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## Sepsis after Total Hip or Knee Joint Replacement in Relation to Airborne Contamination [and Discussion]

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## Sepsis after total hip or knee joint replacement in relation to airborne contamination

BY O. M. LIDWELL

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The beginning of aseptic surgery was marked by the hypothesis that surgical infection might be caused by particles from the air. The importance of other ways of contaminating the wound soon became apparent, however, and these seemed to predominate. With the development of operations for total joint replacement large numbers of operations began to be done on clean tissue with maximal exposure to the air of the operating room. The incidence of infection was high and the airborne hypothesis was advanced as the reason. Extensive investigations with clean-air systems gave support to this. A recently completed control study has concluded that in conventional ventilated operating rooms over 90% of the bacterial contamination of the wound comes from the air and that cleaner air results in a lower risk of sepsis.

### INTRODUCTION

Ever since Lister's epoch-making paper in 1867, when he expounded the 'antiseptic principle in the practice of surgery', the role of the air in the generation of surgical wound infection has been a subject of continuing controversy. Lister based his practice on the hypothesis that the 'living matter of the air' (Tyndall 1881) was the cause of sepsis. 'When it had been shown by the researches of Pasteur that the septic property depended . . . on minute organisms suspended in it . . . it occurred to me that decomposition in the injured part might be avoided . . . by applying some material capable of destroying the life of the floating particles' (Lister 1867).

His practice was brilliantly successful, but over the succeeding years he and most other surgeons became convinced that it was the disinfection of skin, hands and materials that was responsible, rather than any control over the airborne particles. This belief arose from the observation that small bacterial inocula failed to grow in blood or serum. 'The facts . . . seem to indicate that the putrefaction that is so apt to occur in wounds . . . is due rather to septic matter in a concentrated form than to the diffused condition in which it exists . . . in air' (Lister 1881).

Here we meet the either/or argument that has, in no small degree, bedevilled the discussion. Those who hold to the airborne hypothesis point to the ubiquitous presence of airborne microorganisms, not least in the operating room, and argue that because these without doubt settle into open wounds they must be a cause of sepsis and that reducing their numbers in the atmosphere must therefore be of clinical benefit. On the other hand those who discount the airborne genesis of infection point to the facts in regard to small dispersed inocula, as described by Lister above, and argue that only by some breach of aseptic technique can sufficient numbers of bacteria be deposited together into a wound and give rise to infection.

A similar argument is proceeding in regard to upper-respiratory infection. The infective viruses are to be found on airborne particles, but only in very small numbers (Artenstein *et*

*al.* 1968). On the other side are those who, detecting the virus on fingers, and its transfer from hand to hand or from hand to nose, suggest that the indirect contact route is the route of infection (Pancic *et al.* 1980; Gwaltney *et al.* 1980).

Demonstration of the possibility of infection by one route or another does little to answer the question as to which route is responsible for the observed incidence of infection in normal life. Logical consideration of the problem surely leads to the conclusion that its resolution must depend on quantitative assessment. Both routes can, and generally will, deposit potentially infective material at the sensitive site, be it nose or surgical wound. In a particular situation infection will most often arise by that route which most often or most effectively conveys the infective agent. This is not necessarily the same in all situations so that, to postulate extremes, direct wound contamination from the viscera may plausibly be expected to be the origin of most infection in many types of abdominal surgery. On the other hand, prolonged elective operations on clean tissue, exposing large wound areas and involving the insertion of a foreign body, might well be thought the most likely to suffer infection through settlement into the wound of airborne particles.

The question can only be decided by clinical observation and, because there is for the most part no way of labelling the microorganisms so as to associate the infection with their source and route of transmission, this will involve the blocking of one route and comparing the incidence of infection with that observed without the control measure. If, however, infection is predominantly determined by susceptibility, whether immunologically or otherwise, reduction of the bacterial dose by whatever route or by all will lead to no significant reduction in the incidence of infection. Such a situation has been reported with measles among schoolchildren, where the use of ultraviolet light in the classrooms reduced airborne transmission within these rooms but led to no diminution in the overall rate of infection (M.R.C. Report 1954). Transmission at other times, possibly by other routes, resulted in infection of almost all those susceptible to the disease.

Such investigations are not easy. Unless the infection rate is high and the measure highly effective, very large numbers of operations need to be observed. For example, whereas the reduction of a 10% infection rate to zero needs no more than 200 or so, the difference between a rate of 2% and one of 1% can only be usefully investigated, with a reasonable probability of a statistically significant demonstration of a real difference, by observing about 6000.

#### OPERATIONS FOR TOTAL HIP OR KNEE JOINT REPLACEMENT

With the development of a satisfactory technique for the replacement of a diseased hip joint by an artificial prosthesis (Charnley 1979), very large numbers of these operations began to be performed, now more than 40 000 per year in the United Kingdom alone. These operations, which fulfil all the requirements of large exposure of clean tissue in the presence of a foreign body described above, are the most likely to suffer infection by the airborne route. Infection in this situation, whose eruption may be delayed until months or years after the operation, often has serious consequences for the patient and leads to considerable hospital costs. Infection rates associated with this operation have often been high, 10% or more, in spite of the most careful aseptic precautions. The hypothesis of an airborne origin was then put forward and many surgeons devised or obtained equipment designed to reduce the amount of airborne bacterial contamination in the vicinity of the wound. Infection rates generally fell (Lindberg 1979) but

the demonstration that this was a consequence of the cleaner air environment was not wholly convincing, especially because the use of prophylactic antibiotics was also widespread.

In 1973, therefore, the Medical Research Council together with the Department of Health and Social Security sponsored a prospective randomized study in which each surgeon should operate, without altering his techniques in any way, equally in a conventionally ventilated operating room and in one where special equipment was used to reduce the level of airborne contamination. On statistical grounds it was determined that more than 7500 operations would have to be recorded and the outcome observed over a period of around 2 years. This necessitated a multi-centre study in which 19 hospitals took part (Lidwell *et al.* 1982). By the time the study was terminated, in July 1980, over 8000 operations for the replacement of the hip or knee joint had been recorded and the outcome observed over a period of between 1 and 4 years. During that time sepsis in the joint was observed, on subsequent re-operation for failure of the prosthesis, in 86 patients.

TABLE 1. BACTERIAL SPECIES IN INFECTED WOUNDS OR JOINTS AND IN OPERATING ROOM AIR

species	operation type			air§
	contaminated†	clean†	joint replacement‡	
<i>Staphylococcus aureus</i>	32	44	27	9
<i>Staphylococcus albus</i>	5	15	16	37
<i>Propionibacter</i>	—	—	6	10
other skin	—	—	6	13
<i>Streptococcus pyogenes</i>	4	4	—	—
percentage of all isolations	43	67	81	65
Gram-negative bacteria	62	22	11	2
enterococci	8	4	4	1
anaerobes	13	8	1	—
percentage of all isolations	87	36	24	3
other, unclassified, species	—	—	—	33
no isolation	3	8	18	—
total	98	102	86	106

Note: more than one species was isolated from some wounds and joints.

† After Bengtsson *et al.* (1979).

‡ Lidwell *et al.* (1983b).

§ After Lindberg (1979).

#### SPECIES OF BACTERIA RESPONSIBLE FOR INFECTION

As inspection of table 1 will show, the majority of infections in the replaced joints are associated with bacterial species commonly found on the skin. Apart from *Staphylococcus aureus* these are organisms generally regarded as possessing little pathogenic potential. This contrasts strikingly with the organisms isolated from wounds infected after surgery in a contaminated situation, most being abdominal operations, where the infecting organisms are most often of intestinal origin. The range of species is strikingly similar to those usually isolated from the air, which include the anaerobic species among the skin flora (Lindberg 1979; Hambraeus & Benediktsdóttir 1980). This poses the question of whose skin they come from and how they reach the wound.

In an investigation of the bacteria, especially *Staphylococcus epidermidis*, isolated from wound samples obtained during joint-replacement operations, Dr Marples at the Central Public Health

Laboratory has been unable to show any correlation between the strains found in the wounds and those obtained by sampling the patient's own skin (unpublished observations).

During the course of the M.R.C. study there were 27 instances of joint sepsis associated with infection with *Staph. aureus*. In 14 of these, nasal swabs had been obtained at or near to the time of operation from the surgeon, the anaesthetist and the other scrubbed staff, as well as nasal and perineal swabs from the patient. By the use of phage-typing it was possible to show that for six the wound strain was probably the same as that isolated from some person in the operating room at the time of the operation and for one probably the same as that isolated from a regular member of the operating room staff not recorded among the scrubbed staff

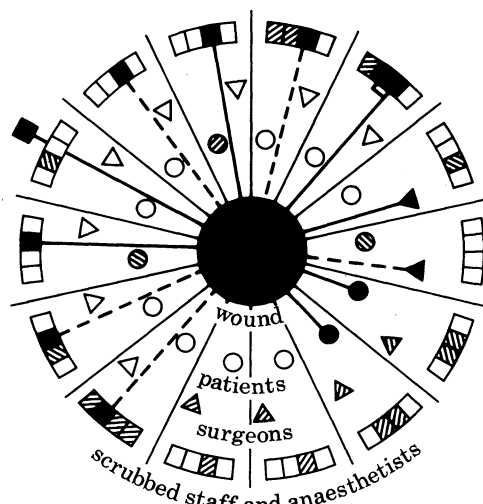


FIGURE 1. Operating-room sources of infection with *Staph. aureus*. Each of the 14 infections is represented by a segment of the circle, the wound in the centre, the patient by the adjacent disc, the surgeon by the triangle and other, scrubbed, staff by the peripheral rectangles. Carriers of *Staph. aureus* are cross-hatched, the wound and the probable or possible source of the infection filled in. Probable sources are linked to the wound by full lines and possible sources by broken ones. The staff source shown outside the circle represents a regular member of the operating room staff not recorded among the scrubbed staff on that occasion.

present at the time of that operation. For five more the wound strain was sufficiently similar to that isolated at the time of operation to consider the carrier of it as a possible source for the infection. For only two could no plausible source be found (Lidwell *et al.* 1983*b* (figure 1). When we consider who were the carriers, then, for only two infections did it appear that the patient himself was the source of his infection, two more may have derived from the surgeon and eight from other staff. These results agree with those of Dr Marples that the infecting strains most often come from persons other than the patient. As against the hypothesis of airborne transmission of these organisms it might be suggested that, since all the personnel in the operating room wear sterile clothing, skin organisms, which are normally dispersed on desquamated skin (MacKintosh & Lidwell 1978), would be unable, or at least substantially hindered, in escaping into the air. This, however, is by no means true. It was shown as long ago as 1948 (Duguid & Wallace 1948) that conventional loosely woven cotten gowns and suits do little if anything to reduce the dispersal of skin squames (Lidwell *et al.* 1978). This is well illustrated in figure 2.



## THE SOURCES OF WOUND CONTAMINATION

If bacterial contamination reaches the wound at the time of operation, it should then be possible by wound sampling to demonstrate this and, if a significant proportion arises from the air, to show a reduction if the level of airborne contamination in the operating room air is reduced. During the M.R.C. study more than 3000 wounds were sampled, after the insertion of the prosthesis but before the start of wound closure, by a wash-out technique (Lidwell *et al.* 1983 *a*). There was a wide variation in the number of bacteria isolated from the samples, even at the same hospital under one set of conditions, but the median values at any hospital

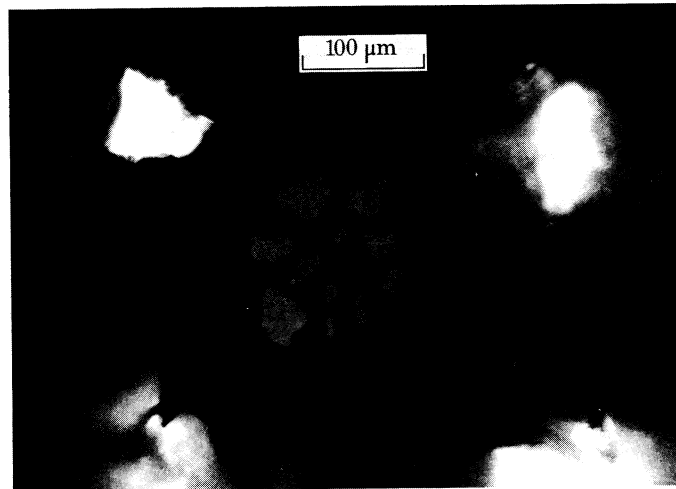


FIGURE 2. Escape of skin squames through operating-room clothing. The figure shows an enlarged view of the intersection of four strands of a loose woven cotton gown, illuminated from behind. Superimposed on this, in the centre, to the same scale, are a group of fragmented skin squames. The thin parts of the weave at each intersection transmit considerable light; in the central part of these are open holes through the fabric. At three of the intersections these are clearly large enough to allow free passage of the squames.

were always less for the operations done in ultraclean air conditions than for those done in a conventionally ventilated operating room. The results from one hospital, where an unusually large number of samples were taken under a variety of conditions, are shown in figure 3. There was also a considerable variation in the numbers isolated at the different hospitals, even at similar levels of air contamination. Figure 4 shows the median results grouped according to the ultraclean air system employed and the resulting median level of air contamination. With the cleanest air system the median number of bacteria isolated was indistinguishable from that obtained in dummy runs. It is clear that the greater proportion of the bacteria isolated from operations in conventionally ventilated operating rooms are associated with the much higher level of air contamination found in these rooms. Analysis of the numerical values shows that the numbers of bacteria isolated from the wounds, not associated with the level of air contamination, are about the same as those derived from an air contamination level of about  $8 \text{ m}^{-3}$ . This implies that in the average, conventionally ventilated, operating room where the median level of air contamination was about  $140 \text{ m}^{-3}$  the proportion derived from the air was about  $\{140/(140+8)\} \times 100 = 95\%$ .

## JOINT SEPSIS AND ULTRACLEAN AIR

The results described above, which indicate a large reduction in the bacterial contamination of the wound when the air contamination in the operating room is reduced, would be expected to lead to a reduction in subsequent sepsis unless joint infection arises in other ways, e.g. by the haematogenous route, or if the development of infection is effectively determined by patient

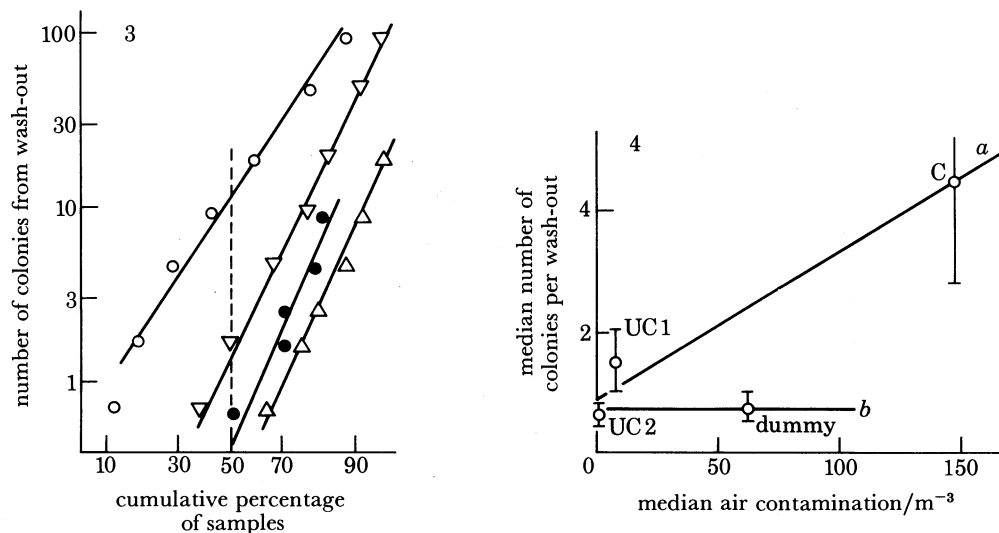


FIGURE 3. Numbers of bacteria isolated from wound wash-out samples at one hospital. The four lines show the distribution of the numbers of colonies grown in samples collected under four different conditions.  $\circ$ , From wounds where the operations were performed in a conventionally ventilated room with the staff wearing conventional clothing and the patients had received prophylactic antibodies;  $\nabla$ , from wounds where the operations were performed in an operating room ventilated by an ultraclean air system, the staff wore conventional clothing and the patients had received prophylactic antibodies;  $\bullet$ , from wounds where the operations were performed in an operating room ventilated by an ultraclean air system, the scrubbed staff wore body-exhaust suits and the patient had *not* received prophylactic antibodies;  $\triangle$ , from wounds where the operations were performed in an operating room ventilated by an ultraclean air system, the staff wore body-exhaust suits and the patients had received prophylactic antibodies.

FIGURE 4. Median numbers of bacteria isolated from wound wash-out samples in relation to the median level of air contamination. The lines show (a) the regression of the bacterial median on the median air contamination, and (b) the median value of the dummy samples. C, from wounds where the operations were performed in conventionally ventilated operating rooms and the staff wore conventional clothing; UC1, from wounds where the operations were performed in rooms ventilated by an ultraclean air system and the staff wore conventional clothing; UC2, from wounds where the operations were performed in rooms ventilated by an ultraclean air system and the staff wore body-exhaust suits (or the operations were performed in a plastic isolator). The short vertical lines indicate for each group its 95% confidence limits.

susceptibility. The clinical observations, which are summarized in table 2, do, indeed show substantial and significant reduction in the incidence of deep joint sepsis after operations for the insertion of a prosthesis in an operating room with an ultraclean air system. This reduction was greater when the operations were done not only with the use of an ultraclean air system but also with some additional barrier, either a body exhaust suit or a plastic isolator, which resulted in a lower level of air contamination.

## SEPSIS AFTER JOINT REPLACEMENT

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## ANTIBIOTICS

The susceptibility of tissue to infection depends on the nature of the tissue, its blood supply and level of oxygenation, on the presence or absence of potential sites for the initiation of infection, clot necrotic tissue or foreign body, and on humoral factors, including the immunological state of the host. This may be influenced by the prophylactic employment of antimicrobial drugs.

The use of these has also been a subject of controversy. The M.R.C. study was not designed to provide a fully randomized prospective study of this. Although there was an even balance of antibiotic use between operations done in conventionally ventilated operating rooms and

TABLE 2. VENTILATION AND SEPSIS AFTER TOTAL JOINT REPLACEMENT

(In parenthesis are given the number of septic joints divided by the number of operations.)

number of hospitals	ventilation	gowns	c.f.u. in air/m <sup>3</sup>	sepsis	percentage
10	turbulent	conventional	158	(36/1798)	2.0
	ultraclean	conventional	7	(16/1604) ratio 2.0	1.0
10	turbulent	conventional	133	(27/2084)	1.3
	ultraclean	b.e.†	0.5	(6/2133) ratio 4.5	0.3

† Body-exhaust suits or plastic patient isolator.

TABLE 3. EFFECT OF ANTIBIOTICS AND VENTILATION

(Number of septic joints divided by number of operations.)

ventilation (clothing)	antibiotics			
	not given		given	
	number	%	number	%
conventional	39/1161	3.4	24/2968	0.8
u.c. (conventional)	8/516	1.6	9/1279	0.7
u.c. (b.e., isol.)	5/544	0.9	1/1584	0.06

Abbreviations: u.c., ultraclean ventilation system; b.e., body-exhaust suit; isol., plastic patient isolator.

those done in ultraclean air rooms, the use or otherwise of prophylactic antibiotics around the time of operation was largely associated with the practice of particular surgeons and hospitals. However, when the results are divided according to the use of prophylactic antibiotics, a substantial benefit from their use is apparent (table 3). It also appears that using prophylactic antibiotics and performing the operation in ultraclean air reinforce one another so that when both are employed to the full the resulting reduction in the incidence of sepsis seems to exceed 15-fold, the overall effect of prophylactic antibiotics alone being about 4-fold and that for a ultraclean air system together with some additional barrier to dispersal about 4½-fold. A fully randomized prospective study of prophylactic antibiotics in joint replacement has recently been published by a French team (Hill *et al.* 1981). Their results fully confirm those given above, with an average reduction due to the use of prophylactic antibiotics of 3.5-fold and of just over 3-fold associated with the use of an ultraclean air system. This last comparison was not randomized with respect to hospitals.



## JOINT SEPSIS AND THE LEVEL OF AIR CONTAMINATION

The comparisons given in table 2 are fully controlled both with respect to surgeons and to hospitals. By dividing the operations into groups, according to the level of air contamination, the relation between this and the incidence of sepsis can be explored. These groups are not fully controlled in relation to each other and the relation obtained (figure 5) depends on the assumption that the number of hospitals included in each of the six groups, six to nine, is such as to balance out the effect of hospital differences. In addition the degree of employment of prophylactic antibiotics at each hospital has been taken into account to derive a sepsis rate

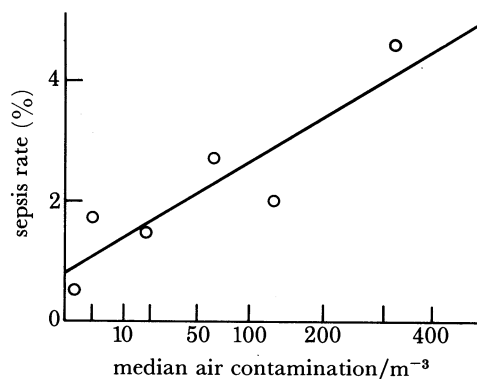


FIGURE 5. The relation between the incidence of joint sepsis and air contamination. Each point represents the median value from a group of 6–9 hospitals within a range of air contamination. The sepsis rates have been computed for operations performed without antibiotic prophylaxis. The line is the regression of joint sepsis on air contamination. The air contamination values are shown on a square root scale.

appropriate to operations without antibiotics. A remarkably consistent relation appears, given by the empirical equation

$$\text{sepsis rate (without prophylactic antibiotics) (\%)} = 0.84 + 0.18\sqrt{A},$$

where  $A$  is the level of air contamination (colony forming units per cubic metre of air sampled, with aerobic cultivation) (Lidwell *et al.* 1983a).

It is interesting to compare the rates of joint sepsis in relation to the bacterial dose to the wound with the rates of colonization resulting from another form of airborne bacterial challenge, namely nasal acquisition of *Staph. aureus* (Lidwell 1981).

Whyte (1982) has made an estimate of the absolute numbers of bacteria deposited in a wound during joint replacement. He calculated this to be about 375 colony-forming units at a level of contamination of 400 bacteria-carrying particles per cubic metre of air, i.e. about one colony-forming unit for every bacteria-carrying particle in a cubic metre of air. Using this figure the data exhibited in figure 5 can be recomputed as dose to the wound and are displayed in figure 6, on a double-logarithmic scale to facilitate comparisons with the nasal acquisition data for *Staph. aureus* referred to above. The parallelism is obvious with a near square-root relation between dose and infection rate for both systems.

## CONCLUSIONS

The arguments and data discussed in this paper lead to the conclusion that infection in the joint after an operation for total joint replacement is most likely to be derived from the airborne flora unless this is reduced to very low levels by an ultraclean air system.

The results may also be interpreted as indicating that the aseptic practices followed by orthopaedic surgeons are very effective so that only a minimal bacterial challenge to the wound is provided by either breaches or deficiencies in these.

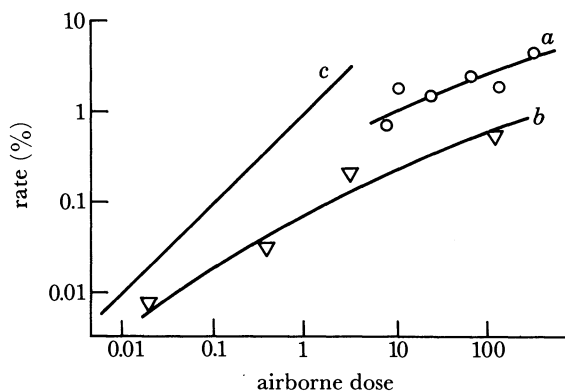


FIGURE 6. The relation between bacterial dose (number of bacteria-carrying particles) and joint sepsis or nasal acquisition of *Staph. aureus*. Curve *a* shows the same data for joint sepsis as those given in figure 5; curve *b* (nasal acquisition) is taken from Lidwell (1981). The straight line (*c*) gives the rates that would result if either acquisition or sepsis resulted from 1 in a 100 of the bacteria-carrying particles.

The extent to which these results can be extended into other forms of surgery is not immediately predictable. The study showed also that the incidence of superficial wound infection was not appreciably affected either by the use of ultraclean air or by the use of prophylactic antibiotics, except for a small minority of infections, classed as major wound infections, which involved the deeper tissues and followed 2.3% of operations performed in conventionally ventilated operating rooms without the use of prophylactic antibiotics. These infections responded to the use of ultraclean air and prophylactic antibiotics in a very similar way to the deep joint infections (Lidwell *et al.* 1983*c*).

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#### Discussion

F. H. HOWORTH (*Ollerton Research Laboratories, near Chorley, Lancashire, U.K.*). To achieve the considerable reduction of wound sepsis that has been reported by Dr Lidwell, it should be stressed that it is not only the wound that is receptive to airborne contaminants, but also everything that is to come into contact with the wound during a surgical operation, such as surgical instruments, the drapes on which they lie and those around the wound, gloved hands, prostheses, etc. The wound and drapes are relatively static in relation to the other items mentioned. They will all become sticky-wet during the course of the operation, and owing to the movement which takes place in and around the wound of all those items that come into contact with it, they will receive whatever bacteria are in the ambient air, by both impaction when they are moving, and by deposition when they are not.

I am often asked why it is only the members of the surgical team who wear the body exhaust gowns and not the anaesthetist and other people in the operating room. The surgical team are in the 3 m × 3 m clean zone and remain there during the operation, whereas the others who remain outside the clean zone are often required to be more mobile and may well leave the operating room and return to it.

It was in 1961 that Professor Sir John Charnley, F.R.S., suspected that the high and unacceptable rate of wound sepsis in joint replacement was caused by airborne contamination. Then he and I worked together to establish that it was so, and subsequently I was able to design a system that overcame the problem in operating rooms in 30 countries.

It is particularly fortunate that the subsequent experimental confirmation of his original suspicions, together with the success of our solution, was published just before he died last year.



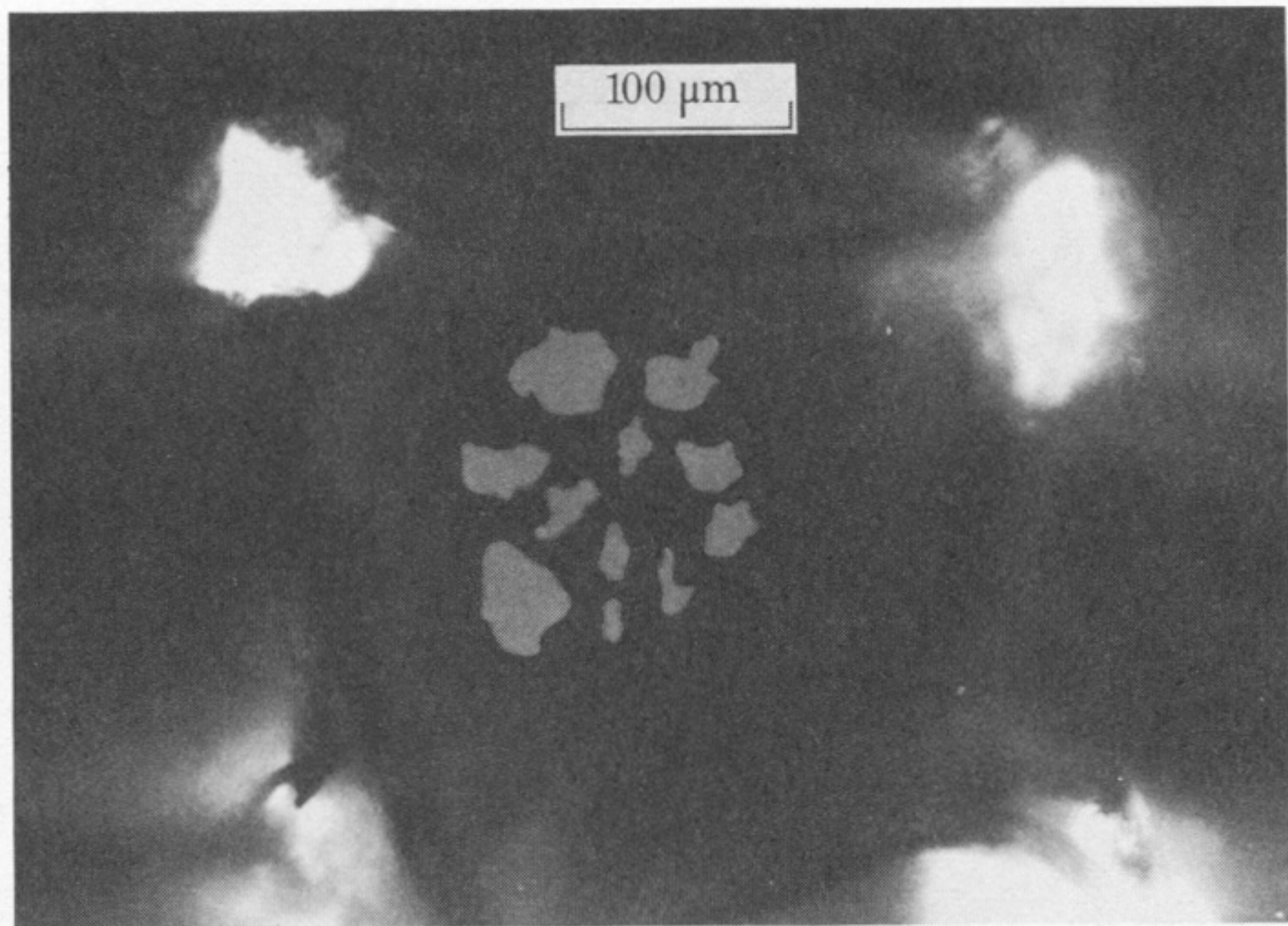


FIGURE 2. Escape of skin squames through operating-room clothing. The figure shows an enlarged view of the intersection of four strands of a loose woven cotton gown, illuminated from behind. Superimposed on this, in the centre, to the same scale, are a group of fragmented skin squames. The thin parts of the weave at each intersection transmit considerable light; in the central part of these are open holes through the fabric. At three of the intersections these are clearly large enough to allow free passage of the squames.