# Dissemination of Staphylococci

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Nasal staphylococci constitute one of the major reservoirs of staphylococci in the hospital.[1-3] Certain nasal carriers disseminate organisms into the environment frequently and in large numbers. These individuals have been termed "disseminators," "dangerous carriers," or "cloud babies" by various authors.[4-6]

Previous studies [1,7] have shown that nasal carriers of large numbers of coagulase-positive staphylococci disseminated staphylococci into the environment more frequently than carriers of smaller numbers.

The present studies were designed to test if dissemination of nasal staphylococci from carriers of similar numbers of these organisms was dependent on the type of staphylococci carried or upon factors in the host.

## Materials and Methods

Two separate groups of patients were studied. Patients with overt staphylococcal infections or patients treated with other antibiotics were excluded from either study. Carriers were defined as patients with at least two of three consecutive quantitative nasal cultures containing coagulase-positive staphylococci.

Carriers were treated with either 10, 50, or 100 mg of methicillin, or 5 mg of oxacillin per gm of petrolatum and lanolin ointment. A small amount of ointment was applied with the patients' fingers completely around the anterior nares three times per day for 1-2 weeks. Quantitative nasal cultures,[8] skin cultures of the forearm, and air samples using slit-samplers[9] were obtained before therapy and 1-3 times a week during and after therapy. Cultures of the air and skin immediately before treatment were compared with similar cultures obtained at least one week after different nasal staphylococci were acquired in numbers equal to pretreatment nasal cultures.

In another study, 100 patients who were nasal carriers of coagulase-positive staphylococci by quantitative nasal cultures were studied for dissemination of these organisms by slit-samplers of air and skin cultures. In this group of patients the frequency of positive air and skin cultures was correlated with the number and penicillin-resistance of nasal staphylococci.

In both groups of patients air samples were collected near the beds of the patients using slit-samplers at the rate of 1 cu ft of air per minute. Since we were attempting to observe conditions that are generally present on the ward, no attempts were made to either increase or decrease activity during the period of sampling. One sampling from each patient was made while the patient was resting quietly in bed, and one sampling was made from each patient while the sheets were shaken lightly for 15 seconds during the minute-and-a-half collection period.

One colony of coagulase-positive staphylococci from each positive air, skin, or nasal culture was phage-typed,[10] and its susceptibility to a variety of antimicrobial agents was determined by plate-dilution methods.[11] Staphylococci were considered resistant to penicillin G if they require 10$\mu$g/ml or more for inhibition.

## Results

Initially, 100 carriers were studied who were not treated with topical oxacillin or methicillin (Table 1). In this group of patients dissemination of staphylococci was compared with the number of nasal staphylococci and their resistance to penicillin G.

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TABLE 1.—*Number of Nasal Carriers of Staphylococci Tested With Air Samples and Skin Cultures*

| Number Nasal Staph | Carriers Sensitive Strains | Carriers Resistant Strains |
|---|---|---|
| $10^1$-$10^3$ | 10 | 5 |
| $10^3$-$10^5$ | 19 | 14 |
| $>10^5$ | 21 | 31 |
| Total | 50 | 50 |

Staphylococci were isolated more frequently from skin cultures and air samples around carriers of more than 100,000 organisms per nasal swab than from skin cultures and air samples from carriers of smaller numbers of staphylococci. This was true regardless of the penicillin-sensitivity of the nasal staphylococci isolated (Tables 2, 3, and 4).

In addition, staphylococci were isolated more frequently from air samples and skin cultures from carriers of more than 100,000 penicillin-resistant staphylococci than from cultures from carriers of more than 100,000 sensitive bacteria. There was no increase in the frequency of positive air and skin cultures obtained from carriers of smaller numbers of penicillin-resistant staphylococci as compared to cultures from carriers of smaller numbers of sensitive strains.

The numbers of staphylococci isolated from the nose of carriers of more than 100,000 penicillin-resistant organisms did not differ from the number isolated from carriers of more than 100,000 sensitive staphylococci (Table 5). Therefore, the increased dissemination of staphylococci by heavy carriers of resistant organisms could not be explained by the presence of larger numbers of staphylococci in the nose available for dissemination.

Heavy nasal carriers of penicillin-resistant strains had been hospitalized more frequently, had a higher mortality rate during the observation period, and had conditions such as uremia or leukemia more frequently than heavy carriers of penicillin-sensitive staphylococci (Table 6). Those host factors might have been responsible for the apparent increased dissemination by carriers of resistant organisms. Therefore, dissemination of staphylococci from carriers of resistant staphylococci was compared to dissemination from the same patients when they were carriers of sensitive organisms.

Twenty-four nasal carriers of coagulase-positive staphylococci were treated for 7-10 days with a nasal ointment containing either oxacillin or methicillin and followed after treatment until they had reacquired coagulase-positive staphylococci of a different phage type and more penicillin-susceptibility than that which was present before therapy. Patients were included in this study only if more than 100,000 staphylococci per nasal swab were isolated both before and after therapy. There were no differences in the numbers of staphylococci isolated from nasal cultures of patients when these were carriers of penicillin-sensitive strains as compared to the numbers isolated from the same patients when they were carriers of penicillin-resistant organisms (Table 7).

Fourteen patients were carriers of penicillin-sensitive strains and acquired resistant ones after therapy, and ten who were originally carriers of resistant strains acquired

TABLE 2.—*Per Cent of Skin Cultures Containing Coagulase-Positive Staphylococci*

| Number Nasal Staph | Carriers Sensitive Strains | Carriers Resistant Strains |
|---|---|---|
| $10^1$-$10^3$ | 10 | 0 |
| $10^3$-$10^5$ | 16 | 14 |
| $>10^5$ | 29 * | 55 * |

* $\chi^2$ $P$ <0.059.

TABLE 3.—*Per Cent of Air Samples Containing Coagulase-Positive Staphylococci Around Nasal Carriers At Rest*

| Number Nasal Staph | Carriers Sensitive Strains | Carriers Resistant Strains |
|---|---|---|
| $10^1$-$10^3$ | 0 | 0 |
| $10^3$-$10^5$ | 16 | 29 |
| $>10^5$ | 19 * | 65 * |

* $\chi^2$ $P$ <0.001.

TABLE 4.—*Per Cent of Air Samples Containing Coagulase-Positive Staphylococci Around Nasal Carriers of Staphylococci During Activity*

| Number Nasal Staph | Strains: Carriers Sensitive — % Positive Air Samples | Carriers Sensitive — % Air Samples 5 col/cu ft | Carriers Resistant — % Positive Air Samples | Carriers Resistant — % Air Samples 5 col/cu ft |
|---|---|---|---|---|
| $10^{1}$-$10^{3}$ | 30 | 10 | 40 | 0 |
| $10^{3}$-$10^{5}$ | 37 | 16 | 50 | 29 |
| $10^{5}$ | 43 * | 24 † | 71 * | 52 † |

* $\chi^2$ $P$ <0.059.
† $\chi^2$ $P$ <0.05.

penicillin-sensitive staphylococci after therapy. The phage types and drug resistance of nasal staphylococci before and after therapy are shown in Table 8.

Despite changes in penicillin-resistance and phage types of nasal staphylococci, there were no significant changes in the frequency of positive skin cultures, positive air samples while resting, or positive air samples during activity (Table 9).

Eighty-five per cent of skin or air samples from individual patients remained positive or remained negative despite changes in nasal staphylococci (Table 10). In the remaining 15% of cultures, positive skin or air cultures became negative or negative cultures became positive following nasal treatment.

## Comment

In this study, two groups of patients were studied with contradictory results. In one group of patients, heavy nasal carriers of penicillin-resistant staphylococci disseminated organisms into the air and onto the skin more frequently than heavy nasal carriers of penicillin-sensitive bacteria. In another group of patients, changes in the penicillin-resistance of staphylococci in the nose did not change the frequency of dissemination.

The study also confirmed previous reports [1,7] that nasal carriers of larger numbers of staphylococci tend to disseminate staphylococci more frequently than nasal carriers of small numbers. However, the increased dissemination by heavy carriers of resistant staphylococci could not be explained by the presence of increased numbers of resistant staphylococci in the nose available for dissemination.

The apparent contradiction of the observations in the two groups of patients suggested that factors other than penicillin-resistance of nasal staphylococci were responsible for increased dissemination by carriers of large numbers of resistant organisms.

The specific host factors responsible for increased dissemination by carriers of penicillin-resistant staphylococci were not identified. However, there were differences in the two groups as demonstrated by increased mortality rates, previous hospital admissions, and uremia in carriers of resistant staphylococci as compared to carriers of sensitive ones.

A series of events would seem to be responsible for additional selective advantages for the dissemination of resistant organisms within the hospital. Patients with a variety of illnesses would increase dissemination of nasal staphylococci because of unknown alterations in the host. The same illnesses would increase the probability that patients would be hospitalized and receive antimicrobial agents. Since the administration of antimicrobial agents to patients in a hospital markedly increases the frequency with which resistant staphylococci are acquired,[12,16] disseminators would tend to acquire nasal staphylococci which were resistant to penicillin and to further disseminate penicillin-resistant staphylococci into the environment.

TABLE 5.—*Numbers of Nasal Staphylococci Isolated From Carriers of More Than 100,000 Penicillin-Resistant Strains As Compared to the Numbers Isolated from Carriers of More than 100,000 Penicillin-Sensitive Organisms*

| | Penicillin-Resistant | Penicillin-Sensitive |
|---|---|---|
| Median | 1,170,000 | 1,290,000 |
| Mean | 1,596.000 | 1,485,000 |
| Standard error of mean | 283,000 | 235,000 |

TABLE 6.—*Other Differences in Carriers of More Than 100,000 Penicillin-Resistant Staphylococci As Compared to Carriers of More Than 100,000 Sensitive Strains*

| | Carriers Sensitive Strains | Carriers Resistant Strains | $\chi^2$ P |
|---|---|---|---|
| No. patients | 21 | 31 | |
| No. previously hospitalized | 5 | 26 | <0.001 |
| No. died | 3 | 13 | <0.05 |
| No. with leukemia | 1 | 4 | >0.1 |
| No. with uremia (BUN >40 mg %) | 0 | 7 | <0.05 |

Although the relationships between man, staphylococci, and the environment are complex, several factors have been identified. One important factor is the drug-resistance of staphylococci in carriers which permits a selective advantage of resistant staphylococci in treated patients as discussed above.

In addition, the number of staphylococci present in the nose is important in the frequency with which staphylococci are disseminated into the environment.[7] There is no established explanation for certain untreated individuals being carriers of large numbers of staphylococci, while others are carriers of only small numbers. In a previous study [14] there was no correlation between antimicrobial resistance or phage types of staphylococci and the numbers which can be isolated from untreated nasal carriers. However, Ehrenkranz has shown that treatment with tetracycline can increase the number of tetracycline-resistant staphylococci in the nose and at the same time increase dissemination into the environment.[15]

Certain staphylococci, such as the 80/81 strain, are frequently isolated from lesions and are readily disseminated from nasal carriers. Other coagulase-positive staphylococci which are readily disseminated are infrequent causes of overt infections. Staphylococci which are disseminated frequently but are infrequent causes of infections have been deliberately introduced into nurseries to control epidemics by preventing colonization of the nose with staphylococci which are frequent causes of infection.[16] Apparently dissemination is not the only factor responsible for clinical infection.

Factors affecting the host can increase the frequency of dissemination. This has been documented in newborn nurseries [6] in which increased dissemination by "cloud babies" was correlated with viral infections due to adenoviruses. As mentioned by the authors, viral infections may have increased dissemination by increasing the number of staphylococci in the nose available for dissemination.

If our interpretation of the findings in the present study is correct, other host factors

TABLE 7.—*Numbers of Nasal Staphylococci Isolated From 24 Carriers of Penicillin-Resistant Strains as Compared to the Numbers Isolated From the Same Patients When They Were Carriers of Penicillin-Sensitive Staphylococci*

| | Penicillin-Resistant | Penicillin-Sensitive |
|---|---|---|
| Median | 1,320,000 | 1,290,000 |
| Mean | 1,467,000 | 1,539,000 |
| Standard error of mean | 179,000 | 105,000 |

TABLE 8.—*Phage Types and Drug-Resistance of Nasal Staphylococci Isolated Before and After Treatment* *

| Treatment: Before | | Treatment: After | |
|---|---|---|---|
| Phage Type | Resistant To | Phage Type | Resistant To |
| 1. 7 | | 80 | P |
| 2. 52a/79 | | N.T. | P |
| 3. 3A/3B | | 77 | P |
| 4. 29 | | 7 | P |
| 5. 3C/6/73 | All | 7/77 | P |
| 6. 7 | | 80/81 | P |
| 7. N.T. | | 80/81 | P |
| 8. 187 | | N.T. | PT |
| 9. N.T. | Sensitive | 81 | PT |
| 10. N.T. | | 80 | PT |
| 11. 80 | | 80/81 | PT |
| 12. 80 | | 80/81 | PTE |
| 13. 79/42D | | 80 | PTEC |
| 14. N.T. | | 80 | PTEC |
| 15. 3B/55 | P | 3a | |
| 16. N.T. | P | 80 | |
| 17. 80/81 | P | 29 | All |
| 18. 187 | P | N.T. | |
| 19. 80/81 | P | N.T. | |
| 20. 80/81 | PT | 3A/3B/55 | |
| 21. 80 | PT | 3B/55 | Sensitive |
| 22. 80/81 | PT | 29 | |
| 23. N.T. | PTE | 3a | |
| 24. 80 | PTEC | 3a/55/71 | |

* N.T., not typeable; P, penicillin G; T, tetracycline; E erythromycin; C, chloramphenicol.

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increased dissemination of nasal staphylococci and at the same time increased the probability that resistant staphylococci were acquired and further disseminated. Dissemination was independent of the drug resistance or phage type of the staphylococci carried, since changes in nasal staphylococci did not change dissemination into the environment.

## Summary

Heavy nasal carriers of penicillin-resistant staphylococci disseminated organisms onto the skin and into the air more frequently than heavy nasal carriers of penicillin-sensitive strains. However, changes in the penicillin-resistance or phage types of staphylococci in the nose of another group of nasal carriers did not alter the frequency of dissemination.

Although staphylococci were isolated more frequently from the environment of nasal carriers of larger numbers of organisms, the increased dissemination by heavy nasal carriers of resistant staphylococci could not be explained by the availability of increased numbers of resistant staphylococci in the nose.

The increase in dissemination of resistant staphylococci was related to the increased frequency with which disseminators had previously received antimicrobial agents within hospitals and thereby acquired resistant staphylococci to disseminate, and not primarily to the staphylococci carried.

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### Generic and Trade Names of Drugs

Sodium Methicillin—Dimocillin-RT, Staphcillin.
Sodium oxacillin—Prostaphlin, Resistopen.

TABLE 9.—*Per Cent of Positive Extranasal Cultures in 24 Patients Who Changed Nasal Staphylococci*

| | Nasal Staphylococci | |
|---|---|---|
| | Penicillin Sensitive, % | Penicillin Resistant, % |
| Positive skin cultures | 33 | 33 |
| Positive air samples at rest | 25 | 25 |
| Positive air samples during activity | 50 | 54 |

TABLE 10.—*Changes in Cultures for Extranasal Staphylococci in Patients With Penicillin-Sensitive Nasal Staphylococci as Compared to Cultures for Extranasal Staphylococci From the Same Patients When They Were Nasal Carriers of Penicillin-Resistant Organisms*

| | No. Patients | | |
|---|---|---|---|
| | Skin Cultures | Air Samples at Rest | Air Samples During Activity |
| Positive cultures with penicillin-sensitive nasal staphylococci; negative cultures with resistant organisms | 1 | 2 | 2 |
| Negative cultures with sensitive nasal staphylococci; positive cultures with resistant organisms | 1 | 2 | 3 |
| Consistently positive | 7 | 4 | 10 |
| Consistently negative | 15 | 16 | 9 |

Tetracycline—Achromycin, Panmycin KM, Polycycline, Tetracyn.
Erythromycin—Erythromycin, Ilotycin.
Chloramphenicol—Chloromycetin, Chloromycetin Palmitate, Chloromycetin Succinate.

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