28	96	5.4
	7 to 10	18	95	5.1

TABLE 3. *Effect of nasal oxacillin on air cultures and skin cultures for coagulase-positive staphylococci*

Treatment day		No. cultured	Per cent positive		
			Skin cultures	Active air samples	Inactive air samples
Before treatment	-1 to -3	26	27	38	15
During treatment	1 to 3	17	0	18	18
	4 to 6	28	7	3	14
	7 to 10	25	8	8	4
After treatment	1 to 3	14	0	43	7
	4 to 6	16	0	31	6
	7 to 10	16	0	25	25

The frequency of coagulase-positive staphylococci in air samples obtained at rest was 15% before treatment, fell to 4% during the seventh to tenth day of treatment, and rose to 25% 7 to 10 days after therapy was discontinued.

Coagulase-positive staphylococci were isolated from 38% of air samples obtained during activity before therapy. During therapy with topical oxacillin, the frequency of positive cultures fell to 3 to 8%, and rose to 25% of the cultures obtained 7 to 10 days after therapy.

There was no significant decrease in the frequency of positive skin cultures, of positive air samples at rest, or of positive air samples during activity in patients treated with placebo ointment.

A total of 226 quantitative nasal cultures were obtained from treated patients at the same time skin cultures, active air samples, and inactive air samples were obtained (Table 4). There was a higher

TABLE 4. *Correlation between quantitative nasal cultures, skin cultures, and air samples*

No. of nasal staphylococci	No. of cultures	Positive skin cultures	Air samples			
			Active		Inactive	
			Positive	5 colonies/ft^3	Positive	5 colonies/ft^3
		%	%	%	%	%
0	144	4	17	3	8	0
10^1 - 10^3	25	4	20	10	4	0
10^3 - 10^5	25	20	32	28	12	4
$>10^5$	32	34	41	34	25	9

frequency of positive skin cultures in carriers of large numbers of nasal staphylococci than in carriers of intermediate numbers or of small numbers. Coagulase-positive staphylococci were isolated from only 4% of skin cultures from patients in whom nasal staphylococci had been completely suppressed.

Coagulase-positive staphylococci were isolated from 41% of the active air samples obtained around heavy nasal carriers, but from only 17% of the active air samples around patients in whom nasal staphylococci had been suppressed. There was also a marked reduction in the number of staphylococci isolated from positive cultures; more than five colonies per ft^3 of air were isolated from 34% of the active air samples around heavy nasal carriers, but from only 3% of the active air samples around patients in whom nasal staphylococci could not be cultured.

Of the coagulase-positive staphylococci isolated from skin cultures or air samples of nasal carriers, 80% were the same phage type as the nasal staphylococci isolated at the same time. Coagulase-positive staphylococci isolated from skin cultures and air samples around patients in whom nasal staphylococci were suppressed were the same phage types as staphylococci isolated from the nose of these patients before suppression in only 8% of the cases.

Discussion

The administration of a large number of antibiotics to either patients or personnel often eliminates the sensitive staphylococci which are in the nose before therapy, but allows replacement of these staphylococci with drug-resistant organisms from the hospital environment. No coagulase-positive staphylococci which are resistant to either methicillin or oxacillin have been detected in this hospital environment. Therefore, there are no resistant strains to replace the sensitive ones during the administration of either of these two antibacterial agents. Topical application of these two penicillins to the presumed nasal reservoir of staphylococci permits study on the extranasal staphylococci uncomplicated by replacement with resistant staphylococci or by the effects of these penicillins on sites other than the nose.

In previous studies (Varga and White, 1961) nasal application of methicillin rapidly decreased both the number of nasal carriers of staphylococci and the number of staphylococci isolated from patients who remain carriers. Depression of nasal staphylococci was followed by a rapid reduction of skin staphylococci and of aerial dissemination of these organisms. These studies confirm previous reports (Moss, Squire, and Topley, 1948) on the effect of nasal penicillin G on skin staphylococci before penicillinase-producing organisms were predominant organisms in hospitals.

In the present studies, oxacillin also rapidly decreased the number of nasal staphylococci and the number of staphylococci isolated from patients who remained carriers. The compound was active both in nasal carriers of staphylococci which were sensitive to penicillin G, and in carriers whose organisms were resistant.

The number of staphylococci isolated from the skin and from the air samples around nasal carriers was roughly proportional to the number of staphylococci isolated from the nose at the same time. Complete suppression of nasal staphylococci was followed by a marked reduction in both skin and aerial staphylococci.

Rapid reduction in skin and aerial staphylococci in these two studies after administration of either oxacillin or methicillin suggests that the maintenance of the skin carrier rate depends upon continued dispersement of staphylococci from the nose onto the skin. This concept is also compatible with the demonstration (Ricketts, Squire, and Topley, 1951) that protection of the skin of the forearm from external contamination as by a nylon film is followed by rapid disappearance of the staphylococci from the protected area.

Similarly, the primary source of aerial staphylococci appears to be in the anterior nose of patients or personnel. Suppression of staphylococci in the nasal site is followed by a marked reduction in the frequency of positive air samples and in the number of staphylococcal colonies isolated in the positive air samples.

Staphylococci have been shown to multiply also on perineal skin, and some perineal carriers disseminate large numbers of staphylococci from this area (Hare and Ridley, 1958). However, this source of dissemination did not appear to be important in the patients reported in this study or in the previous study with nasal methicillin, since nasal methicillin or oxacillin alone suppressed aerial and skin staphylococci.

Acknowledgment

This study was supported by grants E-2561 and AI 05683 from the National Institute of Allergy and Infectious Diseases, U.S. Public Health Service, and grant CC00011 from the Communicable Disease Center, Atlanta, Ga.

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