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CROSS-INFECTION OF WOUNDS WITH ANTIBIOTIC-RESISTANT ORGANISMS*

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The dilemma of hospital infection has been complicated rather than solved by chemotherapy. An appraisal of the problem in terms not only of the disease but of the micro-organism (cf. Okell and Elliott, 1936; Wright, 1940) gave promise of a better insight into and control over the transfer of infection. But the bacteriological index is in some respects much more sensitive than the clinical, and its application has revealed surprising weaknesses in the customary routine for control of cross-infection. A special problem to-day is the frustration of chemotherapy by the spread of resistant organisms among the staff and the patients—a possibility forecast by Miles (1944), when he pointed out the errors of excusing perfunctory asepsis on the grounds that the sulphonamides and penicillin were available. This lesson has, however, been fully demonstrated only during the past few years with the arrival of more antibiotics.

It is in surgery that the new dilemma is particularly evident, because the organisms which cause infection of wounds include some that are outstanding in their ability to acquire resistance to chemotherapeutic agents, and some that are insensitive, or relatively insensitive, to all the agents made available so far. I shall consider separately the two basic problems, prevention of the emergence of resistant bacteria and prevention of the transfer of bacteria—especially of resistant strains—from the environment to the patient. In both of these departments, moreover, it is necessary to consider each chemotherapeutic agent and each bacterial species as a separate problem; indeed, within each species fundamental differences of behaviour may be found, and generalizations about cross-infection or acquired resistance referring to all species are almost sure to be wrong.

Prevention of the Emergence of Resistant Bacteria

Briefly, two mechanisms, selection and adaptation, are generally postulated to account for the phenomena of acquired resistance. Selection of resistant organisms may occur in the presence of an antibiotic, either when these are normally present together with sensitive ones—for example, as a very small proportion of the total—or when they emerge independently as mutants from sensitive parent cells. In either case the resistant organism arises independently of the antibiotic, which merely selects it from a mixed flora (Demerec, 1945, 1948). The other mechanism presupposes modification of the bacterial metabolism caused by contact with the chemotherapeutic agent, an adaptive change for which evidence has been presented by Hinshelwood (1952), Barber (1953), and others. An additional mechanism may be the transfer of resistance from resistant to sensitive organisms in a mixed culture (see Hotchkiss, 1951). It is probable that resistance may be acquired both by selection and by adaptation, and any controversy on this question is pointless except when it refers to the action of a particular agent on a particular organism.

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Special Features of the Commoner Chemotherapeutic Agents

Streptomycin is exceptional among antibiotics in that any (or almost any) bacteria can be rendered resistant to it after relatively short contact *in vitro* or *in vivo* (Florey *et al.*, 1949). Penicillin is also exceptional in that resistance is often due to production of a penicillin inactivator (penicillinase), a property of the organism which may be enhanced by culture in the presence of the antibiotic (e.g., Segalove, 1947). The other antibiotics are not destroyed by organisms resistant to them.

It is of interest that the ease with which an organism may be rendered resistant by subculturing it through media containing an antibiotic is no index of the likelihood that resistant bacteria will emerge during treatment with the antibiotic. For example, it is easy to render staphylococci highly resistant to penicillin *in vitro*, but such resistant strains do not produce penicillinase (cf. Abraham *et al.*, 1941; Bondi and Dietz, 1944). These would seem, therefore, to be different in origin from the penicillin-resistant staphylococci isolated from wounds and from the nares of patients in hospital, which are almost uniformly penicillinase producers (Barber, 1953). We have found it easy, by *in vitro* methods, to produce strains of *Staphylococcus aureus* resistant to neomycin, but such strains have not appeared on burns during a controlled trial of neomycin.

Special Features of the Commoner Wound Bacteria

Streptococcus pyogenes, the most feared of the commoner aerobic organisms, has shown less tendency to acquire resistance to the antibiotics than some of the other pathogens. The successful control of streptococcal infections in recent years must in great measure be attributed to this property. Strains of *Str. pyogenes* resistant to penicillin have not yet been recognized. Resistance to sulphonamides, however, does occur, and strains resistant to the tetracyclines ("aureomycin" and "terramycin") have occasionally been found—for example, on burns (Lowbury and Cason, 1954). Other

streptococci and pneumococci do not share this exceptional vulnerability, and the ubiquitous *Staph. aureus* has, in complete contrast, an exceptional capacity for acquiring resistance to antibiotics and other agents. Phage-typing shows that this property is associated principally with certain phage types and patterns of the species, classified as group III (Williams *et al.*, 1953), which appear to be less stable in their genetic structure than the others (Barber and Whitehead, 1949; Barbour and Edwards, 1953; Lowbury and Hood, 1953), and which have largely replaced the less adaptable members of the species in hospitals, where the use of antibiotics has favoured their survival at the expense of the others.

Among the Gram-negative bacilli, *Ps. pyocyanea* has shown an almost uniform sensitivity to polymyxin, and, surprisingly, no tendency to acquire resistance to this antibiotic either *in vitro* or *in vivo* (Jackson *et al.*, 1951a). This contrasts with its frequent resistance to streptomycin (Seligmann and Wassermann, 1947), and, in smaller measure, to neomycin (Goldin, 1953). Members of the genus *Proteus*, by contrast, are resistant to polymyxin, and not sufficiently or uniformly sensitive to any of the agents at present available (e.g., Poole, 1954). The problem of *acquired* resistance is therefore relevant only in therapy of individual infections with this organism, not in prophylaxis.

Origin of Reservoirs of Resistant Strains in Hospital

There can be little doubt that cross-infection is the important factor which determines the accumulation of resistant staphylococci in hospitals. This is particularly evident in the case of antibiotics against which the organisms do not readily acquire resistance—for example, chlortetracycline. We used chlortetracycline for several weeks in the treatment of burned patients before resistant staphylococci began to appear in the burns of some of them; not long after this, however, the majority of staphylococci isolated from burns were found to be resistant to chlortetracycline, and most of these were isolated from patients who were not receiving the antibiotic. In treatment with streptomycin, resistance is so likely to be induced in wound bacteria that control of cross-infection is not the crucial factor in determining its continued value as an antibiotic—though cross-infection with such organisms is undoubtedly very common.

The importance of cross-infection in producing reservoirs of resistant bacteria receives further support from our experience with *Str. pyogenes*. In contrast with *Staph. aureus*, cross-infection with this organism can for various reasons be substantially limited, and, although chlortetracycline-resistant streptococci have emerged on several occasions in the burns of patients treated with the antibiotic, no reservoir of such organisms has been built up in the Burns Unit.

Methods of Preventing Emergence of Resistant Bacteria

Three procedures may help to prevent, or at least delay, the emergence of resistant bacteria: (1) economy in the use of chemotherapeutic agents; this implies not only restricting their use for cases in which they are specially indicated, but also giving them in sufficient amount to achieve a complete effect in the shortest possible time—an approach to the *therapia sterilisans magna* of Ehrlich; (2) avoidance of agents which readily induce resistance—especially streptomycin—when other agents will do as well; and (3) the use of two or more agents together. This third method has been vindicated in the treatment of tuberculosis by combinations of streptomycin, *para*-aminosalicylic acid, and isoniazid (M.R.C., 1949, 1953). If the resistant organisms emerge by selection of mutants, the use of two unrelated antibiotics will provide a barrier against the emergence of any mutants except those in which resistance to both antibiotics has been acquired at the same time, and the proportion of all divisions which give rise to such double mutation is likely to be exceedingly small. Moreover, two unrelated antibiotics used together will interfere with different metabolic processes and so reduce the chances that the organism will establish an alternative metabolism to the one which has been blocked (Garrod, 1953). If two agents fail to prevent the emergence of resistant strains, three or even four agents may still have this effect (cf. Carpenter *et al.*, 1945).

In addition to its effect in preventing the emergence of resistant bacteria, combined therapy may be associated with synergistic action—enhancement of the bactericidal effects of one agent by combination with other agents (Ungar, 1943; Garrod, 1953). The converse effect—antagonism—may also be found with some combinations (see Jawetz, 1952).

Efforts to Prevent Emergence of Resistant Staphylococci in a Burns Unit

This is essentially a study of *Staph. aureus*, since the other species which have been studied are either resistant to chemotherapy or not liable to become resistant to the chosen antibiotics. Recently in trials of chemoprophylaxis against *Staph. aureus* in burns we have obtained results which give some grounds for hope; but before describing them I must recall some of the earlier hopes which were not fulfilled during studies on burns in the past 12 years.

From the Glasgow burns unit, Colebrook and his colleagues (Clark *et al.*, 1943) reported successful chemotherapy for *Staph. aureus* in burns by local application of a penicillin cream. Five years later this effect was not maintained (Colebrook, Duncan, and Ross, 1948), and when shortly after this we made a controlled prophylactic trial of penicillin cream on burns it showed no prophylaxis whatever against staphylococci, though there was a highly significant effect against *Strep. pyogenes* (Jackson *et al.*, 1951b). During this trial about 70% of the staphylococci isolated from burns were resistant to penicillin. A short trial of dibromopropamidine—brought to an end because of local toxic action (Cruickshank *et al.*, 1955)—was accompanied by an increased resistance of staphylococci in the burns to this compound.

Next we made a trial of chlortetracycline, which had recently been introduced and which was apparently active against all the staphylococci from burns in our unit. An assessment of this trial after a few weeks showed a significant prophylactic effect against *Staph. aureus*; but from about the sixth week we began to detect chlortetracycline-resistant staphylococci, which became predominant in the ward soon afterwards. With this emergence of resistance we found that chlortetracycline was no longer protecting burns against *Staph. aureus* (Lowbury, Topley, and Hood, 1952). Staphylococcal phage was then tried, and after showing promise of prophylactic value it selected a breed of phage-resistant staphylococci in the burns (Lowbury and Hood, 1953). Finally, erythromycin, which we were investigating as an antibiotic for streptococcal infections, left us a legacy of resistant staphylococci—after eight months in which no resistant strains appeared (Lowbury and Cason, 1954).

Before embarking on trials of combined prophylaxis we thought it worth while testing the prophylactic value of certain compounds suitable for topical rather than for systemic administration, including neomycin and a synthetic compound, 1:6-di-4′-chlorophenyl-diguanidohexane (I.C.I. 10,040, or "hibitane") (Davies *et al.*, 1954). Our purpose was to use each of these agents for a short time, and switch from one to another after three months, or as soon as resistant strains began to appear; these, it was argued from previous experience, should soon be diluted out of the resident flora when there is nothing to favour them rather than other staphylococci. Moreover, we were anxious to know whether these agents had any value when used alone.

And then, since sensitive strains—for example, of *Str. pyogenes*—not infrequently appear on burns in spite of the presence of penicillin, it seemed to us that combined therapy may perhaps be relatively ineffective in preventing acquired resistance during prophylaxis of burn infection. Finally, we had reasons, from initial laboratory tests, to believe that staphylococci might be rendered resistant to neomycin and to hibitane less readily than to the other chemotherapeutic agents which we had studied.

Preliminary trials—first of neomycin for three months, and then of hibitane for four months—were carried out as follows.

Eligible patients were those who (*a*) had burns of less than 20% body area, (*b*) were not given skin grafts on admission, and (*c*) were regarded as suitable for treatment by the closed method. These patients were allocated by random selection to groups which received local applications either of penicillin cream (controls) or of penicillin cream plus (in the first trial) neomycin (2 mg./g.) or (in the second trial) hibitane (1 mg./g. of the dihydrochloride) on admission and at all dressings till healing, discharge, or operation. Burns were sampled with moistened swabs on admission and at every dressing or operation. The swabs were inoculated on a variety of media and investigated by methods described elsewhere (see Jackson *et al.*, 1951a, 1951b). The results of the trial of neomycin are shown in Table I.

TABLE I.—*Neomycin Prophylaxis for Staphylococcus Aureus on Burns (During First 14 Days)*

Cream Applied at Dressings Containing	Staphylococcus		Total	% Acquired
	Acquired	Not Acquired		
Neomycin ..	5	28	33	15
No neomycin ..	18	12	30	60
Total ..	23	40	63	

$\chi^2 = 11{\cdot}59$. $P < 0{\cdot}001$.

TABLE II.—*Hibitane Prophylaxis for Staphylococcus Aureus on Burns (During First 14 Days)*

Cream Applied at Dressings Containing	Staphylococcus		Total	% Acquired
	Acquired	Not Acquired		
Hibitane	6	23	29	21
No hibitane ..	28	5	33	85
Total ..	34	28	62	

$\chi^2 = 23{\cdot}11$. $P < 0{\cdot}001$.

Whereas 18 out of 30 (60%) burns treated with the control penicillin cream picked up *Staph. aureus* during the first 14 days after admission, only 5 out of 33 (15%) of the burns treated locally with neomycin and penicillin picked up the organism in that period. Table II summarizes the results of the trial of hibitane. Of 33 burns treated with penicillin cream, 28 (85%) picked up *Staph. aureus* during the first 14 days after admission; by contrast, only 6 (21%) of the 29 burns treated with hibitane cream picked up the organism.

None of the staphylococci isolated from burns during this time has been resistant to either agent. This fact is consistent with our failure to induce resistance of staphylococci to hibitane *in vitro*. Neomycin-resistant organisms, which can be obtained by *in vitro* methods, are small colony forms, and we have found that they show a diminished virulence for mice by the intramuscular test (Selbie and Simon, 1952). In this respect they are different from staphylococci in burns resistant to penicillin, chlortetracycline, chloramphenicol, and erythromycin. It is possible that the neomycin-resistant strains are also less well adapted for survival in the mixed flora of wounds and burns, as the non-penicillinase-producing penicillin-resistant staphylococci appear to be (Barber, 1953).

This study of prophylaxis must not, of course, be held to apply also to therapy of established infection. Separate trials are needed to determine the possible therapeutic value of local applications of neomycin and hibitane. Moreover, three or four months of prophylactic trial is too short a time to justify any confidence that resistant strains may not turn up later.

PREVENTION OF THE TRANSFER OF RESISTANT ORGANISMS

Staph. aureus is the conspicuous organism in this study not only because of its exceptional powers of emerging resistant but also because it occurs normally and abundantly in the nose and on the skin of so many healthy people. The second front of our attack—on the prevention of spread—is therefore again, to a great extent, a problem of *Staph. aureus*.

Barber (1947) and Barber and Rozwadowska-Dowzenko (1948) drew attention to the large and increasing proportion of staphylococci isolated from hospital patients and staff which were resistant to penicillin. These strains were apparently being selected as the result of treating patients with the antibiotic, but their prompt appearance in the nares of nurses and in many patients who had not received the antibiotic showed that cross-infection with resistant strains must be occurring on a large scale. Similar observations in respect of penicillin and of other antibiotics were made by many workers (for example, Rountree and Thomson, 1949; Forbes, 1949; Clarke *et al.*, 1952; Lowbury, Topley, and Hood, 1952), and it is now common knowledge that the classical methods for controlling cross-infection—barrier nursing, cubicle isolation, aseptic techniques—are quite inadequate for the exclusion of resistant staphylococci from susceptible sites of hospital patients.

For the limited objective of preventing cross-infection with resistant, as distinct from sensitive, organisms there is one recommendation—to stop using the antibiotic in question. Resistant strains will then no longer be favoured, and sensitive strains should have an equal opportunity of growing. During a prophylactic trial of chlortetracycline we found that the proportion of resistant staphylococci in the ward tended to fall after use of the antibiotic was discontinued at about the same rate as it increased while the antibiotic was in use, though a residue of resistant organisms persisted in the burns of patients who remained in hospital for many weeks. The dilemma is acute, as we are scarcely justified in withholding an effective antibiotic from a case of severe infection merely in order to preserve its effectiveness, unless equally good alternatives are available. The discovery of new antibiotics is therefore of the highest importance, and there is no pointless redundancy in having half-a-dozen alternative agents for the chemotherapy of *Staph. aureus*, provided that they differ from each other in their mechanism of action and therefore in the pattern of resistance which develops against them.

Prevention of Cross-infection as a General Problem in Surgery

Lister's achievements were apparently so complete that the unsolved problems of cross-infection in surgery were overlooked for some time afterwards, both by surgeons and by bacteriologists. The natural defences of healthy tissues are capable of accounting for many contaminants, and this undoubtedly exaggerated the apparent victory of asepsis. The surgical experience of two world wars and the development of the newer fields of operative surgery, however, revealed that a considerable amount of contamination passed through the aseptic barriers, and gave rise to clinical infection of varying severity (Stokes and Tytler, 1918; Fleming and Porteous, 1919; Miles *et al.*, 1940). But the failure of asepsis was still wider than the clinical data could show, for many wounds in which clinical signs of infection were absent could be found to heal more slowly when certain organisms were present than when they were kept free from those contaminants (Gissane *et al.*, 1944; Clayton-Cooper and Williams, 1945; Jackson *et al.*, 1951b). Such

"silent" infection was demonstrated by controlled study of methods which protected a random selection of the wounds at risk against contamination.

It is well known that transmission of bacteria from the environment to the patient may be through the air (by droplets, droplet-nuclei, or dust) or by contact (immediate or intermediate), but the factors which determine the relative importance of each route are complex and still imperfectly understood. Important factors are the viability of the organism outside the body—for example, Gram-positive cocci in general survive the evaporation of their suspending menstrua better than Gram-negative bacilli (Heller, 1941; Lowbury and Fox, 1953); the presence or absence of organisms in carriers among staff and patients—staphylococci, for instance, are commoner on the hands than streptococci, and therefore more apt to be transmitted by contact; the exposure or protection of the site of entry of organisms—for example, a wound of the hands or feet can be protected against contamination by dressings more easily than one of the trunk or face (Lowbury and Fox, 1954; Lowbury, Crockett, and Jackson, 1954).

Specific recommendations for the elimination of reservoirs of infection, for blocking the routes of transfer, and for increasing the resistance of the patient have been built up piecemeal with our increased knowledge of these mechanisms. After the early development of antisepsis and asepsis in operating theatres, of cubicle isolation, and of barrier nursing, there followed attempts to reduce air contamination by dust-laying with oils (Van den Ende *et al.*, 1940, 1941a, 1941b), by dispersion of chemical disinfectants such as hypochlorites, triethylene glycol, and lactic acid (Douglas *et al.*, 1928; Masterman, 1938; Robertson, 1946; M.R.C., 1948), by ultra-violet irradiation of air or surfaces (Hart, 1936; Hollaender *et al.*, 1944; M.R.C., 1948), and by air-conditioning with filtered air (Bourdillon and Colebrook, 1946).

Some of these methods contributed less than laboratory experiments had led one to expect, particularly ultra-violet irradiation—for example, M.R.C., 1954—and chemical disinfection (for example, Lidwell and Williams, 1954). In these examples the relative failure may have been caused, in part, by the impossibility of sterilizing dust by either of these methods at levels which are safe for the persons exposed (cf. Lidwell and Lowbury, 1950). Even dust-laying and air-conditioning, however—methods which do not depend on the killing of bacteria—achieve only a partial effect, not only because they too are imperfect but because they attack only one of the vectors of cross-infection. The relative importance of this vector probably varies greatly in different kinds of ward and with different organisms; this may explain the conflicting reports on protection against cross-infection by oiling of floors and bedclothes (Wright *et al.*, 1944; Clarke *et al.*, 1954).

The newer methods of combating contact infection involve the extension of aseptic methods beyond the operating theatre to the dressing of wounds in casualty dressing-rooms and wards. The value of no-touch technique was demonstrated in the dressing of neurosurgical wounds (McKissock *et al.*, 1941), and has been further validated in studies on added infection rates of a wider range of wounds in hospital (Williams *et al.*, 1945) and in factory surgeries (Clayton-Cooper and Williams, 1945). Involving no antibiotic barrier, such prophylaxis is equally effective against sensitive and resistant contaminants.

Colebrook's machinery for excluding bacteria from burns also involved the extension of aseptic principles—in this case to a field which Lister had ignored and in which asepsis had been thought unattainable. So, indeed, it remained in all but the smallest burns, if by asepsis was meant the total exclusion of bacteria. But the exclusion of some pathogens from some of the lesions—a lessening of the risks of sepsis—is an end worth attaining. It is the end that was achieved in trials of the no-touch dressing technique. For burns, Colebrook introduced more complex machinery of physical and chemical barriers against contamination by contact and from the air—the use of no-touch technique in an air-conditioned dressing-station with filters, together with local application of penicillin cream under ample dressings (Colebrook, Duncan, and Ross, 1948; Colebrook, 1950). The one organism which responded to this combined prophylaxis—*Str. pyogenes*—happened to be the most formidable pathogen commonly found on burns. It was also the one which was uniformly sensitive to penicillin. A trial of local penicillin (Jackson *et al.*, 1951a) confirmed the prophylactic effect of penicillin against *Str. pyogenes* and the absence of any effect on the other common flora—for example, *Staph. aureus*, which was predominantly resistant to penicillin at this time, and the coliform bacilli, *Ps. pyocyanea* and *Proteus*, which were uniformly resistant. This aroused a suspicion that the benefits which Colebrook reported after the combined attack on cross-infection with penicillin and dressings under filtered air might be attributable entirely to penicillin.

We found an answer to this question in a controlled trial of the air-conditioned dressing-station in the Burns Unit here (Lowbury, 1954). A significantly smaller proportion of burns dressed in the ventilated room acquired *Ps. pyocyanea, Proteus,* and antibiotic-resistant staphylococci than were acquired by the burns treated in the room with the ventilators switched off. *Str. pyogenes* was uncommon in burns during the trial, and the chances for its transfer were small, because burns carrying the organism were dressed at the end of each dressing list. Coliform bacilli appeared on approximately the same number of burns in the two groups—an indication that these organisms were probably acquired by self-contamination. A further point of interest in this trial was the significantly higher proportion of *Staph. aureus* resistant to chlortetracycline and penicillin and showing the "hospital strain" phage patterns (group III) which we found in the nares of patients dressed in the room with the air-conditioning plant switched off. This index of added infection is of special interest, as the patients spent only a small fraction of their total hospital time in the dressing-station.

The benefits of air-conditioning with filters, like those of the no-touch technique and other physical methods, cannot be lost through the emergence of resistant mutants.

Relative Importance of Wards, Dressing-stations, and Operating Theatres as Sites of Cross-infection

The trial which I have just described showed that the frequency of cross-infection could be reduced by changing the dressings, not in the ward but in a special room ventilated by filtered air under positive pressure. In spite of the elimination of this ward risk, however, the opportunities for transfer of infection to patients while they are in the ward must be great. Blankets, sheets, clothing, handkerchiefs, and other fabrics are known to be potential sources of cross-infection (Hare, 1941; Duguid and Wallace, 1948; Dumbell *et al.*, 1948), but soiled dressings must be regarded as a more important reservoir, from which both airborne and contact spread are liable to occur—the latter particularly if the dressings become soaked through with infected exudate. At the receiving end, burns or wounds which are imperfectly covered, and those with dressings that have become soaked with sterile exudate (Colebrook and Hood, 1948), present a good target for contaminants. Exposed burns, before their exudate has dried, are liable to pick up the airborne bacteria, and do in fact show *Str. pyogenes, Ps. pyocyanea, Staph. aureus,* and other bacteria more often than perfectly covered burns of feet and hands (Lowbury, Crockett, and Jackson, 1954).

Evidence that much of the cross-infection occurs in the ward if dressings are done in a separate room has come to light in recent studies on one organism, *Ps. pyocyanea* (Lowbury and Fox, 1954). For a period of seven months all the *Ps. pyocyanea* from burns in this unit were typed by an agglutination method (Christie, 1948; Fox and Lowbury, 1953). It was possible to divide the strains into three major groups, each consisting of a large number of apparently variable subgroups or patterns. The patients

from whom the strains were isolated were in two wards, E and F, but had their dressings and operations in the same dressing-station and operating theatre. Nevertheless, each ward had for a time its own predominant strain, which was serologically different from the predominant strain of the other ward.

How much added infection occurs in operating theatres? For many years the efficiency of our aseptic drill has been taken for granted, though individual flaws have from time to time been exposed. For example, Devenish and Miles (1939) found that a proportion of rubber gloves used in the operating theatre had minute holes through which skin staphylococci and other organisms could pass into the wounds. Cleansing fluids—for example, 1% cetrimide, 10% "dettol," soap solution—were commonly found to be contaminated with *Ps. pyocyanea* when dispensed in bottles with corks—the organism apparently being protected by the cork (Lowbury, 1951). Reports of tetanus (Sevitt, 1949) and of gas gangrene (Sevitt, 1953) apparently acquired in an operating theatre focused attention on the unsatisfactory air hygiene of the standard operating theatre, which is ventilated by extractor fans over the sterilizers; by this method air is sucked into the theatre through doors, windows, and other apertures, carrying with it a representative selection of hospital and street flora. The need for a new style of operating theatre ventilated with filtered air under positive pressure was demonstrated by Cairns (1939), and, more recently, by Girdlestone and Bourdillon (1951), and is now being recognized more widely. Such a theatre should be planned to incorporate other features which are likely to reduce the chances of contamination—for example, designed to minimize movements and personnel in the zone of operation (Gissane *et al.*, 1944). The frequency of wound contamination and infection at operations carried out in theatres of the old and new types is the subject of an extended investigation by Dr. Sevitt and myself in this hospital, to be reported later.

DISCUSSION AND CONCLUSION

Each of the measures found to have some effect in preventing the emergence or the transfer of antibiotic-resistant organisms makes, by itself, only a fractional contribution. Added together they contribute rather more, but still do not nearly solve the problem, which demands an extension and improvement of existing methods and the search for new ones. Elimination of the primary reservoirs of infection (places where pathogens breed) and of the targets for infection are obviously of the first importance. Sometimes—for example, in the primary excision and grafting of burns—both objects may be achieved by the same procedure. Some idea of the difficulty of setting up effective barriers is given by Rogers (1951), who found that cross-infection with infantile gastro-enteritis and the transfer of specific serological types of *Bact. coli* was not prevented by strict cubicle isolation. In open hospital wards, Anderson *et al.* (1954) have shown that the standard of nursing has little influence on the rate of cross-infection with these organisms. Sauer (1935), however, reported success in preventing cross-infection with gastro-enteritis at a special unit for premature infants by an elaborate series of barriers, including ultra-violet screens, special kitchens, and cubicle isolation. This experience suggests that our failures in preventing cross-infection may be due simply to insufficient standards of asepsis—such as might be expected, for example, in operating theatres where rubber gloves or masks were not used.

Whether such elaborate measures for preventing cross-infection (assuming that they work) are justified depends on the clinical hazards of infection in each particular field. In any case, however, it would be of the greatest value to have special units in which a maximum level of asepsis could be assessed for effectiveness in preventing different kinds of infection, and for guidance in planning of hospitals tomorrow. It is not enough (cf. Goodall, 1952) to attribute our failures to faulty nursing or to inadequate fulfilment of the recommendations laid down in the memoranda of the Medical Research Council (1941, 1951) on control of hospital infection. Scrupulous observance of these recommendations may not, as we have seen, prevent some kinds of cross-infection. If the recommendations are to be saved from merely ritual observance—or uncritical disuse—they must be subjected to a more detailed assessment than has yet been possible.

Even without such elaborate special units, however, there is scope for the investigation of many ideas—for example, the admission of mothers as auxiliary nurses for their own children in hospital (Pickerill and Pickerill, 1954); the use of a disinfectant barrier to prevent contamination through soaked dressings (Lowbury and Hood, 1952); the use of rubber gloves for many duties in hospital wards; the use of chemotherapeutic agents for suppressing the skin carriage (Murray and Calman, 1955), and the nasal carriage (Moss *et al.*, 1948; Valentine and Hall-Smith, 1952) of *Staph. aureus*—methods which may cause some reduction in the cross-infection rate with that organism (Gould and Allan, 1954).

There is some danger that advances in surgery which were made possible by the arrival of antibiotics will be relinquished as the staphylococci surmount each new chemotherapeutic obstacle. The physical obstacles, such as air-conditioning, cannot be surmounted in this way; nor, apparently, can the older chemical obstacles—for example, disinfectants such as phenol and the cresols. Although our attention to-day is drawn to combined chemotherapy as the most hopeful weapon against the emergence of resistant forms, it is too early to assume that no substance will be discovered which is as safe as penicillin and as permanent in its effects against *Staph. aureus* as phenol, and perhaps hibitane.

Summary

The prevalence of antibiotic-resistant organisms—especially staphylococci—causing added infection of wounds in hospital patients has emphasized the limitations of chemotherapy and of hygiene applied in this field.

Emergence and spread of resistant organisms are considered in this paper as separate problems. To combat the former, efficient dosage and a combination of two or more agents has been advocated. In our hands, local application of neomycin and of "hibitane" has had some prophylactic effect against staphylococci in burns, so far not accompanied by the emergence of any resistant strains. Methods to control the spread of bacteria by air and by contact have been considerably developed in recent years, but more knowledge of their performance is needed. Some further improvements are suggested by existing data—for example, the general use of positive-pressure ventilation with filtered air for operating theatres and dressing stations. For the more complex task of limiting the transfer of infection in the ward, many changes (in hospital design and in nursing routine, for example) require investigation.

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PATHOGENIC STAPHYLOCOCCI IN THE ENVIRONMENT OF THE NEWBORN INFANT

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Improved hygiene and the development of potent antibacterial agents have been responsible over recent years for a considerable reduction in the amount of neonatal infection, particularly infection of the alimentary and respiratory tracts. Staphylococcal infection of the newborn, especially in hospital, is, however, still a problem, and the marked tendency of the staphylococcus to acquire resistance to antibiotics has retarded its control and increased its relative importance.

The objects of the present investigation are to report and compare the carriage rates and antibiotic resistance of staphylococci in three maternity hospital units of different types; to compare these hospital results with corresponding data obtained from domiciliary confinements; to correlate staphylococcal carriage with clinical infection; and to study the mode of spread of the organism between mothers, babies, and hospital staff.

Materials and Methods

The hospital units concerned are (*a*) a maternity unit adapted from an old building, somewhat crowded and part of a general hospital (hospital W); (*b*) a newer and more spacious unit, also part of a general hospital, with better facilities for isolating infected patients (hospital E); and (*c*) a small self-contained maternity hospital with adequate accommodation situated in the country (hospital M). The period of the investigation was from March to July, 1952.

Altogether 608 vaginal swabs and 701 nasal swabs taken on admission from 770 mothers in these three hospital maternity units and 44 nasal and 44 vaginal swabs from mothers confined at home were examined for the presence of pathogenic staphylococci, and their sensitivity to four antibiotics and to sulphonamide was determined. Specimens taken from the offspring of these mothers included 683 conjunctival and 639 umbilical swabs, from a total of 774 babies. Eye swabs (E_4) were taken four days after delivery of the infant, since it has been shown that the carrier rate reaches its maximum about this time (Torrey and Reese, 1945). Umbilical swabs (U_8) were taken as soon as the cord had separated—that is, about the eighth day after birth. From the medical, nursing, and domestic staff attending these cases during the period of the survey, 245 nasal swabs were examined.

In order to ascertain whether mothers acquired pathogenic staphylococci while in hospital, 293 nasal and 297