CARRIERS
CI

entucky,
a,

iers of staphy-
d in those who
quantities of

hods

a 35-bed male
d three to five
ve methods for
staphylococci
r surgery, pa-
fected if frank
of incision or
runcles, pneu-
of infection.
hylococci from
m lesions were
r, and Knight,
lity to penicil-
omycin, chlor-
and kanamycin
ution methods
51). Patients
ady if they re-
gs before the
e admitted with
e quantitative

et al., 1959; Public Health Laboratory Service, 1960; Moore and Gardner, 1963; Bassett et al., 1963). In the present study, quantitative nasal cultures were obtained from a group of patients before surgical operations; the frequency of infections after surgery was compared in

nasal cultures were obtained.

## Results

The overall frequency of staphylococcal infections after surgery in 451 patients was 11%; 8% of patients who were not carriers of coagulase-positive staphylococci before surgery, and 10% of patients who were nasal carriers of fewer than 100,000 staphylococci per

[1] Markle scholar in academic medicine. Present address: Department of Medicine, Medical College of Georgia, Augusta.

# INCREASED INFECTION RATES IN HEAVY NASAL CARRIERS OF COAGULASE-POSITIVE STAPHYLOCOCCI

ARTHUR WHITE[1]

*Department of Medicine, University of Louisville, Louisville, Kentucky, and Department of Medicine, Medical College of Georgia, Augusta, Georgia*

## Abstract

To study the association of nasal staphylococci with infection rates, quantitative nasal cultures were obtained three times weekly from over 400 patients who did not receive antimicrobial drugs before surgery. There was a significantly increased infection rate in heavy nasal carriers (more than 100,000 colonies per swab) as compared with noncarriers, but no significant increase in infection rates in light nasal carriers as compared with noncarriers. There was no significant difference in the numbers of staphylococci isolated from untreated carriers of different phage types or from carriers of staphylococci of different antimicrobial resistance. In these studies, only heavy nasal carriers were greater risks in postoperative infection. The predominance of resistant staphylococci or of certain phage types from infections could not be explained by the differences in the number of staphylococci in the nasal reservoir of untreated carriers.

There have been conflicting reports over the increased frequency of infection rates in nasal carriers of coagulase-positive staphylococci as contrasted to noncarriers (Weinstein, 1959; Williams et al., 1959; Public Health Laboratory Service, 1960; Moore and Gardner, 1963; Bassett et al., 1963). In the present study, quantitative nasal cultures were obtained from a group of patients before surgical operations; the frequency of infections after surgery was compared in patients who were not carriers of staphylococci before surgery and in those who were carrying different quantities of staphylococci.

## Materials and Methods

All patients admitted to a 35-bed male surgical ward were cultured three to five times a week by quantitative methods for nasal coagulase-positive staphylococci (White et al., 1959). After surgery, patients were considered infected if frank pus issued from the site of incision or if the patients acquired furuncles, pneumonia, or other evidence of infection.

Coagulase-positive staphylococci from each nasal culture and from lesions were phage-typed (White, Foster, and Knight, 1959), and their susceptibility to penicillin G, tetracycline, erythromycin, chloramphenicol, methicillin, and kanamycin was tested by plate dilution methods (Jackson and Finland, 1951). Patients were excluded from the study if they received antimicrobial drugs before the operations, or if they were admitted with infections existing before quantitative nasal cultures were obtained.

## Results

The overall frequency of staphylococcal infections after surgery in 451 patients was 11%; 8% of patients who were not carriers of coagulase-positive staphylococci before surgery, and 10% of patients who were nasal carriers of fewer than 100,000 staphylococci per

[1] Markle scholar in academic medicine. Present address: Department of Medicine, Medical College of Georgia, Augusta.

swab, acquired infections after surgery (Table 1). In patients with progressively larger numbers of staphylococci in the nose before the operation, the infection rates rose progressively, so that the postoperative infection rate in patients with more than 1,000,000 coagulase-positive staphylococci was 29%.

TABLE 1. *Postoperative infection rates in nasal carriers of different numbers of coagulase-positive staphylococci**

| No. of nasal staphylococci | No. of patients | Infection rate |
|---|---|---|
| | | % |
| 0 | 345 | 8 |
| $10^1$ to $10^3$ | 14 | 7 |
| $10^3$ to $10^5$ | 28 | 11 |
| $10^5$ to $10^6$ | 26 | 19 |
| $>10^6$ | 38 | 29 |

*Total number of patients was 451; mean infection rate was 11.

In infections acquired by patients who were nasal carriers of coagulase-positive staphylococci before surgery, the staphylococci isolated from the nose before the operation were the same phage types and had the same antimicrobial susceptibility as did the staphylococcus isolated from the lesion of the same patients in 66% of the cases. There were no significant differences in ages, types of operations, or types of illnesses in noncarriers, light nasal carriers, or heavy nasal carriers.

Staphylococci isolated from the lesions of 31 of the infected cases were phage-typed, and their susceptibility to antimicrobial agents was determined by plate dilution methods; 55% of the staphylococci were phage type 80/81, and the remainder either were in phage group III or were nontypable. Two-thirds of the staphylococci were highly resistant to penicillin and tetracycline; one-third were sensitive to all antimicrobial agents tested.

Only 25% of the staphylococci isolated from untreated nasal carriers were penicillin- and tetracycline-resistant, and only 21% were phage type 80/81. There was then a greater frequency of 80/81 phage types and of penicillin- and tetracycline-resistant staphylococci in lesions than could be explained by the prevalence of these staphylococci in the nose of untreated patients. This predominance might be explained in part if phage type 80/81 staphylococci were present in larger numbers in the nose of 80/81 carriers than in carriers of other staphylococci, or if drug-resistant strains were present in the nose in larger numbers than were drug-susceptible strains. However, there was no significant difference in the number of penicillin-sensitive staphylococci in positive cultures as compared to penicillin-resistant or multiple drug-resistant strains (Table 2). Similarly, phage type 80/81 staphylococci were not present in significantly larger numbers in 80/81 nasal carriers than were other phage types in the nasal carriers of staphylococci of different phage types (Table 3).

The administration of antimicrobial drugs did not decrease the frequency with which staphylococci could be isolated from nasal carriers. However, the

TABLE 2. *Quantitative counts of nasal staphylococcal strains with different antimicrobial resistance in untreated carriers*

| No. of nasal staphylococci | Sensitive | Only penicillin-resistant | Penicillin- and tetracycline-resistant | Resistant to three drugs | All penicillin-resistant |
|---|---|---|---|---|---|
| $10^1$ to $10^3$ | 54 (16%) | 7 ( 8%) | 10 (15%) | 22 (20%) | 39 (15%) |
| $10^3$ to $10^5$ | 181 (54%) | 54 (62%) | 40 (64%) | 48 (44%) | 142 (55%) |
| $>10^5$ | 100 (30%) | 27 (30%) | 13 (21%) | 38 (36%) | 78 (30%) |
| Total | 335 (100%) | 88 (100%) | 63 (100%) | 108 (100%) | 259 (100%) |

TABLE 3. *Quantitative counts of nasal staphylococcal strains of different phage types in untreated carriers*

| No. of nasal staphylococci | I | II | III | Not typable | Miscellaneous | 80/81 | All not 80/81 |
|---|---|---|---|---|---|---|---|
| $10^1$ to $10^3$ | 4 (16%) | 6 (8%) | 21 (17%) | 39 (25%) | 13 (21%) | 18 (11%) | 83 (19%) |
| $10^3$ to $10^5$ | 14 (59%) | 43 (55%) | 65 (54%) | 73 (50%) | 23 (38%) | 83 (57%) | 218 (51%) |
| $>10^5$ | 6 (25%) | 29 (37%) | 34 (29%) | 36 (25%) | 25 (41%) | 46 (32%) | 130 (30%) |
| Total | 24 (100%) | 78 (100%) | 120 (100%) | 148 (100%) | 61 (100%) | 147 (100%) | 431 (100%) |

staphylococci which were isolated from carriers or patients treated with penicillin, tetracycline, or with multiple drugs were resistant to at least penicillin and tetracycline significantly more frequently than were the staphylococci isolated from patients who received no therapy (Table 4).

## Discussion

These studies showed that untreated patients who have high quantitative nasal counts of coagulase-positive staphylococci before operations have a significantly higher postoperative infection rate than do either patients who are carriers of smaller numbers or patients from the positive cultures than in patients in whom fewer staphylococci are present in the positive cultures (White, 1961*a*). In addition, heavy nasal carriers of coagulase-positive staphylococci disseminated their organisms onto their skin and into the air more frequently than did either whom no staphylococci are isolated from the nose before surgical operations. Previous studies showed that staphylococci can be isolated from the nose more consistently from patients in whom large numbers of staphylococci are present in nasal carriers of smaller numbers or noncarriers (White, 1961*b*). All of these studies suggest that quantitative nasal cultures help differentiate heavy nasal carriers, who are greater hazards to themselves and who disseminate their organisms more widely, from carriers of smaller numbers who are less important in staphylococcal diseases.

TABLE 4. *Nasal carrier rates for coagulase-positive staphylococci and frequency of multiple drug-resistant strains in treated and untreated patients*

| Treatment | Treatment day | No. of cultures | Per cent positive | Per cent resistant to penicillin G and tetracycline |
|---|---|---|---|---|
| Untreated patients | 1 to 3 | 562 | 12 | 33 |
| | 4 to 6 | 356 | 22 | 28 |
| | 7 to 9 | 250 | 24 | 40 |
| | 10 to 12 | 164 | 23 | 28 |
| Tetracycline treatment | 1 to 3 | 83 | 16 | 23 |
| | 4 to 6 | 56 | 20 | 82 |
| | 7 to 9 | 35 | 40 | 93 |
| | 10 to 12 | 22 | 54 | 83 |
| Penicillin treatment | 1 to 3 | 165 | 23 | 21 |
| | 4 to 6 | 188 | 22 | 67 |
| | 7 to 9 | 83 | 23 | 63 |
| | 10 to 12 | 30 | 23 | 71 |
| Multiple drug treatment | 1 to 3 | 42 | 33 | 43 |
| | 4 to 6 | 36 | 28 | 80 |
| | 7 to 9 | 19 | 37 | 100 |
| | 10 to 12 | 7 | 43 | 100 |

Differences in the quantity of staphylococci in the nose of 80/81 carriers or penicillin- and tetracycline-resistant carriers, as compared to nasal carriers of other strains or carriers of sensitive organisms, were not sufficient to explain the increased frequency of 80/81 penicillin- and tetracycline-resistant staphylococcal lesions. Carriers of resistant organisms tend to disseminate their organisms more widely onto the skin and into the air than do carriers of equal numbers of sensitive strains, probably because disseminators are more likely to have received antimicrobial drugs and, therefore, acquired resistant forms to disseminate (White, Smith, and Varga, 1963). Although dissemination was not tested in this study, it is possible that increased dissemination by untreated patients or personnel of resistant staphylococci was partially responsible for the increased prevalence of resistant staphylococcal infections. In addition, treatment with antimicrobial agents markedly increased the prevalence of resistant staphylococci in the nose of treated patients. All of the factors would selectively increase the availability of drug-resistant staphylococci in the environment.

The discrepancy between this and other studies (Weinstein, 1959; Williams et al., 1959) showing increased infection rates in carriers of staphylococci as compared to noncarriers, and studies which did not show such a correlation (Public Health Laboratory Service, 1960; Moore and Gardner, 1963; Bassett et al., (1963), is not completely explained. The present study is the only one which quantitated the nasal-carrier state, and only heavy carriers had a significantly increased infection rate. Other methods of collecting nasal cultures may detect larger numbers of carriers of small numbers of staphylococci who do not have an increased risk of postoperative infections, and therefore mask increased infection rates in heavy carriers. Further quantitative studies of nasal and skin carriage should help clarify these discrepancies.

Although it is attractive to postulate that the increased quantity of staphylococci in the nose is responsible for the increased postoperative infection rate, it is equally possible that the presence of large numbers of staphylococci in the nose is only an indication of decreased host resistance of a general or type-specific nature. The increased emphasis on studies of host resistance to staphylococci is a logical approach to this and other problems in staphylococcal disease.

## Acknowledgments

This work was supported by grants E-2561 and AI-05683 from the National Institute of Allergy and Infectious Diseases, U.S. Public Health Service, and CC-00011 from the Communicable Disease Center, Atlanta, Ga.

## Literature Cited

Bassett, H. F. M., W. G. Ferguson, E. Hoffman, M. Walton, R. Blowers, and C. A. Conn. 1963. Sources of staphylococcal infection in surgical wound sepsis. J. Hyg. 61:83-94.

Jackson, G. G., and M. Finland. 1951. Comparisons of methods for determining sensitivity of bacteria to antibiotics. A.M.A. Arch. Internal Med. 88:446-460.

Moore, B., and A. M. N. Gardner. 1963. A study of postoperative wound infection in a provincial general hospital. J. Hyg. 61:95-113.

Public Health Laboratory Service. 1960. Incidence of surgical wound infection in England and Wales. Lancet 2:659-663.

Weinstein, H. J. 1959. The relation between the nasal staphylococcal carrier state and the incidence of postoperative complications. New Engl. J. Med. 260: 1303-1308.

White, A. 1961*a*. Quantitative studies of nasal carriers of staphylococci among hospitalized patients. J. Clin. Invest. 40:23-30.

White, A. 1961*b*. Relation between quantitative nasal cultures and dissemination of staphylococci. J. Lab. Clin. Med. 58:273-277.

White, A., F. Foster, and V. Knight. 1959. Propagation of staphylococcal phages in liquid medium. Antibiot. Chemotherapy 9:81-86.

White, A., T. Hemmerly, M. P. Martin, and V. Knight. 1959. Studies on the origin of drug-resistant staphylococci in a mental hospital. Am. J. Med. 25:26-39.

White, A., J. Smith, and D. T. Varga. 1963. Host factors in dissemination of staphylococci. Clin. Res. 11:212.

Williams, R. E. O., M. P. Jevons, R. A. Shooter, C. J. W. Hunter, J. A. Girling, J. D. Griffiths, and G. W. Taylor. 1959. Nasal staphylococci and sepsis in hospital patients. Brit. Med. J. 2:658-662.