Epidemiology of Airborne Staphylococcal Infection

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INTRODUCTION ................................................................. 660
Material Reviewed ......................................................... 660
DISPERSAL OF STAPHYLOCOCCI INTO THE AIR ......................... 661
Nose and Skin Carriers ..................................................... 661
Mechanism of Dispersion .................................................. 661
Frequency and Magnitude of Dispersion ................................ 661
Factors Influencing Dispersion .......................................... 663
Infected Lesions .................................................................. 663
Air Contamination Resulting from Dispersion .......................... 663
TRANSFER THROUGH THE AIR ........................................... 664
Viability in Air ..................................................................... 665
ACQUISITION OF AIRBORNE STAPHYLOCOCCI ....................... 665
Operating Room Infection ................................................... 665
Airborne transfer from without ............................................ 665
Locally generated aerial contamination .................................. 666
Air counts and infection rates ............................................. 666
Infection in Wards ............................................................. 667
Minimal infective dose ....................................................... 668
Relevance of Nasal Acquisition .......................................... 669
CONCLUSION ...................................................................... 670
LITERATURE CITED ........................................................... 670

INTRODUCTION

It is a characteristic of the airborne route of infection, in contrast to transfer by food or water, that whenever there is the possibility of aerial transfer there is almost always also the possibility of transfer by other routes. This is perhaps especially true of the forms of staphylococcal infection that have been most extensively studied, namely, those occurring in hospitals. But, during the last few years, there has been a great volume of work based on the assumption that airborne spread is an important route in the spread of the human staphylococcal disease, and there is therefore a considerable body of information for review.

It is logical and convenient to discuss first the studies on dispersal of staphylococci into the air and, second, the survival of the cocci in, and their carriage by, the air. These aspects can be presented in some precise and quantitative detail. When we come to consider acquisition, we enter an area in which extrapolation and analogy loom large, but sufficient quantitative data have now been accumulated to give some factual foundation to the discussion. Nevertheless, the final summing up as to the probable importance of airborne transfer in relation to other modes of spread is of necessity a product of judgment rather than arithmetic.

Material Reviewed

For the most part this paper is based on a selective review of published reports, with special reference to those on a series of investigations (44, 45, 58, 59) carried out with R.A. Shooter at St. Bartholomew's Hospital, London, England (referred to as S.B.H.).

Use has also been made of a recent study of my own at St. Mary's Hospital, London, England (S. M.H.), a report of which is in preparation. In this study, we sampled the air in two surgical wards, one having a total of 14 or 15 patients in four rooms and the other having 22 beds in an open ward. Petri dishes [diameter, 6 inches (15 cm)] of serum-agar containing phenol-phthalein phosphate (2) were exposed in the rooms for 12 hr (or in part of the experiment for 24 hr) on each of 5 days each week. Nasal cultures were examined from each patient weekly.

The total number of staphylococcus-carrying particles on the air plates was recognized by the phosphatase reaction and either all or, when the numbers of colonies on the plate were larger than three to five, a portion were subcultured and tested for coagulase and for phage type. It was thus possible to make some estimate of the number of coagulase-positive staphylococci settling from the air, and of the proportion with various phage patterns, for attempted correlation with
the strains isolated from the patients' nasal cultures.

For airborne particles with a diameter equivalent to those found to carry *Staphylococcus aureus*, that is about 14 μ (38), the settling rate in colonies per square foot per minute is numerically approximately equal to the volume count expressed as colonies per cubic foot. A 6-inch petri dish has an area of approximately 0.2 ft²; in round figures, therefore, the count on such a plate exposed for 24 hr is about 60% of the number of particles inhaled by an adult person in the same time, since the volume inhaled is ordinarily about 0.3 ft³ per min.

**Dispersal of Staphylococci into the Air**

The frequency with which normal individuals harbor *S. aureus* in the nose and on the skin is now well known (56), and such normal carriers are an important source from which the cocci are dispersed. The other source from which staphylococci may be dispersed, especially in hospitals, comprises patients with infected lesions—of skin, wounds, respiratory tract, or gut.

*Nose and Skin Carriers*

Hare and his colleagues were among the first to define the frequency with which nasal carriers of *S. aureus* liberate the cocci into the environment; they counted the numbers shed into the air of a very small cubicule during exercise. Hare and Ridley (21) found that all but 6 of 19 carriers liberated staphylococci, and 7 gave substantial numbers; this and subsequent work (41) pointed to the special importance as dispersers of persons who harbor staphylococci on the perineum. On the other hand, White (54, 55) emphasized the relation between dispersal of staphylococci and the total numbers present in the nose and on the skin.

One feature that also emerged from these and other studies was the wide individual variation in the number of staphylococci shed into the air by carriers. The individuals at the upper end of the distribution seemed to differ sufficiently from those at the lower end to justify the use of the term "heavy disperser" for them, and the suggestion that such heavy dispersers might be responsible for epidemics of hospital infection stimulated further study of the mechanism of dispersal.

**Mechanism of Dispersal**

Hare and his colleagues showed that very few staphylococci are liberated into the air directly from the nose of carriers during ordinary activity; Hare (19) described the liberation by other routes as "outflow" and emphasized the importance of friction with the skin. White (54) had found that the extent to which patients contaminated their bedding was correlated with the numbers of staphylococci found in their nasal cultures. Subsequently, Davies and Noble (14) demonstrated that large numbers of skin fragments are dispersed into the air during the activities known to liberate bacteria; they suggested that most of the staphylococci are carried on such fragments, and they were able to cultivate *S. aureus* from epithelial squames liberated by a known carrier (15).

It thus seemed that the differences among individual carriers in the number of staphylococci that they disperse might be related to (i) the number of cocci on the skin, (ii) the particular area of skin colonized, or (iii) the rate of desquamation. By parallel sampling of air for skin squames and staphylococci, Noble and Davies (37) showed that the last of these was not likely to be the explanation; they thought that the extent of skin carriage was probably the most important determinant. Hare and Ridley (21) had previously suggested that carriage on the skin of the perineum was particularly likely to lead to dissemination, and Solberg (49) not only confirmed this but also showed that, in the absence of perineal carriage, there is a correlation of numbers of staphylococci disseminated with the number found on the nose or on the skin (in his experiments, of the fingers and hand). The importance of the perineal skin as a source for dispersal receives indirect support from observation that, in operating-room clothes, the greatest liberation of skin bacteria seems to be from below the waist and especially through open trouser ends (5, 8). It may be noted that most observers have measured air contamination while the subjects were exercising in some form of cubicle and generally making quite vigorous leg movements; this may perhaps over-emphasize the contribution of the perineum to aerial dispersal.

**Frequency and Magnitude of Dispersal**

It was clear from the early work of Hare and Ridley (21) that many nasal carriers shed staphylococci into the air while exercising. This has been amply confirmed. On the basis of experiments in small cubicules, Bethune et al. (5) reported that 14 of 38 nasal carriers (from a group of 150 normal people) generated an air contamination level of one *S. aureus* particle per ft³ or more, corresponding to a total liberation of about 100 particles or more in 2 min of walking-on-the-spot. Noble and Davies (37) examined 127 persons, 54 of whom were normal adults whereas the rest...
were hospital patients, many with skin disease. The subjects removed all their clothing and then dressed again in a 100 ft³ cubicle from which the air could be sampled. Of the whole group, 30, including only 2 of the 54 normal adults, liberated S. aureus to 1% of the total flora in the cubicle; this corresponded to the liberation of about 25 staphylococcus-carrying particles or more. Eight liberated more than 10,000 S. aureus particles.

More precise estimates of the numbers of staphylococci liberated by carriers have been provided by Solberg (49; personal communication), who estimated the aerial contamination resulting from a standardized agitation of a group of persistent carriers' bedding in a special chamber. Solberg found the air counts of staphylococci dispersed during the making of the beds of his carriers to be distributed in a log-normal fashion, and at least 20% of the 126 carriers (drawn from 2,014 patients surveyed) dispersed more than 10,000 staphylococcus-carrying particles in the standard test (Fig. 1).

Our own studies of air counts in a hospital ward offer another basis for estimating the frequency of dispersal. In Fig. 2 are plotted the mean daily counts of S. aureus of the phage type carried by each of the patients who were carriers on admission to the subdivided S.M.H. ward, excluding those who were carrying strains of types already known to be present in the ward; some of the patients, in contrast to Solberg's subjects, were only transient carriers. The counts are clearly also distributed log-normally. About 50% of carriers generated air counts below 5 colonies per ft³ per 24 hr, but 10% generated counts that averaged more than 50 colonies per ft³ per 24 hr during their stay in the ward, at times when they were the only carriers known to be present. Some rough estimates as to the ventilation rate of the ward suggest that this implies the liberation of $10^6$ to $10^9$ staphylococcus-carrying particles in 24 hr.

It seems likely, therefore, that the heavy dispersers of staphylococci represent the top end of a continuous distribution. This is compatible with the idea that the degree of dispersal depends largely on the extent of skin contamination with staphylococci, and that the shedding of the staphylococci into the air is due to the continuous desquamation of skin fragments carrying cocci, which either may be transients recently deposited there from the reservoir area in the anterior nares, or may be actually multiplying in or on the skin. The rate of desquamation is presumably related in part to friction of the skin and clothes or other skin areas.

It is, perhaps, remarkable how many bacteria are shed on exercising, even when the subjects

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**Fig. 1.** Air counts of Staphylococcus aureus. (A) Generated by disturbance of bedding of persistent carriers [after Solberg (49), supplemented by a personal communication]; (B) during undressing and redressing [after Noble and Davies (37)]. Plotted on a probability scale, so that a straight line represents a normal distribution.

**Fig. 2.** Air counts (particles per square foot settling in 24 hr) of Staphylococcus aureus generated by patients admitted as carriers to a hospital ward (S. M. H.).
are naked (50). Also, in a few unpublished observations in coal mines, O.M. Lidwell and I found that nearly naked miners distributed skin bacteria into the air in quite large numbers. It may also seem surprising that carriers liberate as many staphylococci as they do when it is considered how relatively scarce staphylococci appear to be when carriage is determined by swabbing; however, the area of skin generally examined is very small, and most methods for the bacteriological examination of skin are known to be very inefficient (62).

Factors Influencing Dispersal

Blowers and McCluskey (8) commented that they have not yet encountered a heavy disperser of staphylococci among the normal women they have examined, whereas they found nearly 10% of men to be dispersers. None of the other studies has discussed the influence of sex, but, of the 10 heavy dispersers reported by Solberg, 3 were women, and in general his results do not show any significant differences between men and women carriers in the numbers of staphylococci dispersed. In my ward studies, one of the five heaviest dispersers was a woman.

It has been found that treatment of a nasal carrier of tetracycline-resistant staphylococci with tetracycline led to an increase in the number of staphylococci dispersed into the air, presumably as a result of increased nasal carriage (17), or possibly as a result of increased skin carriage resulting from a reduction in the normal flora and a consequent reduction in the fatty acid content of sebum (18). A similar phenomenon was observed in debilitated or dying patients by Solberg: an increase in the number of organisms in the nose and a corresponding increase in the number shed. M.T. Parker (personal communication) has made a similar observation. One observation that a concomitant virus infection might increase dispersal (16) does not seem to have been confirmed.

A very substantial increase in the number of staphylococci liberated has been found to follow the taking of a shower bath (4, 62). The increase may be 10-fold or more, and the effect persists for at least 60 min. The mechanism of this increase is not known, though it is presumed that the washing in some way allows an increased loss of the superficial squames.

Within broad limits, clothing makes remarkably little difference to the liberation of skin bacteria, and indeed Speers et al. (50) found that some of their subjects liberated as many bacteria when exercising naked as they did when fully dressed, either in street clothes or in a sterile operating room suit. The only practicable method so far described for reducing the rate of liberation is the use of very closely woven clothing, with a trouser suit tightly closed at the ankles (4, 8).

Infected Lesions

The discussion to this point has been concerned with healthy carriers of staphylococci, without any staphylococcus-infected lesions. As would be expected, patients with staphylococcal infections of the skin tend to be especially heavy dispersers (1, 20, 37). Thom and White (52) found, however, that there was little dispersion from septic wounds during the performance of wound dressing, and it seems likely that the effect of skin lesions is, partly at least, to increase the load of staphylococci on the skin. There may also be an increase in the rate of desquamation, for example, in some patients with psoriasis, and one such has been implicated as the source of an epidemic of surgical wound infection in an operating room (32a), though generally in such patients many of the skin particles dispersed are too large to remain airborne (37). Our own observations (59) indicated that carriers can be as important as sources of cross infection as patients with septic lesions. Burke and Corrigan (13), on the other hand, found patients with septic lesions to disperse more staphylococci than healthy carriers; but they studied only 44 carriers. Patients with chest infections have been thought from time to time to be especially dangerous as dispersers (e.g., 44), but there is little direct evidence on this point. The possible effect of antibiotic treatment on dispersal needs to be considered when patients with septic lesions are being compared with healthy carriers.

Air Contamination Resulting from Dispersal

It can thus be concluded that most persons who carry staphylococci in the nose, all of whom must from time to time contaminate their skin, liberate their staphylococci into the air around them. A small proportion of the carriers are especially heavy dispersers and give rise to a high level of aerial contamination. It is not surprising, therefore, that there are considerable variations in the counts of staphylococci in hospital ward air (Fig. 3). The variations in the air counts are, of course, directly related to the presence or absence of heavy dispersers in the ward (34). When the air count in the ward was high, it was virtually always found that the air staphylococci were almost all of one phage type and usually attributable to spread from one person. In the large ward, there were occasions when two dispersers contributed significantly to the air count, but those occasions were relatively uncommon (34).
WILLIAMS


FIG. 3. Air counts (particles per square foot per 24 hr) of Staphylococcus aureus in three rooms of the divided S. M. H. ward.

But, as in other situations, the air counts in hospital wards have been found to conform to a log-normal distribution. In Fig. 4, the air counts from the divided ward are plotted as logarithms on a probability scale and are seen to fall close to a straight line. For comparisons between wards, therefore, the median is the most appropriate statistic. Lines depicting the distributions in five different wards are shown in Fig. 5, and the medians from some of them are given in Table 3.

In the S.B.H. open ward, the median count of S. aureus was about 0.1 colonies per ft³. This count was derived from two periods of 2-hr sampling each week, and it might be thought that this could be no more than generally indicative of the total daily exposure of the particles to airborne staphylococci. However, a very similar median and distribution of staphylococcal counts were observed in the open ward at S.M.H., tested by exposure of 12-hr sedimentation plates.

It is instructive to present the counts in terms of the numbers of staphylococcus-carrying particles that might be inhaled by ward patients in 24 hr. In the two open wards, the median numbers that would be inhaled per day were about 18 and 23 particles; the daily dose exceeded 100 particles on about 15 to 22% of days. In the divided wards at S.M.H. and S.B.H., the median was about 4, and a dose of 100 was exceeded on only about 3% of days.

It is interesting to note that in a small series of tests in a ward at the Queen Elizabeth II Hospital, Welwyn, which consists of four-bed bays opening off a wide corridor, the air counts are intermediate between those of the open and the divided wards (data kindly supplied by R. W. Payne). The explanation of these differences clearly demands further investigation, and it is of obvious relevance to the acquisition of nasal carriage of staphylococci, discussed below.

TRANSFER THROUGH THE AIR

For a proper understanding of the mode of spread of airborne staphylococcal infection, a knowledge of the size of the airborne particles and of their load of staphylococci is needed. Studies with the size-grading sampler devised by Lidwell (26) indicated that the mean "equivalent diameter" of particles carrying S. aureus was about 14 μ (the "equivalent diameter" is the diameter of a sphere of unit density settling in air at the same rate as the particle in question); the interquartile range was about 8 to 20 μ (38). A much smaller proportion of large particles was observed by Walter et al. (53), using the Andersen sampler, but this is doubtless attributable to the characteristics of that instrument (29). Earlier work by Lidwell and his colleagues (27) indicated that, on the average, airborne staphylococcus

FIG. 4. Distribution of air counts of Staphylococcus aureus in the divided S. M. H. ward, based on a total of 1,037 12-hr sedimentation plates.
particles carried about 4 viable cocci, the range being from 6 for the particles greater than 18 \( \mu \) in diameter to about 1 for those less than 4 \( \mu \). These sizes and numbers of bacteria are consonant with the idea that most airborne \textit{S. aureus} cells are associated with desquamated fragments of skin (37).

In normally turbulent air and in a room 10 ft high, particles 14 \( \mu \) in diameter settle at a rate equivalent to about six air changes per hour, so that 50\% of the particles remain suspended for 6 min and 20\% for 15 min. Directional air currents of 40 to 50 ft per min are not uncommon in occupied buildings, so that transfer of staphylococci for considerable distances is clearly possible.

In a few studies, in an open surgical ward in which we have found large numbers of staphylococci being dispersed near one sampling point, the mean counts at sampling points about 20 and about 70 ft distant were, respectively, 26 and 11\% of the count at the point nearest to the disperser.

When a heavy disperser was present in one of the rooms in the four-room S.M.H. ward, the count in the other rooms has been on average about 5\% of that in the room with the disperser. Lidwell and his colleagues (27a) have studied a ward divided into nine rooms and found that the count in rooms other than that containing a source of staphylococci is about 10\% of that in the source room.

In studies of staphylococcal infection in a surgical operating room, Shooter et al. (46) demonstrated what appeared to be aerial transfer over the distance of 90 ft that separated the wards from the operating room.

The actual extent to which staphylococci can be conveyed within a ward or between rooms must depend on the local circumstances of structure, site, and ventilation, but enough has been said to show that aerial conveyance over considerable distances is quite possible.

The aerial route is not, of course, the only way by which staphylococci can be conveyed from one room to another, and hospital routines commonly prescribe quite elaborate rituals for dealing with potentially infected dust on floors, shoes, trolley (cart) wheels, and the like, which is thought to generate secondary airborne spread. But, though many workers have estimated the bacterial content of floors, few have made any useful studies of actual transfer by this route (see 53).

**Viability in Air**

There is a considerable amount of laboratory work to show that staphylococci commonly survive in the dried state for periods measured in days or weeks. Whether there is any significant alteration in their infectivity on storage is not certain. Indications of some loss of infectivity were obtained by Hinton et al. (23) and by Taylor et al. (51); other workers have found no such effect (e.g., 28, 42). Noble’s (35, 36) experimental work in animals has suggested that any effect on infectivity from desiccation is limited to an extension of the lag period and that, if staphylococci are protected from body defenses immediately after introduction into the tissues, they are as virulent as fresh organisms.

**Acquisition of Airborne Staphylococci**

There are two important ways in which airborne staphylococci might infect patients in hospitals: by inhalation or by settling directly into some susceptible area, such as a wound, or onto instruments or dressings that subsequently come into contact with the wound. Inhalation infection may occur anywhere and at any time; sedimentation infection is of particular importance in operating rooms and treatment rooms where surgical wounds are exposed, often for long periods of time. It will be convenient to deal with sedimentation infection in operating rooms first.

**Operating Room Infection**

Airborne transfer from without. Recent studies of air hygiene in surgical operating rooms date largely from the work of Bourdillon and Colebrook (10) in a Burns Unit treatment room, but it was the application of their work to the control of a high incidence of postoperative staphylococ-
cal wound infection by Blowers et al. (6) and by Shooter et al. (46) that brought the subject to general attention. Shooter et al. estimated that, in an 8-month period, the incidence of operating-room infections was 9% of 427 wounds; 0.07 particles per ft² containing *S. aureus* were found in samples from the air during operations. A simple alteration of the ventilation so as to generate a positive pressure in the operating room and exclude staphylococcus-contaminated air from the wards was followed by a substantial reduction in the general air bacterial count (the number of *S. aureus* was not reported), and by a reduction to less than 1% in the incidence of sepsis of presumed operating theater origin in 532 wounds. It is reasonable to assume that this reduction in sepsis was attributable to a reduction in the number of staphylococci settling from the air into the wounds and onto the sterile instruments and equipment. No other investigation has been reported in which alteration of the ventilation was the only change made, but the published report of Blowers et al. (6) and subsequent unpublished experience (Blowers, personal communication) supported the general idea that the prevention of contamination of operating room air with bacteria from other parts of the hospital by the introduction of positive-pressure ventilation has often been associated with a reduction in the incidence of postoperative sepsis. Blowers and Crew (7) recorded a mean *S. aureus* count of 0.6 colonies per ft² in an exhaust-ventilated operating room, compared with 0.03 colonies per ft² in a plenum-ventilated operating room.

**Locally generated aerial contamination.** The work just cited concerned contamination of operating room air with staphylococci from other parts of the hospital, drawn into the operating room by air currents. It is this form of transfer that is controllable by positive-pressure ventilation. But aerial contamination can also be generated within the operating room, either by disturbance of the patients' bedclothes and drapes or from the skin of the operating room personnel, as discussed already.

**Air counts and infection rates.** The bacterial count observed in the air of an operating room is clearly the sum of that produced by infiltration of contaminated air from without and that generated locally. It would be of great value for the monitoring of operating room hygiene if it were possible to relate the staphylococcal (or even the total bacterial) count in the air to the risk of postoperative sepsis. The difficulties of deriving such a relationship are, however, very great. The incidence of wound sepsis is in any case generally very low—perhaps between 1 and 5%. Only a part of the septic cases are infected during operation, and this portion is difficult to estimate, and in any case is not all attributable to sedimentation of airborne staphylococci. In addition, the numbers of staphylococci actually settling onto susceptible areas are so small as to be difficult to measure.

Burke's (11) study is in many ways the most detailed available. By using a very sensitive technique, he was able to recover *S. aureus* from 46 of 50 wounds examined at the end of operation; most wounds yielded two or more different strains, and the mean number of viable units of staphylococci was 14 per wound. Potential sources for the staphylococci found in the wounds were: air, 68%; carrier site on patient, 50%; hands or nasopharynx of the surgical team, 20%. (In some cases, there were two or more potential sources.) Only 2 of the 50 wounds developed any clinical sign of postoperative infection; the rate for wounds that had not been carefully washed out for bacteriological examination was not presented.

In a comparable study of the sources of infection in 35 patients who developed wound sepsis apparently resulting from operating room infection, Bassett et al. (3) thought that a member of the surgical team was concerned in 31% and the patient himself in 17%, the source of the remainder being untraced.

There are several other published studies in which an attempt was made to relate postoperative infection to airborne staphylococci found in the operating room (e.g., 24, 53, 60), but they do not allow easy summary. The general impression is that staphylococci of the type responsible for postoperative infection were rarely found in the air, but this may well reflect the very small air samples generally examined.

In general, it appears that, in reasonably well-ventilated operating rooms with good staff discipline, the *S. aureus* count is of the order of 0.01 to 0.05 colonies per ft²; in a series of operating rooms, we have observed a mean settling count of about 0.01 colonies per ft² per min, while an American cooperative study reported a count as low as 0.001 colonies per ft² per min. (33).

The operating room ought to be a situation in which it would be possible to determine the average infecting dose of staphylococci for man. Taking a figure of 0.01 colonies per ft² per min, and assuming an effective target area of 1 ft² (to include instruments, etc.) and a duration of operation of 2 hr, a frequency of operating room infections of 1% would imply that the 1% infective dose is about 1 staphylococcus-carrying particle. But, to put any real meaning into the
figures, we need to measure the air count and the sepsis rate in a far greater number of patients than has yet been attempted and to carry out at the same time elaborate bacteriological cultures on the patient himself and on the ward to try to assess the relative importance of routes of transfer other than air. And we should remember Burke’s (12) thesis that sepsis is often determined largely by the condition of the actual tissue on which the staphylococcus alights, and on the state of the patient; if his observations are generally applicable, there are usually plenty of staphylococci.

**Infection in Wards**

There is ample documentation of the rate at which both newborn infants and adult patients become nasal carriers of the prevalent staphylococcus in many hospital wards (56). It was reasonable to postulate in the first place that these staphylococci reached the nose by way of the air. Evidence has been sought on this point in several ways—by examining the order in which different parts of the body are colonized, by attempting to interfere with transfer by one route or another, by trying to identify the source of the staphylococcus more precisely, and by relating the acquisition rate to the staphylococci found in the air.

The most precise investigations in this field concern newborn infants. It was shown, first, that the umbilicus and abdominal skin are generally colonized before the nose (25, 48). Second, Rammelkamp and his collaborators showed that a nurse carrier only conveyed her staphylococci to infants if she handled them (61), and later that the colonization of the infants could be delayed by increasing the precautions against contact infection (31, 32). With very strict precautions against cross infection, the rate of acquisition of staphylococci was reduced from 43 to 14%; the latter infections were assumed to be due to aerial transfer. The relative unimportance of inhalation infection in newborn infants is perhaps hardly surprising when one considers that the infant has a minute volume of only about 500 ml (about 0.02 ft³), and that he has to be handled frequently, usually by nurses who handle a good many other infants. But a 14% acquisition rate in a 4-day hospital stay is equivalent to some 3 to 4% per day, which is of the same order as observed in adult wards.

With the evidence from the newborn infants in mind, it is pertinent to ask whether the nose or some skin site is the first area to be colonized in the adults who acquire staphylococci in hospitals. It is obviously more difficult to obtain evidence on this for the adult than for the infant, but in a study of surgical patients (22) R. A. Henderson examined swabs daily from the nose, skin of the hands, skin near the wound site, wound, bedclothes, and environment (Table 1). Some 20% of the 81 patients who became nasal carriers yielded staphylococci of the relevant phage type from one or other of the two skin sites before its appearance in the nose, and a further 15% had yielded the staphylococci from the wound. In the remaining 66% of acquisitions, the nose was the first site on the patient found to yield the staphylococcus. Two important provisos have to be entered here: there was a striking dominance of staphylococci of one phage type among the acquisitions in the ward, which means that there is a serious risk of regarding as related two independent acquisitions; and the area of skin examined was very small and perhaps not representative. Additionally, even skin or clothing contamination might result from aerial transfer, which need not operate only to give inhalation infection. However, the evidence, such as it is, does not contravert the idea that direct inhalation infection is important in the acquisition of the nasal carrier state in adults.

In our recent study at St. Mary’s Hospital, 53 patients were observed to acquire nasal carriage of *S. aureus* while in the ward. The same phage type had been recovered from the air prior to its recovery from the patient in 64% of cases (Table 2). In this ward, there was no marked dominance of one type, and indeed 25 types are represented among the 53 acquisitions. Again, this is not formal evidence that the nasal carrier state was acquired by inhalation of cocci, but it is consistent with such an explanation.

Further evidence for the importance of aerial transfer comes from studies of different ward

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**Table 1. Primary site of colonization in adults**

<table>
<thead>
<tr>
<th>Carrier sites, etc., positive before nose for staphylococci of same phage type</th>
<th>No. of patients who became nasal carriers in ward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nose positive twice or more</td>
<td>Nose positive only</td>
</tr>
<tr>
<td>None</td>
<td>19</td>
</tr>
<tr>
<td>Clothing only</td>
<td>6</td>
</tr>
<tr>
<td>Dressing or wound</td>
<td>7</td>
</tr>
<tr>
<td>Hand or other skin sites</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
</tr>
</tbody>
</table>

* Patients swabbed daily; apparent acquisitions on first 3 days of hospital stay, and acquisitions of untypable strains, excluded.
structures. In an open 22-bed ward we found that separation of patients by the full length of the ward (about 50 feet) only reduced the rate of acquisition of staphylococci by about one-half, as compared with the acquisition rate for a patient in a neighboring bed (59). At the other extreme, very low nasal acquisition rates have been found in patients nursed in single rooms opening to fresh air, that is, when the chance of aerial transfer from one room to another is very low indeed (40). There also appeared to be very little spread of tetracycline-resistant strains from patients nursed in isolation rooms fitted with exhaust ventilation, and the acquisition rate for such strains was greatly reduced in a ward in which all patients harboring such strains were isolated (59).

In adult patients, there are technical difficulties in recognizing the acquisition of nasal carriage that are not present with infants, since truly per-

sistent carriers may fail to yield staphylococci on some occasions. However, since carriage of tetracycline-resistant staphylococci is even now relatively rare (at least in Britain) in people outside hospitals, such strains form a convenient indicator of hospital acquisition. Some rates of acquisition of tetracycline-resistant staphylococci in various wards are presented in Table 3. Unfortunately, data for tetracycline resistance of staphylococci isolated from air samples in these wards are not available, so it is only possible to compare the ranking of the wards with respect to the two parameters. The very limited results suggest that the acquisition rate was higher in the wards with the higher counts of air staphylococci. For various technical reasons, it has not yet been possible to test directly the relation of the acquisition rate to the exposure to particular staphylococci, though this clearly needs to be done.

Minimal infective dose. If we are to understand the epidemiology of airborne infection, we must know the minimal dose of microbes ordinarily needed to effect colonization or infection; this number is not known, but it is so important that it seems justified to indulge in some extrapolation from the few figures available. Shinefield and his colleagues, in their investigations of bacterial interference, found that they could set up a carrier state in the nose of 50% of newborn infants by the inoculation of between 200 and 400 cocci. As noted already, most airborne staphylococcus-carrying particles appear to contain no more than one to six viable cocci.

In experimental infections, it is generally found that the relation between dose and attack rate is not linear, but conforms to an S-shaped curve. For extrapolation to be possible, it is therefore necessary to apply some transformation to the data, e.g., to plot the logarithm of the dose inoculated against the probit of the percentage attack rate. This has been done in Fig. 6 for the data obtained by Shinefield and his colleagues (43, supplemented by a personal communication from

Table 2. Number of patients showing apparent acquisition of nasal carriage in relation to previous air exposure (S. M. H.)*

<table>
<thead>
<tr>
<th>No. of weeks nose negative for the acquired staphylococcus before acquisition</th>
<th>Staphylococci of acquired type—</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found in air previously</td>
<td>Not found in air previously</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>15 (9)*</td>
<td>11 (8)</td>
</tr>
<tr>
<td>2</td>
<td>9 (6)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>3</td>
<td>3 (2)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>4</td>
<td>3 (1)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>5+</td>
<td>4 (3)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Total</td>
<td>34 (21)</td>
<td>19 (15)</td>
</tr>
</tbody>
</table>

* An additional 13 (9) patients were found on admission to the ward to be carriers of a staphylococcus previously found in the air and so may well have acquired their nasal carriage in the ward.

Numbers in parentheses give patients carrying the acquired strain on one occasion only.

Table 3. Acquisition of nasal carriage of tetracycline-resistant Staphylococcus aureus in relation to daily exposure to airborne staphylococci

<table>
<thead>
<tr>
<th>Reference</th>
<th>Type of ward</th>
<th>Median exposure (particles/24 hr)</th>
<th>Acquisition rate (per cent per day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al. (59), Noble (34) Shooter et al. (47)</td>
<td>22-24 bed open, S. B. H. 22-24 bed divided in two parts, S. B. H.</td>
<td>18</td>
<td>0.7</td>
</tr>
<tr>
<td>Williams (in preparation)</td>
<td>14 beds in 4 rooms, S. M. H.</td>
<td>9*</td>
<td>0.6</td>
</tr>
<tr>
<td>Lidwell et al. (27a)</td>
<td>30 beds in 9 rooms, S. B. H.</td>
<td>4*</td>
<td>0.3</td>
</tr>
</tbody>
</table>

* These values are estimates based on mean counts provided by O. M. Lidwell, converted to medians on the assumption that the distribution was similar to that in the earlier S. B. H. studies.
Dr. Shinefield), and the points lie very close to a straight line. Extrapolation of the line back would suggest an attack rate of about 0.02% for a dose of five cocci. The observations of Shinefield et al. were made on newborn infants who are presumably more susceptible to staphylococcal colonization than adult subjects, but, in the absence of any other figures, the calculation may be worth pursuing.

The data in Fig. 5 suggest that the median number of staphylococcus-containing particles inhaled in the S.B.H. wards may have been about 18. Each of these particles probably contained, on the average, about 4 viable cocci, so that the total daily dose inhaled could be estimated at about 70 cocci; if the dose-response relation observed by Shinefield were applicable to the adults, this dose might be expected to generate a "take-rate" of just over 10% per day if all the inhaled particles co-operated to set up the carrier state, or 0.16% if they acted independently. Unfortunately, we do not know how many of the airborne staphyloccoci were tetracycline-resistant, but the apparent acquisition rate for tetracycline-resistant strains was about 0.7% per day.

In the S.M.H. divided ward, the median dose of sensitive and resistant staphylococci inhaled was about 16, which on Shinefield's figures would indicate a take-rate of 0.6%, or less than 0.01% if all the particles acted independently; the actual rate of acquisition of tetracycline-resistant strains was 0.3% per day.

These and some other similar data are presented in Table 3. Although quite insufficient to indicate a clear relation, they suggest that the staphylococcal acquisition rate in different wards may well be related to the air count. In fact, the acquisition rates in the wards are, considering the amount of extrapolation involved, clearly of the same order as those predicted from Shinefield's figures. But at least these calculations clearly indicate that there is no wild improbability in the idea that the acquisition of the nasal carrier state in surgical patients results from the inhalation of such airborne staphylococci as can be shown to occur in the wards. The number of complicating factors in any precise analysis is formidable.

In the first place, as already noted, the figure for a median bacterial count conceals enormous variations, and we clearly need to know whether a short exposure to a large number of airborne staphylococci is equivalent to a more prolonged exposure to smaller numbers. A second complication arises from the fact that staphylococci appear to vary in their ability to colonize the nose (57), so that there is reason to think that inhalation of large numbers of cocci of some strains may be less effective in setting up the carrier state than inhalation of others. The third complication arises from differences in the recipients. The phenomenon of bacterial interference, studied in detail by Shinefield et al. (43, 43a) in infants, almost certainly operates in adults also. Several workers have shown that patients admitted to hospital as carriers of S. aureus are less liable to acquire hospital strains than patients admitted as noncarriers (e.g., 58). The fact that, at least in open wards, patients treated with antibiotics acquire hospital staphylococci in the nose more often than those who are not (e.g., 39) is presumably another example of the same phenomenon, which was well demonstrated experimentally by Boris et al. (9). At the same time, antibiotic treatment probably prevents nasal acquisition in other patients.

Relevance of Nasal Acquisition

In the operating room, we must assume that, whatever the dose-response relation, the aerial transfer of staphylococci to the wound itself is potentially important. It may be asked whether there is any corresponding relevance in the nasal acquisition of staphylococci in the wards. There seem to us to be two ways in which the nasal spread is important.

In the first place, it appears that, at least in some circumstances, nasal carriage of staphylococci predisposes to postoperative infection
There has been some discussion on the significance of these observations (3, 22, 30), but scrutiny of the records of a considerable number of patients leaves no doubt in my mind that the phenomenon is real, even if not generally so frequent as suggested by our original observations.

But nasal carriage is also relevant in that it seems to be the mechanism by which the endemic staphylococci persist in the hospital. Such persistence can often be for a long period. For example, at Saint Bartholomew's Hospital we observed the spread of a staphylococcus of phage type 75/77 which continued from the start of the study in one ward in February 1959 until the end of January 1960. During this period of 1 year, there were only 39 days when there was not present a patient who was either known or reasonably presumed to be a carrier of the strain. A total of 23 patients were infected with the strain, but only 6 of them had any clinically infected lesion.

**CONCLUSION**

The commensal association of staphylococci with man is universal (56) and to a large degree harmless. The transfer from one individual to another must, under ordinary circumstances, very often be by direct or indirect contact. But ability to disperse *S. aureus* into the air in large numbers is a characteristic—sometimes temporary and sometimes persistent—of a number of healthy people, and wherever we go indoors there is a chance that we shall inhale staphylococci. (A few observations in two Post Offices in London have given an average sedimentation count of 0.01 colonies per ft$^3$ per min, a figure quite similar to that for hospital wards (J. Corse, personal communication). But it is only in hospitals that any detailed study of the processes of transfer has been made.

Airborne transfer in hospitals gains its special significance from the fact that, if this route is actually operative, a single disperser is potentially able to infect a considerable number of other patients, who need not be confined within the same room, or even perhaps on the same floor; and the transfer of infection cannot be contained by ordinary methods of asepsis.

The evidence that has been reviewed seems to leave little doubt that airborne transfer can be of importance. It appears that the acquisition of nasal carriage of *S. aureus* by patients nursed in hospital wards can be explained if the dose-effect relationship determined experimentally in infants is approximately applicable to adults. If the results obtained in the studies reviewed can be confirmed elsewhere, we should have a rational basis for assessing one aspect of hospital hygiene in relation to the prevention of staphylococcal infection. We still lack, however, a precise measure of the relative part played by this airborne spread in the etiology of staphylococcal hospital-acquired infection generally.

To take surgical wound infection as an example, we have to recognize that infection can be derived from: (i) staphylococci carried by the patient on admission to hospital; (ii) staphylococci that the patient has come to carry in the nose and on the skin after admission, which subsequently enter the wound; and (iii) staphylococci that reach the wound directly without the prior intervention of the nose or skin carrier state. It appears that aerial transfer plays a major part in the second of these categories and a part—sometimes major and sometimes minor—in the third. But we have insufficient precise evidence on the relative importance of the three categories themselves. The proportion will clearly differ greatly from one hospital to another, and within one hospital, from one sort of surgical operation to another, and from time to time.

The challenge with which we are faced is to provide much more firmly based estimates of the relative frequencies in these categories and the factors that determine them. The practical justification for attempting such an analysis is that it can provide the only basis for judging how best to construct and ventilate hospitals. And the fundamental difficulty of performing the analysis is that in any hospital, where the analysis would be practicable, the overall incidence of infection is probably no more than 1 to 2%, and this small proportion must be distributed over all the various routes and sources.

**ACKNOWLEDGMENTS**

I am grateful to H. R. Shinefield, C. O. Solberg, and W. C. Noble for providing me with additional details of their experimental results. I am also greatly indebted to O. M. Lidwell for allowing me to see, in advance of publication, some of the data from a further study at St. Bartholomew's Hospital, and for numerous valuable discussions on the whole topic of the review. The work at St. Mary's Hospital was supported by a grant from the Hospital Endowment Fund.

**LITERATURE CITED**


Discussion
ALEXANDER D. LANGMUIR
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Dr. Williams has presented a perceptive review of our knowledge of the occurrence of *Staphylococcus aureus* in the air of hospital wards and surgical operating rooms and of its spread to patients. It is impressive how much work has been reported during the past decade and what a

ERRATUM

Epidemiology of Airborne Staphylococcal Infections

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Volume 30, no. 3, p. 664, column 2: on Fig. 4, the left-hand scale should read “cols. per 0.2 sq. ft. per 24 hour” and the figures on the right-hand scale should read, from top to bottom, “0.05, 0.025, and 0.005.”