Some aspects of the transfer and acquisition of *Staphylococcus aureus* in hospitals

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SUMMARY

An efficient typing system for distinguishing strains of this common organism has made possible detailed studies of transfer and acquisition in a variety of hospital environments. Although the nose is the most usual site of colonization perineal carriage may be of particular epidemiological significance since dispersal into the environment is generally by means of desquamated skin fragments, which are most heavily contaminated from the perineum. Direct contact transfer via hands or clothing is significant in infant nurseries and other situations where infected lesions demand frequent handling, e.g. burns units. Self-infection of the surgical wound is not uncommon, presumably from the skin edges adjacent to the wound. There has been much controversy as to the significance of direct infection by airborne organisms deposited directly into the wound at the time of operation. The available evidence would indicate that this must occur but the relative contribution of this route to the sum of surgical sepsis will depend on the operation concerned and remains uncertain. The build up of antibiotic resistant strains to develop the characteristic hospital population, the 'hospital staphylococcus', appears to take place principally by interchange of nasal strains through inhalation of airborne organisms. The airborne particles involved, however, are not always, or perhaps, often, carried by air movement directly from the room housing a carrier into other rooms in the hospital but are redispersed into the air of these rooms from nurses clothing which has become contaminated in the course of nursing the carrier concerned. As a consequence ventilation systems aimed at reducing the airborne spread of micro-organisms may be ineffective in controlling the spread of the staphylococcus so long as the nursing staff move between the rooms, either of the general wards or of the isolation unit. Control of

transfer, direct or indirect, via contaminated clothing has proved difficult to achieve.

INTRODUCTION

During the 25 years following the end of the Second World War *Staphylococcus aureus* can lay claim to being the most extensively studied micro-organism ever. There were several reasons for this interest and effort. The combination of the use of penicillin and, probably, some changes in the character of the organism itself reduced concern over streptococcal infections. The development of an effective typing system (Wilson & Atkinson, 1945, and see Parker, 1962) provided the technical means for distinguishing between individual strains of the *S. aureus* with sufficient precision to identify possible and probable sources for acquisition and infection. The emergence of a particularly spreading and invasive strain, first in Australia (Ibister *et al.,* 1954) but rapidly appearing all over the world with a speed and virulence that called to mind the influenza pandemic of 1917 soon illustrated the value of this method in elucidating the nature of a highly dramatic epidemiological event. The consequence of the '80/81' outbreak inevitably stimulated extensive study of the phenomenon and of the problems posed by staphylococcal infections in hospitals. Studies over the following years demonstrated the varying pattern of staphylococcal prevalence and showed that the strains present in the hospital and those causing disease were continually changing so that the overall effect was the result of the summation of a series of overlapping 'epidemics' (Noble, 1962; Williams, 1966). From this viewpoint the '80/81' epidemic is an extreme example of a general phenomenon. The '80/81' strain began to decline in significance during the 1960s (Parker, 1966) and although there have been lesser outbreaks associated with particular strains none have approached its world-wide impact. Following on this the pace of investigation into the characteristics of *S. aureus* began to slacken somewhat and attention was directed or redirected to other species also responsible for substantial amounts of hospital sepsis. The at least relative, rise in the incidence of infections due to gram negative bacteria (Pollack *et al.,* 1972) led to somewhat premature statements as to the decline and death of the *Staphylococcus* as a significant cause of hospital infection. The *Staphylococcus* is a tough and adaptable creature and like the premature announcement of the death of Mark Twain, 'the report was exaggerated'. Infections due to *S. aureus* have continued to form a substantial part of all infections (Bengtsson *et al.,* 1979). With such a mass of published material it is impracticable to attempt anything approaching a comprehensive overview and even within the limited range of topics included in this paper the presentation is inevitably highly selective.

THE HOSPITAL SITUATION

Since *S. aureus* is a common inhabitant of the nose, many patients arrive in hospital carrying this organism. During their stay they are in close proximity to a large number of persons and there are many opportunities, by remote or close juxtapositions, for the transfer of micro-organisms between them. As a consequence the rate of nasal carriage generally increases with the duration of hospital stay (fig. 1). The two examples illustrated have been chosen as being recent, observed in general hospitals, and covering extended periods of stay. They differ entirely in the epidemiological method by which they were obtained. The values form the Greenwich District Hospital (Lidwell *et al.,* 1975) are the result of an intensive study over a 3-year period of three wards in that hospital. The Birmingham data were obtained by means of a series of cross sectional prevalence studies involving short visits to the wards of no less than 38 hospitals over a period of 6 years (Ayliffe *et al.,* 1977).

The characteristic feature of both these sets of observation is the increase in nasal carriage of strains of the staphylococcus resistant to antibiotics. In both studies tetracyline was the marker used but the great majority of these organisms were resistant to a wide range of antibiotics, including penicillins. In addition to the carriage rates shown in fig. 1. for tetracycline resistant strains, about 20 per cent of the patients in the Greenwich hospital carried other strains, of which over half were resistant to penicillins only and the remainder sensitive to all antibiotics. Although these strains not infrequently changed during patient stay their numbers remained approximately constant. Differing patterns have been observed at other times and places and the absence of increase in the carriage rate of antibiotic resistant staphylococci has been interpreted as an indication that control measures designated to limit the transfer of staphylococci between patients have been successful (Lidwell, 1970). However it is not entirely certain that this has been the reason for the observed phenomena or whether the apparent success was due to the absence at the time of any spreading strain of the organisms. Certainly when such a strain appeared in the hospital wards described in the above paper the procedures that had appeared effective in earlier years were no longer so.

Studies of the spread of staphylococci in hospitals can be divided into two classes. Those which are concerned with the incidence of sepsis, which has most often meant sepsis in a wound following surgical operation, and those which observe the changes in carriage of the organism, generally in the nose. Although carriage is not in itself a disease and generally is unaccompanied by any unwanted consequences for the individual, it is not without

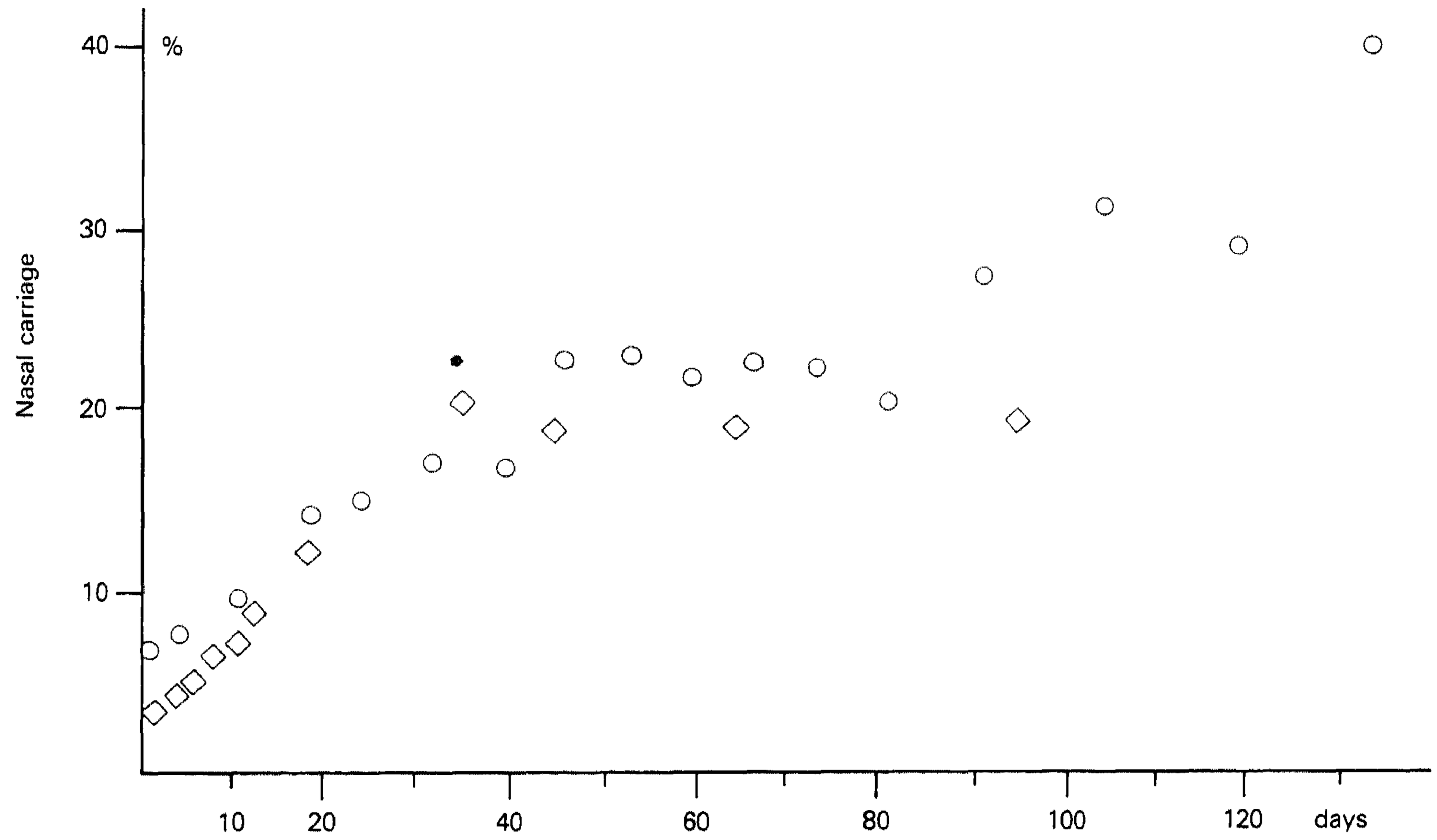

Fig. 1 Acquisition of the 'hospital' staphylococcus. The increase in the proportion of patients carrying tetracycline resistant staphylococci in the nose during stay in hospital. Circles: patients in the medical wards of the Greenwich district hospital (after Lidwell *et al.*, 1975). Diamonds: patients observed in the Birmingham cross-sectional survey (after Ayliffe *et al.*, 1977).

clinical significance. Several studies of surgical sepsis have found that infection with the staphylococcus is more frequent among those who carry this organism pre-operatively (Williams *et al.*, 1959; Bengtsson *et al.*, 1979). In addition the increase in carriage is particularly an increase in the prevalence of antibiotic resistant strains and infection due to these is often more difficult to treat than similar infections with sensitive strains. The mechanisms by which the changes in the population of staphylococci in the noses of hospital patients take place are, in their own right, a fascinating example of natural selection resulting from environmental pressures on a genetically variable population. There are two aspects to this, first the genetic processes whereby the genes responsible for antibiotic resistance arise within a given strain and second the interchange of strains between hosts which allows the environmental effects to act on the genetic system. I shall only be concerned here with the second of these.

Carriage and its estimation

Any study of changes in the rate of carriage is dependent on the accuracy with which this can be estimated. This involves quantitative elements, how profuse must the organism be at the site sampled for it to be detected; qualitative elements, how many, how often and which sites are to be examined; and discriminating capacity, if more than one strain is carried by the same individual what are the probabilities that these will be discovered?

TABLE I

	S. aureus isolated		
Site	by direct plating	by enrichment only	Total
Nose	128	18	146
Hand	13	74	87
Axilla	2	22	24
Perineum	20	25	45

Samples from 361 patients

After Polakoff *et al.,* 1967

The most frequently employed method is to use a swab moistened in nutrient broth, to rub this over the site being examined and then to smear this over the surface of a petri dish containing a blood agar or serum agar medium. Colonies resembling *S. aureus* are examined after incubation and one or a few tested for coagulase production, and phage typed if positive. In a study designed to explore some of the limitations of this procedure (Polakoff *et al.,* 1967) not only were nasal, skin and perineal sites sampled at the same time but the swabs were also examined by an enrichment technique. The results of the observations are shown in table I. While direct plating was fairly satisfactory in detecting nasal carriers (88 per cent) fewer than half the perineal carriers (44 per cent) were detected by the method and only 8 per cent and 15 per cent respectively of axilla and hand carriers. Although only 1/4 of the perineal carriers were not also nasal carriers these amounted to 4 per cent of the patients and half of them were heavy carriers. Light carriage, detectable only by enrichment, may indicate no more than recent contamination from an extraneous source, 'picnickers'. Carriage on the non-perineal skin was often only light and when heavy appeared to be related to carriage elsewhere.

In addition to the, perhaps 10 per cent of nasal carriers, usually light carriers, which are likely to be undetected by a simple nasal swabbing technique (Shooter *et al.*, 1963) and the 4 per cent of patients who are perineal carriers but not nasal carriers it is probable that more than one strain is carried by the carriers detected on perhaps 10 per cent of occasions (Solberg, 1965). Just as more sensitive methods of detection may indicate carriage when only the transient presence of an organism recently deposited at the site is involved so frequent sampling may also suggest changes which are no more than ephemeral phenomena. An attempt to make a detailed allowance for these sources of uncertainty was made for the data obtained in the Greenwich study (Lidwell *et al.*, 1975). The result of these calculations, admittedly of limited accuracy, was to increase the total number of carriers in the wards to which an individual was exposed by about one third above that detected by weekly nasal sampling but the distribution of these carriers in the different parts of the hospital section studied was not significantly affected.

Dispersal

From the earliest studies it was apparent that there was a very wide variation in the numbers of staphylococci dispersed into the air by carriers and that although the numbers dispersed into the air were correlated with the numbers present in the nose few organisms were directly liberated from this site during ordinary activity. (Hare & Ridley, 1958; White, 1961). A critical observation was that of Davies & Noble, (1962, 1963) who demonstrated that not only are large numbers of skin fragments dispersed into the air by activities known to disperse bacteria but also that *S. aureus* could be cultivated from epithelial fragments dispersed by known carriers. These fragments had an equivalent particle diameter of about 13 μm, i.e. a settling rate in air of about 30 cm/min (Noble *et al.*, 1963) but probably carry only a few viable cells each. In a series of samples of ward air the mean value was estimated to be about 4 (Lidwell *et al.*, 1959). As a consequence the capacity for dispersal is directly correlated with the density of skin carriage. This was well demonstrated in an extensive and systematic study carried out by

Solberg (1965) on 100 nasal carriers. He sampled the nose, throat, faeces, skin (lip, fingers and hands) the axillae and vagina, as well as dispersal in a standardised test. The best correlation to dispersal was given by the skin counts. In conformity with all other investigators he found a wide range in the density of carriage and the degree of dispersal. His figures are illustrated in fig. 2. While there was no significant difference between men and women nasal carriers in their capacity to disperse staphylococci this was not the case for a group of 15 perineal carriers who were only relatively weak nasal carriers. All dispersed much more extensively than the nasal carriers and this was much more marked among the men studied. In all Solberg found 17 carriers who dispersed more than 10^4 staphylococci in his tests, of these 13 were men and only 4 women.

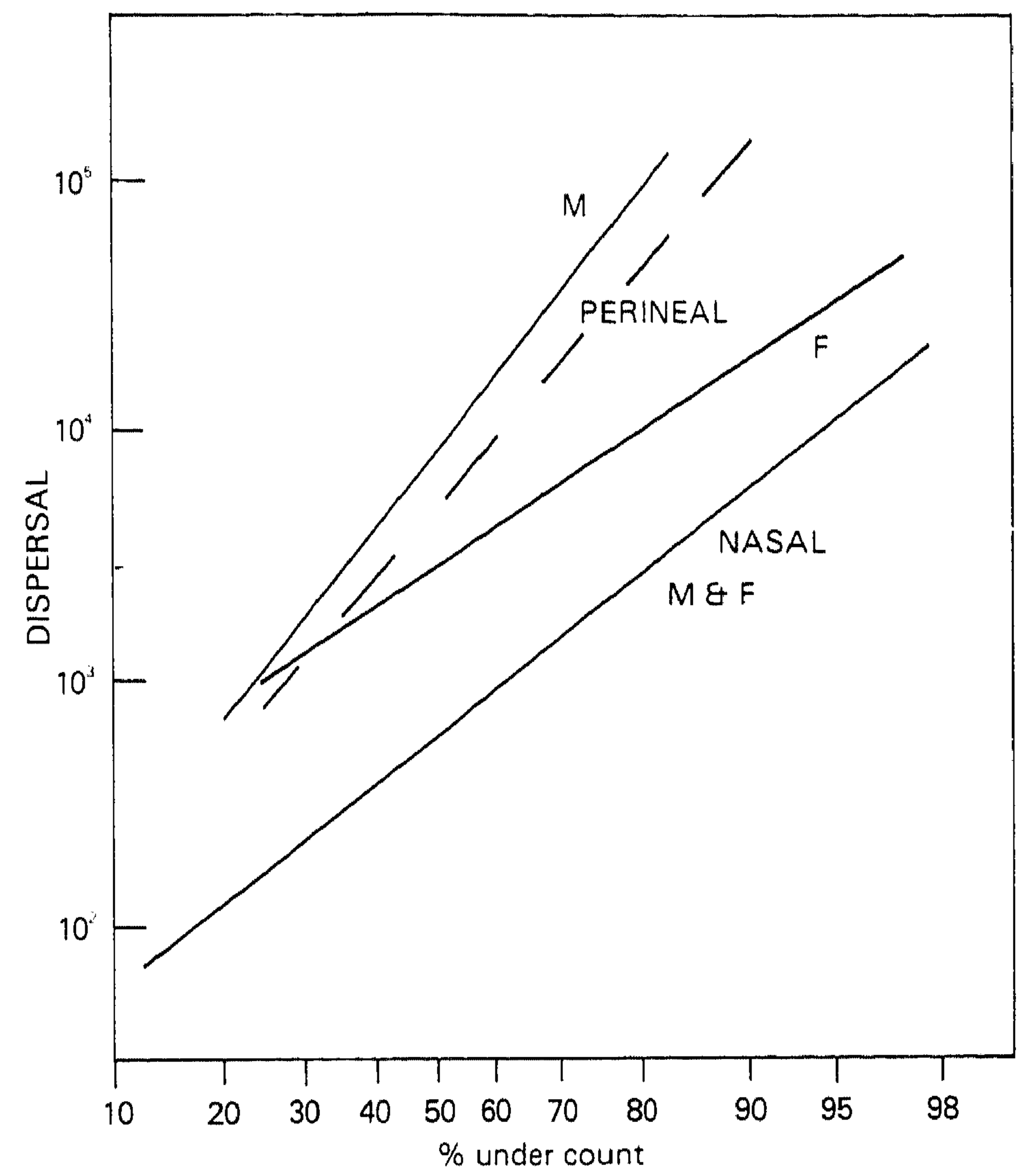

Fig. 2 Dispersal from 100 nasal carriers, male and female, and from 14 perineal carriers, 9 men and 5 women (after Solberg, 1965).

Twelve of them, including 11 men, were perineal carriers. These figures emphasize the potential significance of the minority of perineal carriers as dispersers of the organism. Solberg also demonstrated the significance of skin contamination and its dependence on the actual carriage site by a series of experiments in which the carriage site alone was treated by some antibacterial agent. Fig. 3(a) shows the results of nasal treatment on a nasal carrier and fig. 3(b) that of treating the perineal area of a perineal carrier. A similar result followed treatment of the infected area of patients suffering from skin lesions. These patients, like the perineal carriers, dispersed large

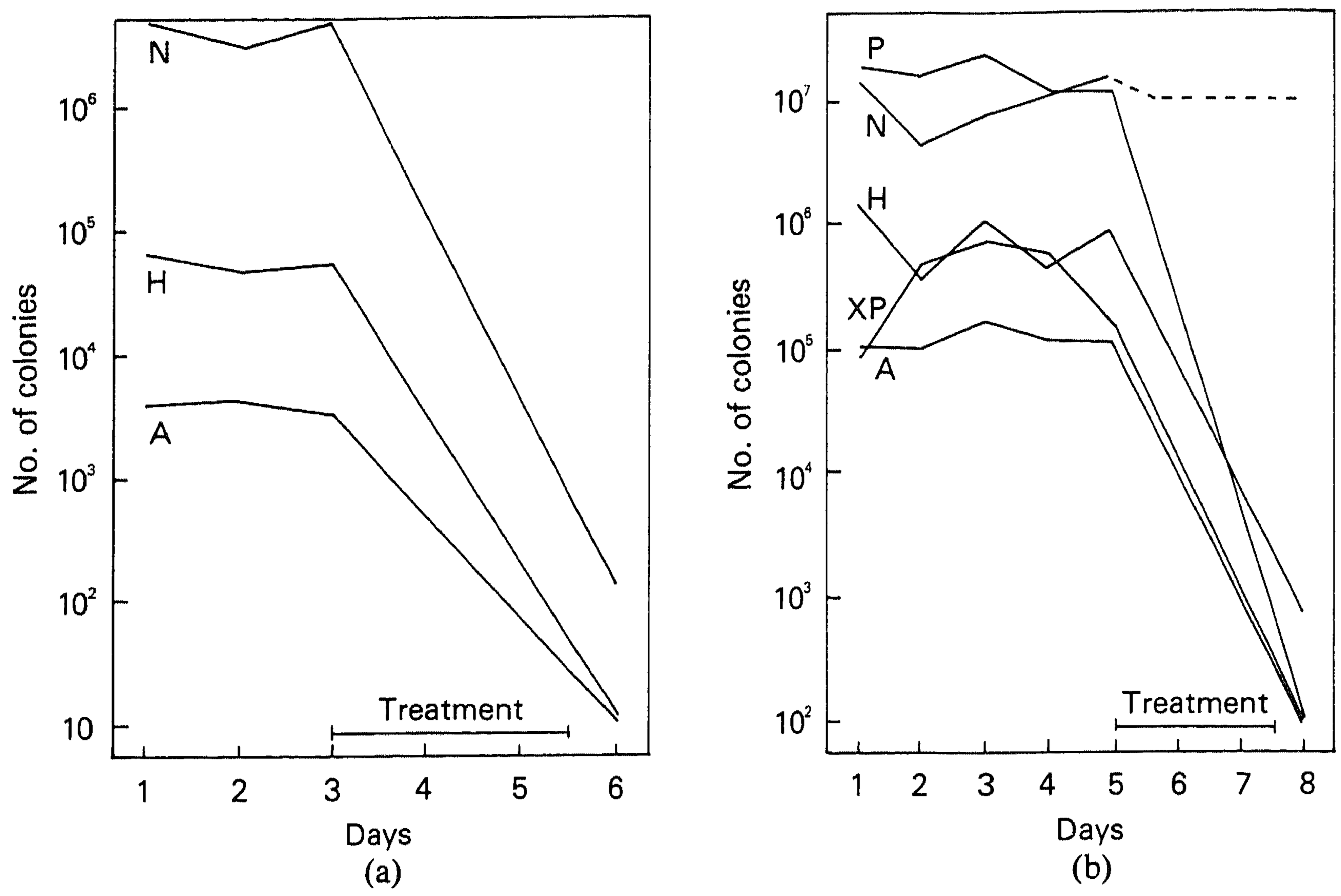

Fig. 3 Treatment of carriers (after Solberg 1965). (a) Left hand: dispersion of staphylococci by nasal carriers treated with antibiotic nasal spray. The logarithmic vertical scale gives the numbers of *S. aureus* recovered in samples taken in a standardized manner from, the nose N, the hands H, and the air of the room during and after bedmaking A. During the treatment period the carriers were subjected to a nasal spray of a framycetin-gramicidin preparation 4 times a day. Data based on 40 carriers.

(b) Right hand: dispersion of staphylococci by a perineal carrier treated with hexachlorophane emulsion. The logarithmic vertical scale gives the numbers of *S. aureus* recovered in samples taken from: the skin of the perineum P, the nose N, the hands H, the skin just outside the perineal area XP, and the air of the room during and after bedmaking A. During the treatment period the patient rubbed a 3 per cent emulsion of hexachlorophane over the perineal area twice daily. Data from a male patient.

numbers of staphylococci. There has been some diversity of opinion as to the relative frequency of 'dispersers' among men and women. Blowers & McLuskey, (1965) reported 10 per cent among the men they studied but no women. Noble & Davies (1965) on the other hand, although finding greater dispersal of skin scales and micro-organisms from men than women, clothed in their usual garments, reported that this difference disappeared when both sexes were examined in identical clothing. This would accord with the absence of any sex difference reported by Lidwell & Brock (1972) from the Greenwich Hospital wards.

Two exceptions to the general association of staphylococcal dispersal with skin contamination have been reported. In 1960 Eichenwald and his colleagues reported on an outbreak of staphylococcal infection in an infant nursery. While infants suffering from impetigo dispersed actively there was

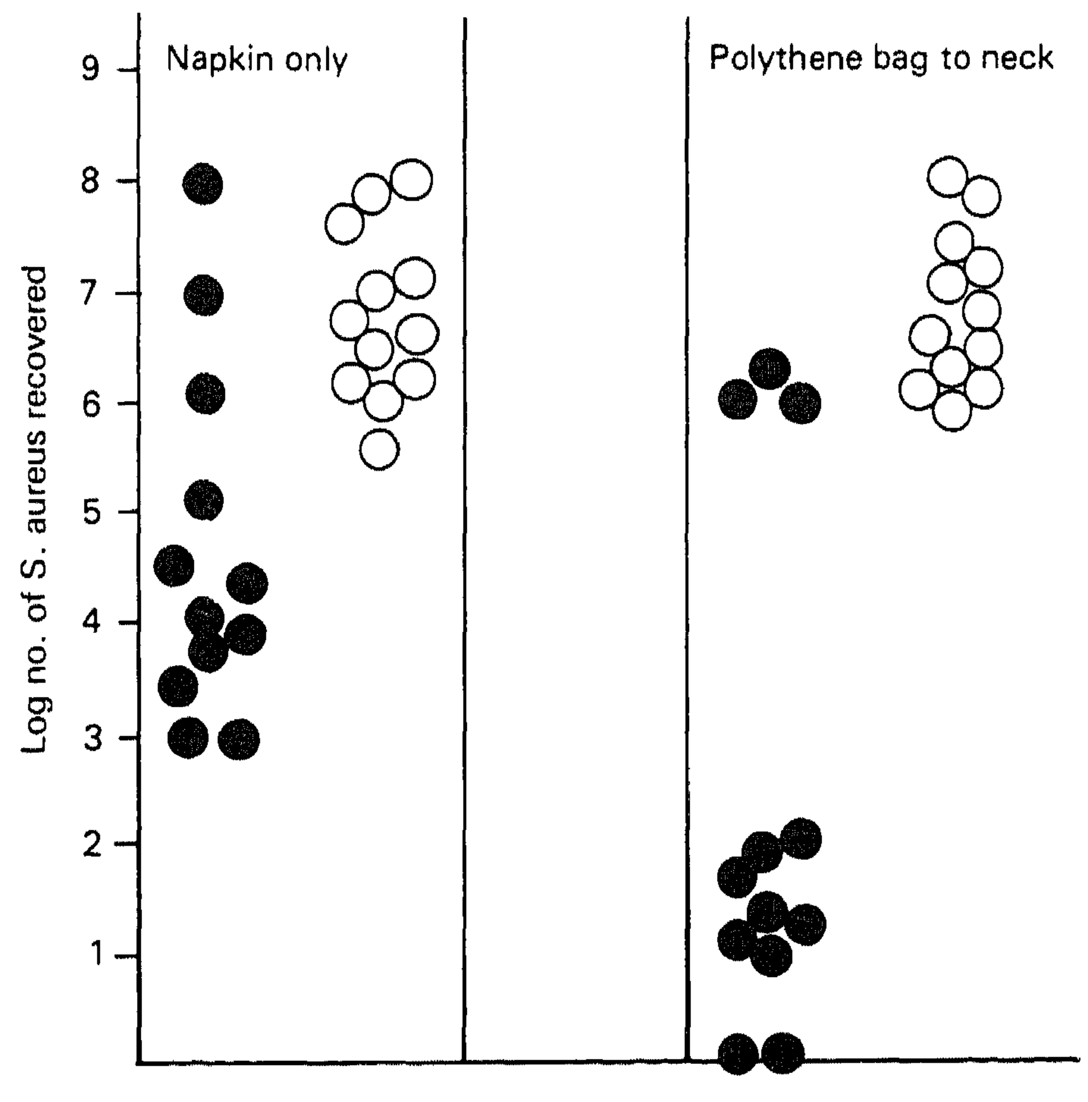

Fig. 4 Dispersal of *S. aureus* by babies with concomitant adenovirus infection (after Eichenwald *et al.*, 1960).

also a group of infants without lesions who were also active dispersers. This dispersal appeared to be directly from the upper respiratory tract as was demonstrated by the results obtained when the bodies of the infants were enclosed in a polythene bag tied around the neck (fig. 4). In addition the size distribution of the particles was quite different to that for normal skin dispersal, almost all the particles were below 5 μm. Further study showed that this dispersal was associated with infection with a respiratory virus. Whether the phenomenon is a regular occurrence is not known but no such experience has been reported since. The strain involved was a variant of 80/81 which undoubtedly differed from the generality of staphylococci.

Another instance of staphylococcal dispersal in small particles has been reported from a burns unit (Hambraeus, 1973). While the median particle size of the airborne material was usually close to that commonly found, about 11 μm, during periods of heavy dissemination this fell to no more than 4 μm (fig. 5). These patients had extensive wet lesions without skin covering but the mechanism of dispersal was not apparent.

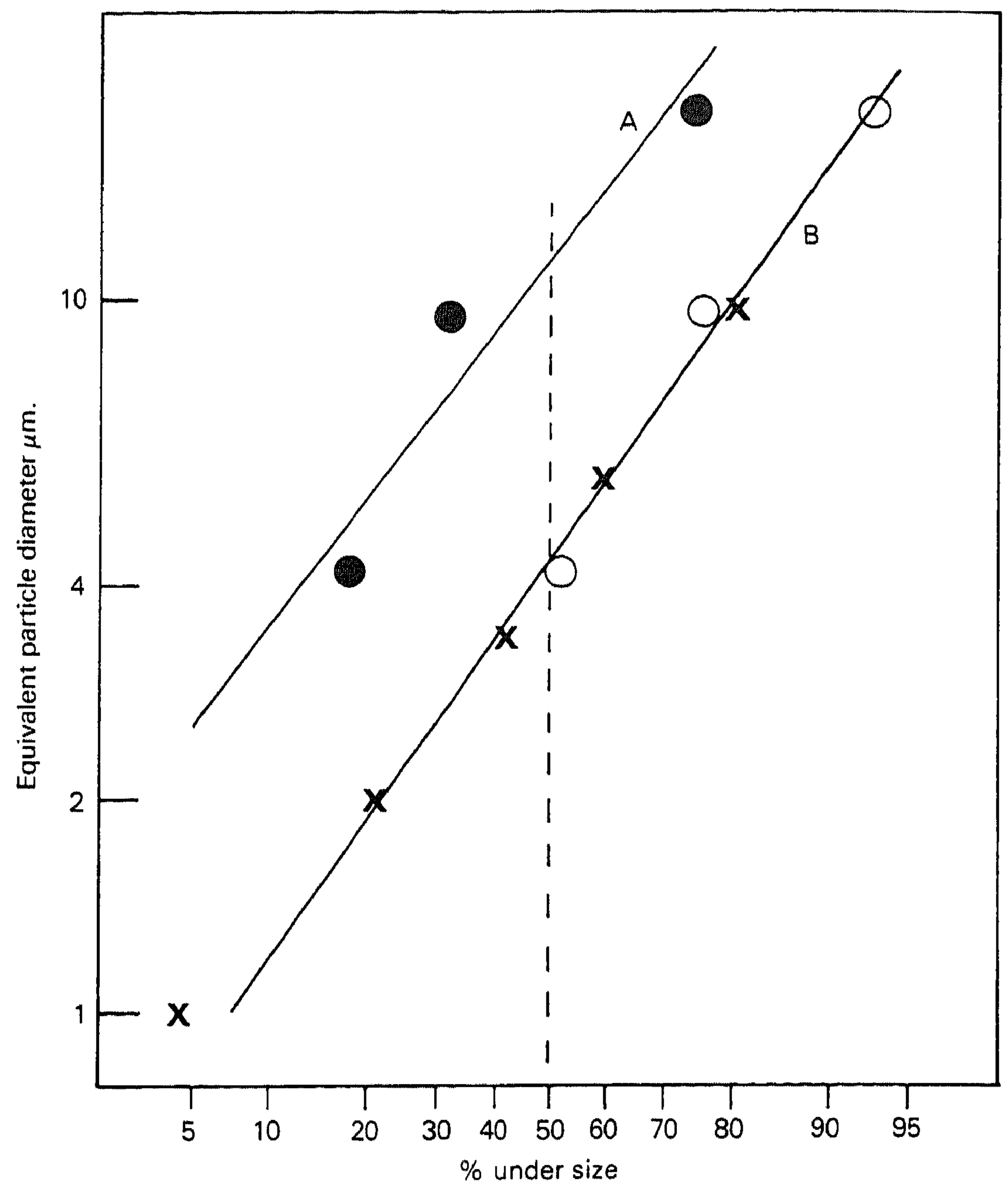

Fig. 5 *Particle size of airborne S. aureus* in a burns unit (v. Hambraeus, 1973(a)). A, filled circles: normal, low or moderate dispersal.
B, open circles and crosses: massive dispersal from patients with extensive infected lesions.
The circles are from samples taken with the size-grading sampler (Lidwell, 1959), the crosses from samples with the Anderson multi-stage sampler (Anderson, 1958).

Studies of dispersal have invariably employed aerial dispersal as an easily estimated quantity, either during standardized exercise in a test chamber or in the natural situation. Carriers who disperse in this manner must inevitably contaminate their surroundings. As dispersal is usually via contamination of the skin, air dispersal is a good index of the capability of transfer by contact routes as well as by means of airborne particles. However, it is not necessarily the case that those who do not disperse into the air are not potential sources of infection by other than airborne routes. This is applicable to all kinds of localized lesions for example infected surgical wounds. Where these require repeated handling, for dressing or treatment, contamination of the nurses' hands or clothing provides a mechanism for the spread of the organism.

Transfer and acquisition

The circumstances governing the transfer and acquisition of *S. aureus* will vary widely in different parts of the hospital so that the effective routes for transfer will also differ. In almost every situation however distance between the source and the potential recipient will diminish the risk of infection. It is therefore not possible to draw conclusion as to the likely route of infection merely from such spatial data but the extent to which the different routes are affected by distance will differ and knowledge of these differences may enable inferences to be drawn as to the probable way in which infection is transferred between two situations. Transfer between A and B may also involve a sequence of more than one route, in which case careful and detailed analysis may be needed to unravel the connections. These and other points can be best illustrated by a consideration of the evidence available in some situations which have been studied in detail.

Infant nurseries

It is appropriate to start with the infant nursery. The newborn child lacks a bacterial flora but rapidly acquires this in the first hours and days of life. Staphylococcal infection is not only a hazard to the newborn but infection of the child is the principal route by which the mother becomes infected, leading to the development of a breast abscess, often after discharge from hospital (*Hospital Infection,* 1960). The environment of the infant nursery with the necessary frequent handling of the child provides easy opportunities for the spread of the staphylococcus and it was in this situation that the 80/81 strain first appeared. Controlled experimental studies are rare in the study of staphylococcal epidemiology but two sets of observations were made by Wolinsky, Mortimer and colleagues (Wolinsky *et al.,* 1960, Mortimer *et al.,* 1966) in which babies naturally colonized in the main hospital nurseries were placed in rooms with 7 and 8 cots respectively, one in the 7-cot room, study A, and 2 in the 8-cot room, study B. The other cots were occupied with babies admitted direct from the delivery room. The results are shown in table II. In the absence of any special precautions almost 2/3 of the babies were colonized with the strain carried by an 'index' baby during their stay in the nursery, which averaged 4 days. Washing the hands with a hexachlorophane containing detergent before handling a uninfected infant reduced this to not much over 1/3 while the use of different nurses for the two sets of infants further reduced the proportion infected to no more than 1/10. The site where the acquisition was first

TABLE II

Transfer of *S. aureus* in infant nurseries

Nursery	Index baby	Nurses' hands	Aquisitions from Index baby	
A	H	NW	45/49	92%
	H	W	17/32	53%
	NH	W*	3+?5/91	(3)9%
B	H	NW	46/105	44%
	H	W	3/21	14%
	NH	W*	16/158	10%

H index baby handled, NH not handled, by nurse before dealing with other babies in the room.
W nurses' hands washed, NW not washed, before dealing with other babies.
* Different nurses from those handling the index babies.
The numbers of aquisitions/the number of infants exposed relate to a hospital stay of 3–5 days.

After Wolensky *et al.,* 1960

detected was most frequently the umbilicus and only in a small proportion the nose. With the combination of frequent handling and a small breathing volume, only about 1/20 that of the adult, it is not surprising that the contact route was the most frequent way in which infection was transferred. The simple procedure of a 10 s hand wash halved the rate of transfer. However either the washing was not fully effective (Midland group, 1976) or there were other contact possibilities since there was a further fall of around 25 per cent in the proportion infected when different nurses handled the two groups of infants. The residual infection rate of 10 per cent may still include some contact transfer mediated by indirect routes but is presumptively due to airborne transmission. Since, in the second experiment, 146/830 settle plates exposed for 2 h were positive a single staphylococcal carrying particle would fall on the area of a plate about every 12 h.

This represents a very low dose rate, no more than 10 such particles in the whole duration of nursery stay. Shinefield and his colleagues (v. Williams, 1966) have made an attempt to measure directly the infecting dose for the infant nose. While a dose of 800 cocci led to a take of over 90 per cent, for a dose of 50 this was no more than 10 per cent. Extrapolation from these figures to low doses is hazardous but on the assumption that each coccus acts independently, i.e. the chance of colonization is equal to $1-(1-p)^n$ where p is the chance for a single cell and the number inoculated is n, the chance of infection was approximately 0.0030 for each cell. In the nursery each infant will have breathed in about 3 m^3 of air during its stay. The effective sampling rate of a petri dish, 10 cm in diameter, for a particle settling rate of 0.3 m/min is about 220 l in 2 h. The observed rate of one particle in 12 h is then equivalent to one particle in about 1.3 m^3 of air and a total of no more than 2.3 inhaled over the whole period of stay, corresponding, perhaps, to 10 cocci. With an infection risk per cell of 0.0030 this would lead to a nasal acquisition rate of 3.0 per cent. During the second experiment the nose was the first site colonized in 4 of the 158 infants exposed, without direct contact. This is 2.5 per cent. The close agreement is certainly fortuitous but the orders of magnitude correspond.

The spread of staphylococcal infection in nurseries can be controlled by appropriate skin treatment, which both protects the principal sites of acquisition and prevents dispersal.

Isolation units

Each type of unit has its own problems. Extensive studies have been carried out in the Burns unit of the Academic Hospital Uppsala (Hambraeus, 1972; 1973(a); 1973(b); 1973(c)). The unit consists of 5 patient rooms each communicating via a ventilated air lock with a central corridor. In spite of a considerable degree of malfunction of the ventilating system the degree of isolation between patient rooms for direct airborne transfer was very high. The concentration reduction between a source room and any other room averaged 4.5×10^4 (tests with the ventilation correctly adjusted led to the much higher value of 3.4×10^5). However, the numbers of airborne staphylococci found in other rooms than the room containing the dispersing source were much higher than this, the reduction with respect to the source room being of the order of 10^3 only. Although clean gowns were worn when nursing a patient with an infected burn contamination penetrated to the dress beneath. When a second nurse wore this dress with a second clean gown over it and then nursed another patient the strain of organism carried by the infected patient was found in the air of the second room and on the bed and clothing of the second patient. The use of gowns did reduce transfer but even when relatively impermeable gowns were worn it was still considerable. The relationships observed are illustrated in fig. 6 (Lidwell, 1976). Although it has long been known that normally woven textiles, as used for hospital gowns, offer little or no obstacle to the passage of fragmented skin scales, the gaps in the weave are often as much as 100 μm

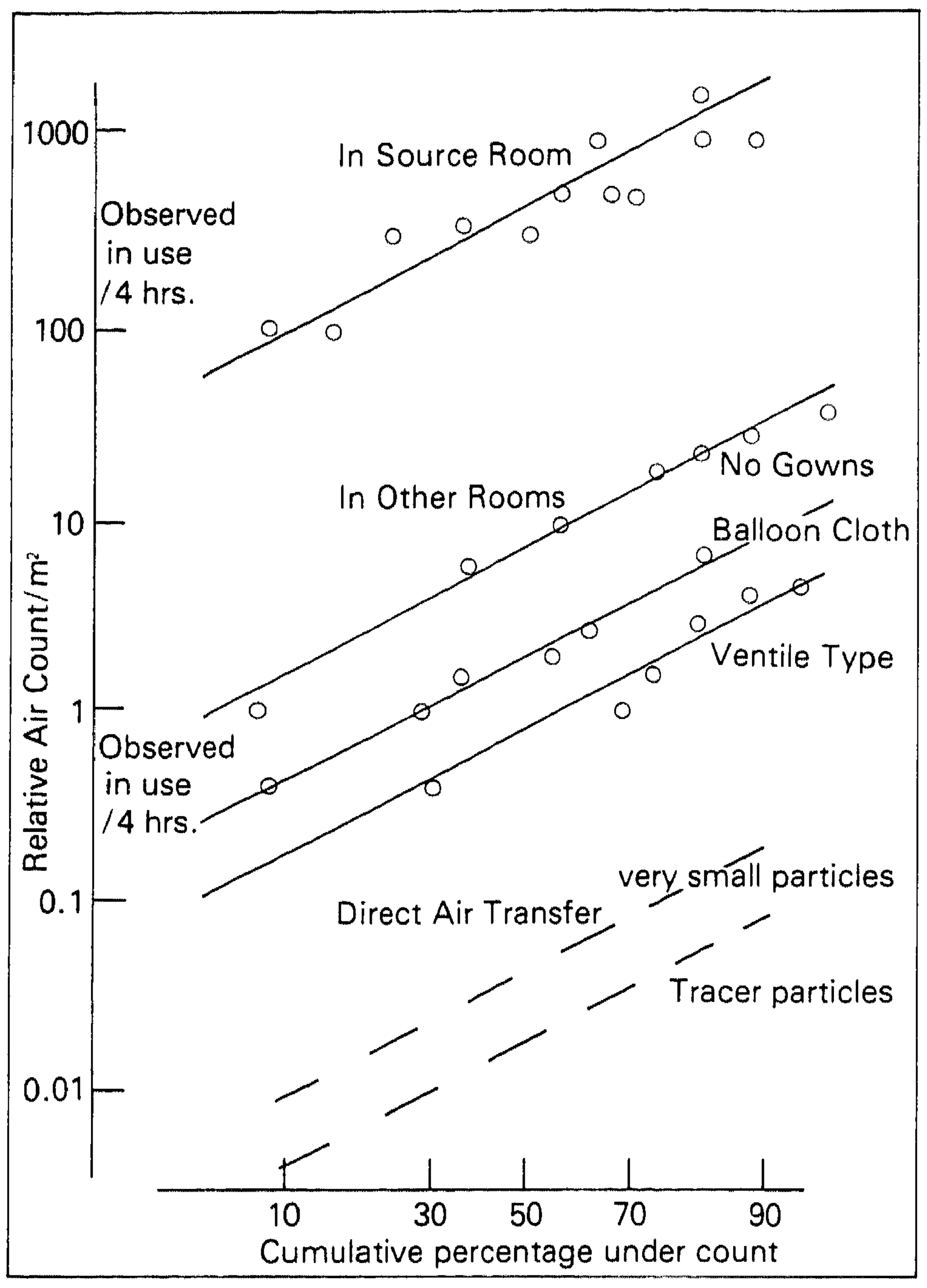

Fig. 6 Transfer of *S. aureus* in a burns unit, comparison with the extent of direct airborne transfer of tracer particles and the effect of different gowning regimes (Lidwell, 1976).

while a whole unfragmented squame is no more than 30–40 μm in its longest dimension, the failure of closely woven gowns, which have been shown to reduce dispersal substantially when worn in operating rooms, was disappointing. Several types of non-woven gowns were also tried with little if any benefit to the patients and the staphylococcal infection rate remained high, nearly 2/3 of all patients.

Heavy dispersal of staphylococci in this unit was often associated with very small particles. These would be transferred to a greater extent via the air than the tracer particles studied but this effect is quite inadequate to explain the observations. Such small particles might also pass more readily through the fabrics. A further consideration is that the infected burns were often very wet and the gowns grossly contaminated with liquid. Fluid may penetrate gowns quite differently to dry particles. It seems that in this situation the airborne route was almost certainly not significant.

TABLE III

Air contamination and infection in a burns unit (relative to the open ward)

System	Air contamination	Nasal acquisition MRSA	Colonization of burns SA	Pseudomonas	Other
Open ward	100	1	1	1	1
Air curtain bed	10–20	1.7	1.0	1.0	1.6
Plastic isolator: in cubicle					
Open top	30	1.0	1.75	0.0	1.2
Filtered air supply	1	0.4–0.65	0.75	0.17	1.1

SA = *S. aureus*
MR = resistant to more than one antibiotic

After Lowbury *et al.,* 1971

In another study of burned patients in Birmingham (Lowbury *et al.,* 1971) a plastic isolator was used and compared with the open ward and an air-curtain bed, table III. Although nasal acquisition and colonization of burns was slightly reduced the effect was very small. On the other hand colonization with *Pseudomonas* was greatly reduced. The results of this study were interpreted to indicate that both airborne and contact routes are important for infection with *S. aureus* but that direct contact is predominant with respect to Pseudomonas.

The operating room

The acquisitions of infection following surgical operation have been the most intensively studied field. This is natural in view of the substantial incidence of staphyloccocal wound infection and the relative ease of investigations within the limited and well controlled environment of the surgical suite.

Attention has already been drawn to the greater frequency of infection among carriers. Table IV gives the results of a recent study on this aspect (Bengtsson *et al.*, 1969). These figures include operations where contamination with intestinal organisms was likely.

TABLE IV
Post operative sepsis in carriers of *S. aureus*

		S. aureus infections			
	No.	Own strain		Other strain	Other micro-organisms
Non carriers	1797	—		23(1.3)	116(6.5)
Carriers	1174	32(2.7)		21(1.8)	78(6.6)
Skin carriers	198		32(7.6)		17(8.6)

( ) = Percentage figures

After Bengtsson *et al.*, 1969

S. aureus was associated with infection in 45 per cent and intestinal organisms with only 35 per cent of 'clean' operations. It was also found in 32 per cent of the 'contaminated' cases while intestinal organisms were found in over 80 per cent of these. The figures show that, in this hospital, self-infection was responsible for about 60 per cent of the staphylococcal infections. The risk of infection from other sources was about one half of that from an autogenous source and in about one half of these infections a possible source could be found either in the air or from among the operating room staff. The operating rooms concerned were in a modern suite with a good ventilation system. The airborne counts recorded were low, probably not more than $50/m^3$ which is considerably less than the $180/m^3$ recommended as an upper limit (Report, 1972).

An indication of the extent to which staphylococci may be dispersed within an operating room and reach the surgical wound is provided by some observations of Burke (1962). In this series of 50 wounds *S. aureus* was recovered from 46, many yielding more than one strain, and the average number of units per wound was as many as 14. These figures are much higher than any reported since. Possible sources for the strains were found in the air for 68 per cent, from a carrier site on the patient for 50 per cent and from the nose or hands of the surgical team for 20 per cent (in some cases there were several possible sources). Only 2 of the wounds developed sepsis. Other studies have attempted, generally without much success, to relate strains of staphylococci recovered from the air or even from the wound to those causing sepsis. The sampling techniques are however comparatively inefficient so that the strains found may be only a few among a greater number actually present. If this were so the chance that they would be those responsible for infection must be small. An average figure for the numbers of particles carrying *S. aureus* which settle from the air in a well ventilated operating room is of the order of $0.1/m^2$ min (Williams, 1966; Bengtsson *et al.*, 1979). The expected numbers reaching an open wound with an effective exposed area, including instruments, etc., of 0.1 m^2 for 1 h would then only reach 0.6 or a single particle in about 2 out of 3 operations. The Uppsala figures, with a staphyloccocal settling rate of about half this, presented a staphyloccocal sepsis rate from all sources other than the patient of 1.5 per cent, about one in 20 of the operations which might have been expected to suffer staphyloccocal contamination from the air. On this estimate the infection risk for a single coccus, taking 4 cells to each infected particle, would be about 1/80. This might be compared with the value deduced for inoculation into an infant's nose of 0.0030, 1/330, but all these calculations are extremely uncertain. There are a number of reports incriminating particular individuals as sources for outbreaks of surgical sepsis. One reported by Payne, (1967) concerned an anaesthetist with a skin condition who was shown to be an active dispenser. Although he certainly handled the patient this was relatively remote from the wound and the airborne route affords the most plausible explanation of the incident.

This is not the place to discuss the many attempts to control infection in clean elective operations, such as total hip joint replacement, by special ventilation systems and clothing which reduce the disseminations of airborne organisms by 100 fold or more. Some aspects of this are discussed by McLauchlan (1980). Unpublished observations made in the course of a multi-hospital trial of these systems (Lowbury & Lidwell) indicate that when the airborne count is reduced to this extent there is a concomitant reduction in the numbers of micro-organisms recovered from the wounds by washing out with sterile saline. The magnitude of this reduction is such as to suggest that, for these operations of relatively long duration on a bacteriologically clean site with a large area of wound exposure, as high a proportion as 95 per cent of the organisms deposited in the wound may derive from the air when the operations are carried out in operating rooms with conventional ventilation with a mean bacterial count in the air of the order of $150/m^3$ (Lidwell, 1980).

The hospital ward

The wards, where the greatest number of patients are nursed, are the place where interchange of strains results in the characteristic hospital population of antibiotic resistant staphylococci. The fact that acquisition and colonization is most commonly in the nose, whose primary physiological function is to act as a protective filter for the lungs, and that the airborne particles carrying staphylococci are of a size that is efficiently intercepted by the nasal passages must lead to a first hypothesis that the airborne route is that principally involved. This is not, however, easy to prove. Based on this assumption many attempts have been made to reduce the acquisition of new strains of staphylococci by patients and so, hopefully, the incidence of sepsis by schemes of ventilation. Proposals of this kind go back to the beginnings of microbiology. Thus John Simon in 1863 (Report) writes:

> To provide throughout the whole of a really active hospital that the means of cleanliness and the means of ventilation shall be proportionate to the many sources of foul and infective material. . . . The ventilation must be such as should leave no corner unsearched by its currents. These, within the wards, must never for a moment cease flowing from inlet to outlet . . . so largely that every unwholesomeness is at once removed by them.

He does not ignore direct transfer by contact and indeed refers to this in the first place, but relates the need for ventilation to those contagions spread by 'matters like pus abundantly floating in the air'.

The low rate of acquisition in an infectious disease hospital where each patient was nursed in a cubicle opening off a covered way (Parker *et al.,* 1965), so that direct transfer of airborne micro-organism between them was obviated might seem to support this approach but the use of mechanical ventilation to protect patients during the pre-operative period (Lidwell *et al.,* 1970) and the installation of a balanced ventilation system in a 'race-track' ward (Whyte *et al.,* 1969) was not very effective. In contemplation of moving into a new hospital, with a mechanical ventilation system designed to reduce air-borne transfer between the patient rooms and with a high proportion of patient beds in single rooms (40 per cent), a prospective study was carried out by the surgical department in Aberdeen over the years 1964–6, before the move, and 1966–8, after (Smylie *et al.,* 1971; Davidson *et al.,* 1971). There was a substantial reduction in the numbers of airborne staphylococci in the wards from a very high figure of around 1/cu ft to about 0.1/cu ft. The last figure is much closer to that which has been found in other hospitals (Lidwell, 1979). Although the nasal carriage rates on admission were similar in the two periods the rate of acquisition of antibiotic resistant strains was much less in the new building. The wound infection rates were also lower. These last are tabulated in table V. It is notable that the reduction in infections with intestinal organisms, which are most often likely to be of autogenous origin, was as great as that for the staphylococcal infections. The study was complicated by the presence in the old hospital over the period studied of an outbreak of infection associated with phage type 84/85 which accounted for over half of the infections. This strain died away after the move into the new hospital. It is impossible to say

TABLE V

Wound infections before and after moving into a new hospital

Infecting organism	Intestinal		*S. aureus*		*SA* not 84/85	
Hospital	Old	New	Old	New	Old	New
Nature of operation						
All						
No. of patients	493					
No. of infections	54	24	42	25	19	22
per cent	11.0	4.7	8.5	4.9	3.9	4.3
Clean						
No. of patients	314	355				
No. of infections	13	8	16	11	7	11
per cent	4.1	2.2	5.1	3.1	2.2	3.1
Potentially dirty						
No. of patients	179	152				
No. of infections	41	16	26	14	12	11
per cent	22.9	10.5	14.5	9.2	6.7	7.2

After Davidson *et al.,* 1971

with confidence whether this was related to reduced opportunities for transfer in the new environment or whether the strain faded away at that time for totally unconnected reasons, as often happens with particular strains. The incidence of infections due to strains of staphylococcus other than this was not affected by the move. As the authors conclude, it is not possible to say which factors were responsible for the improvement in the clinical experience.

The rebuilding of St Alphage's hospital in Greenwich in South East London presented some complex architectural problems. The solution adopted involved a 4 level building, about 100 m square with only a few small internal wells inserted for amenity considerations. Such a deep plan necessitated mechanical ventilation throughout (Drury & Skegg, 1969). The design made it possible to vary the ventilation arrangements and in particular the direction of air flow between the patient rooms, typically containing 6 beds, and the corridors. Over the 3½ years from 1970–3 physical measurements of air transfer and bacteriological observations on the air and of nasal carriage by patients and staff were carried out in three linked ward units comprising in all about 100 beds. Two ventilating regimes were studied. The first with the input and extract to the patient rooms approximately in balance so that there was negligible directed air flow through the doors to the corridors. In this condition considerable interchange of air took place across the doorways which were often open. The second with excess input to the patient rooms so that there was a net outflow from these rooms into the corridor, the same arrangement as that studied in Aberdeen. Under these conditions air exchange across the doorways should be much reduced. Gas and particle studies (Foord & Lidwell, 1975 a and b) showed that there was indeed a substantial reduction in air transfer and transport of airborne particles between rooms when the second, directed, pattern of ventilation was obtained. The difference was as great as 100 fold in some circumstances. The extent of particle transfer between rooms was however never great, the mean concentration ratio observed between sets of rooms rarely falling below 1000: 1 under any conditions. There was, moreover, no significant reduction in the levels of airborne contamination and the rates of nasal acquisition of *S. aureus* compared with other hospitals previously studied (Lidwell *et al.,* 1975) and the development of the characteristic hospital population of antibiotic resistant strains proceeded in the usual way, (fig. 1). More detailed analysis showed that transfer of strains from identified sources in particular positions occurred into all parts of the three wards studied (Fig. 7). Examination of the air samples, eliminating the effect of unrecognized carriers, showed that the extent of transfer, measured by the air count in the receiving room, was indeed proportional to that in the room containing the source carrier, fig. 8, but that the apparent extent of transfer exceeded the observed transfer of airborne tracer particles by more than tenfold. How then did the airborne particles in the second room arise? Examination of all the evidence suggests that this was a consequence of contamination of the nurses' clothing when handling patients and that the organisms were redispersed when the nurse entered another room (Lidwell & Brock, 1970). A similar mechanism has already been suggested for the apparent air transfer of staphylococcal strains observed in the Uppsala burns unit.

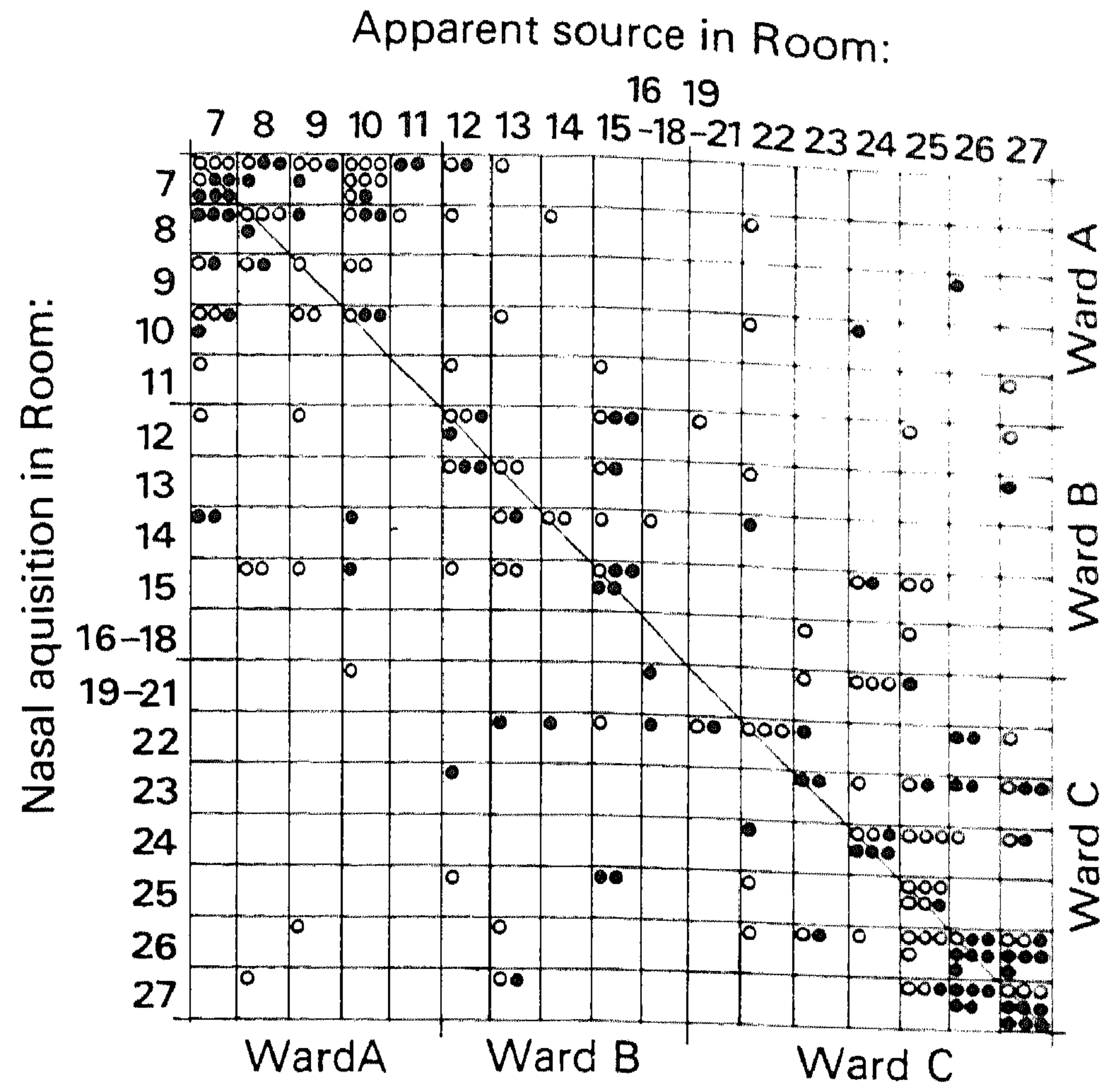

Fig. 7 Nasal acquisition of *S. aureus* apparently derived from unique patient sources (carriers) in known positions in the wards. The numbers along the top of the figure marking the 17 columns specify the room which contained the apparent source. The numbers marking the 17 horizontal rows specify similarly the room in which the acquisition occurred. The three single-bed rooms associated with ward B, rooms 16–18, have been grouped together. Rooms 19–21 have been treated similarly. The grouping of the rooms within the wards is given at the bottom and right-hand side of the figure. The location and apparent source of each of the 217 acquisitions is indicated in the appropriate cell. The filled circles indicate acquisition of strains resistant to tetracycline.

These and similar studies also provide data for the estimation of the nasal acquisition rate in relation to the exposure to airborne particles carrying the organism. No useful correlation has been obtained by comparing the overall number of airborne staphylococci of all strains with the total nasal acquisition rate. However when the exposure to airborne particles per single potential source is compared with the nasal acquisition rate from those sources there appears to be a functional relationship (fig. 9). The acquisition rate is not proportional to the dose rate but varies less than this, approximately as the square root. This might be a true dose response relation but is perhaps more likely a consequence of the heterogeneous nature of the population exposed. The rate never reaches as much as 1 per cent of the population exposed inhaling a single particle. If each particle carries 4 viable cells this is equivalent to a risk of acquisition of 0.0025 per

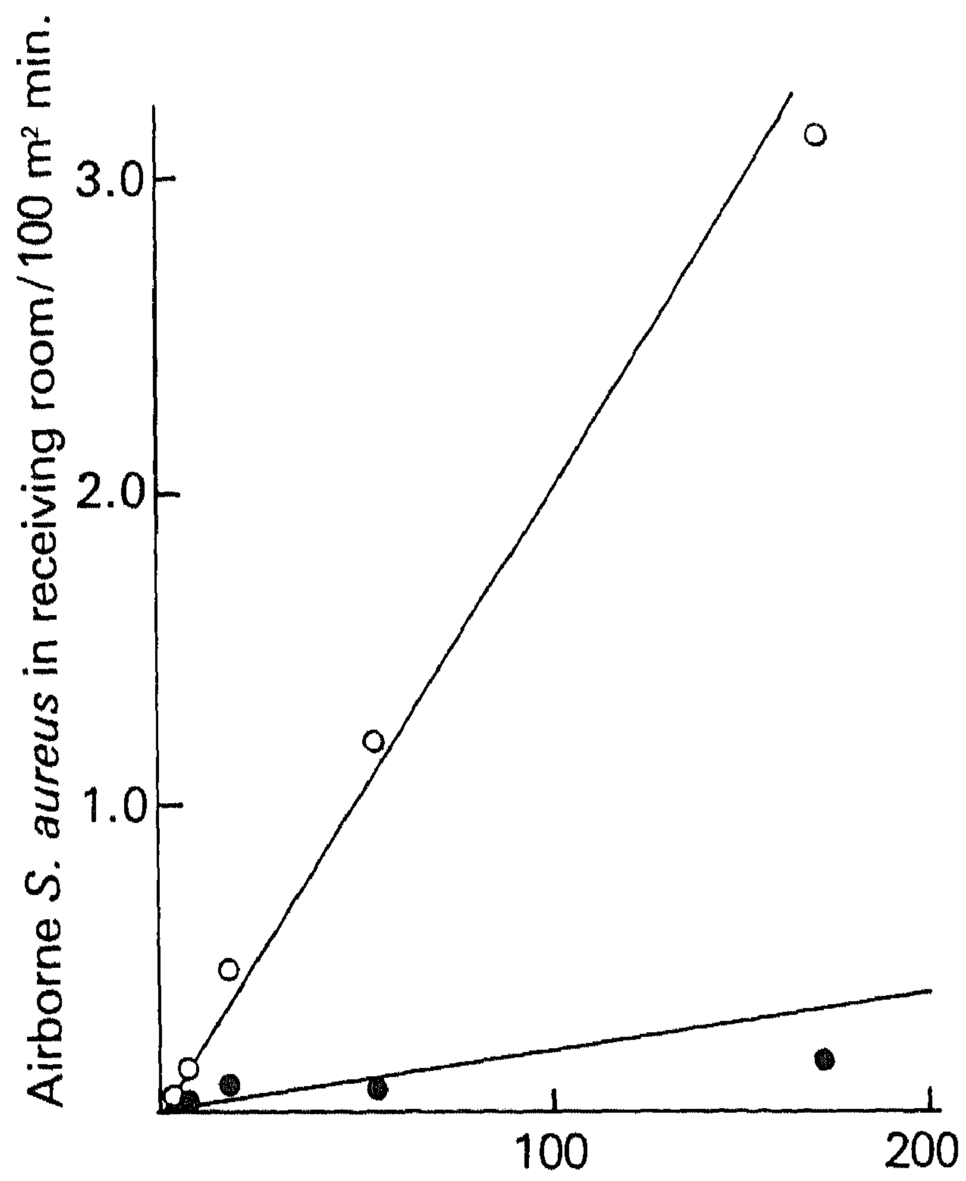

Fig. 8 The numbers of airborne *S. aureus* found in rooms other than in which a dispersing source was located. Only those occasions when the highest count was found in the room containing the apparent source have been included. The data have been divided into groups according to the numbers found in the samples taken in the source room, i.e. 1–3, 4–9, 10–99, 100–300 and the points plotted at the geometric mean of the range. The upper curve ○, gives the numbers found in samples taken in other rooms of the same ward as that containing the source. The lower curve ●, gives the numbers found in rooms in an adjacent ward.

coccus. This may be compared with the figure of 0.0030 deduced from the experiments of Shinefield, quoted earlier, on the inoculation of staphylococci directly into infants noses.

However, unlike new born infants, the population of the hospital wards is highly heterogeneous. Susceptibility to acquisition of a particular strain will vary very widely. In particular patients receiving antibiotics will be highly resistant to the acquisition of a sensitive strain but may readily acquire a resistant one. It is not surprising therefore that the acquisition rate for tetracycline resistant strains has been observed to be several times greater than that for other strains (Lidwell, Polakoff *et al.*, 1966). The corrected figures for acquisition in relation to exposure shown in fig. 9 are compatible with a J shaped distribution of susceptibility, the majority of the population have an extremely low susceptibility so that the observed rates of

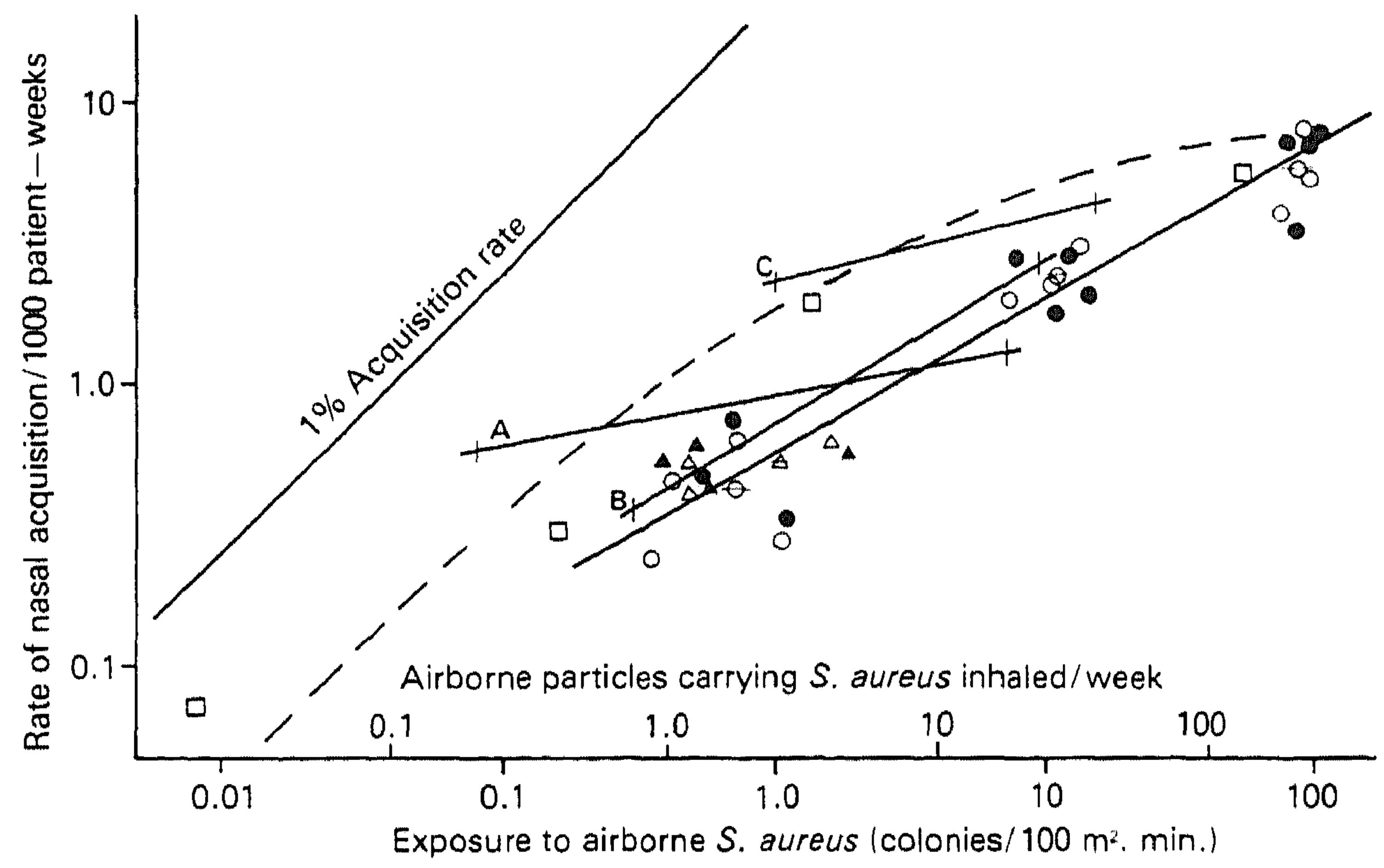

Fig. 9 Exposure to airborne *S. aureus* and the rate of nasal acquisition. The vertical scale is the rate of acquisition of a new strain in the nose, per single potential source (carrier) per 1000 patient-weeks. The horizontal scale is the exposure to airborne *S. aureus*, per single potential source (carrier), expressed as the number of colony forming particles settling per 100 m^2 (1080 ft^2) min during daytime hours. Above this scale is given, approximately, the corresponding number of airborne particles carrying *S. aureus* which would be inhaled by a patient during one week. For this purpose the mean breathing rate been taken as 10 l/min and the exposure during the 12 night hours as one-half that during the daytime. All the scales are logarithmic. The acquisition rates from the detected patient sources are shown by circles and those from staff carriers by triangles. The open symbols correspond to data for the three wards taken separately and the filled symbols for the four periods of the investigation. The open symbols crossed by short horizontal bars refer to the average values for the whole investigation. The group of 8 circles in the upper right hand corner of the figure relates to acquisitions from patient sources in the same room as the recipient; the centrally placed group to patient sources in another room of the same ward and the lower left hand group to patient sources in another ward. The 'best' straight line through these points has been drawn by eye. The results of previous calculations of this kind have been included in the figure, for purposes of comparison, as shorter lines on which short vertical bars indicate the range of values covered; A, B and C. For acquisition from patient sources at Greenwich, corrected values have been derived which attempt to take account of undetected (missed) possible sources. These have been plotted on the figure as squares which correspond, in order of decreasing exposure to airborne *S. aureus*, to nasal acquisition from patient sources in the same room as the recipient, in other rooms of the same ward, in rooms in an adjacent ward and in rooms in a remote ward. The curved broken line has been drawn through these four points as described in the text. Also indicated on the figure is the rate of nasal acquisition which would result if 1/100 of the particles carrying *S. aureus* inhaled were to result in acquisition of that strain in the nose.

acquisition derive entirely from the tail of the distribution, comprising only a few per cent of the patients exposed. The broken line on the figure shows the relationship calculated for such a distribution where the chance of acquisition from a single coccus is less than 10^{-5} for more than 97.5 per cent of the population but reaches 10^{-1} for the most susceptible 0.5 per cent. For the purpose of the calculation each air-borne particle carrying *S. aureus* has been assumed to carry 4 cocci on the average.

Even this apparent relationship between the airborne challenge and the rate of nasal acquisition does not unequivocally demonstrate that this occurs by means of nasal inhalation of particles from the air. The airborne exposure is likely to parallel the risk of bacterial transfer in other ways. The studies of nasal acquisition in wards including those in the Greenwich hospital do however indicate strongly that hospital ventilation *per se* is unlikely to have any major effect on the transfer of staphylococci infection.

A direct experiment on nasal acquisition by hospital patients analogous to that carried out by Wolinsky, Mortimer and colleagues on babies has been done by Solberg (1974). Three patients who were not themselves nasal carriers were placed in a 4-bed room ventilated mechanically at 4 air changes per hour. In the fourth bed was placed a nasal carrier who was nursed by different nurses to those who dealt with the others. Of those exposed to vigorous dispersers (more than 10^5 particles by a standardized test) 30 per cent became carriers of the strain in the course of 10 days. If the carriers were only weak dispersers (less than 100 particles by the test) then only 5 per cent became carriers over the same time. There is no guarantee that the strains were equally capable of nasal colonization but the figures correspond to a 6 fold reduction in the acquisition rate for a 100 fold or more expected reduction in exposure. No determination of the actual exposure was made.

Following application of a thorough isolation policy for carriers of the strain, Selkon and his colleagues (1980) were successful in controlling an epidemic of infection with a particular strain of a methicillin resistant staphylococcus (fig. 10). The policy involved transferring all carriers, nasal or with infections, into a purpose-built isolation unit. The rooms in this were constructed with individual ante-rooms containing a wash basin and a gown, put on by a nurse before entering the patient room. The corridor was positively pressured by the air supply, which was exhausted from the rooms. The nursing staff were peculiar to the unit. Such a system provides a barrier against transfer both by direct airborne routes and by routes which involve contamination of the nurses' clothing. As the authors are aware the decline in infection could have been due to spontaneous changes in the character of the strain but the balance of evidence would seem to be against this. There was no reduction in the use of flucloxacillin during the period and there was no significant reduction in the rate of infection with methicillin sensitive strains until carriers of these strains were isolated.

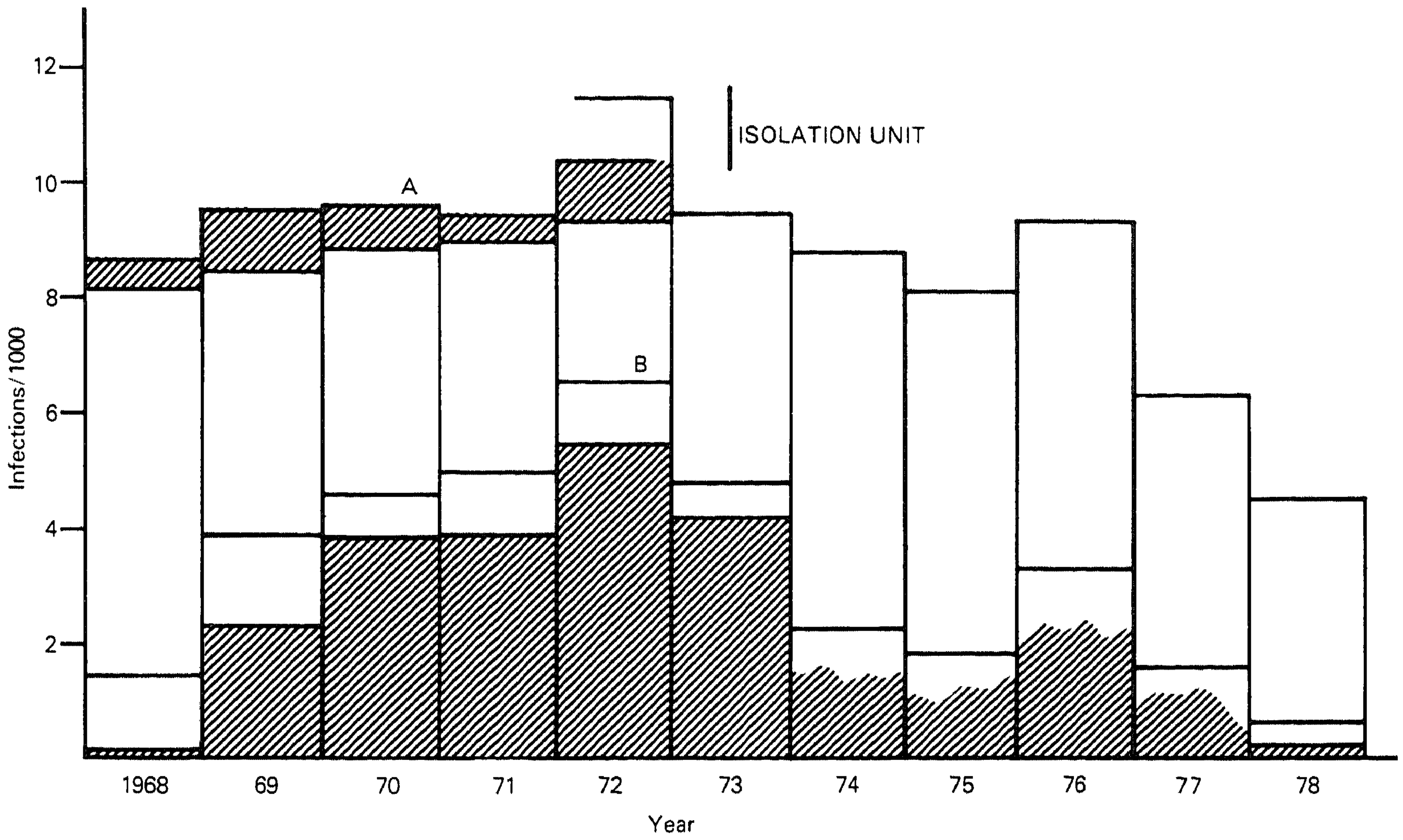

Fig. 10 Infection with methicillin resistant strains of *S. aureus* in a general hospital before and after the introduction of an isolation unit.

The upper boundary, A, shows the rate of infection with 'hospital strains' i.e. those resistant to penicillin and tetracycline, the lower boundary, B, that with strains resistant to methicillin. The hatched areas indicate infections with strains of phage type 75/85, the upper those sensitive to methicillin, the lower those resistant to this antibiotic.

The isolation unit came into use, for methicillin resistant strains, in June 1973 and was applied to all departments of the hospital by 1976. Carriers of methicillin sensitive strains were also isolated in 1978.

(There was a change in the definition of 'hospital' strains from 1972 onwards and a nurse shortage in 1976 which led to deficiencies in the application of the isolation policy during that year. No data are given for the numbers of infections with strains of phage type 75/85 after 1972 except for methicillin resistant strains in 1973 and 1978.) After Selkon *et al.,* 1980.

CONCLUSION

It is only possible in a single paper to give a very cursory account of all the work on the transfer of staphylococcal infection which has appeared over the last 35 years. Evaluation is particulary difficult in a field which has generated many opinions but fewer established facts. One factor which is probably responsible for a great part of the uncertainties is the variable character of the organism itself. In any hospital the strains present vary with time and the appearance of a particularly spreading strain may change the whole pattern. There is some evidence that differences in capacity for spreading depend on the density of growth at the carriage site but it is almost certain that strains vary also in their ability to colonize. This is manifest in the relation of antibiotic treatment to the acquistion of resistant strains but probably applies in relation to other patient characteristics also.

A significant fact which has become apparent over the last years is the part played by contamination of nurses' clothing in spreading the organism. Control over this is difficult to achieve but it would seem that this is at least one area which must be explored further if we are to make any substantial improvement in the spread of *S. aureus* in hospitals.

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