Staphylococcal antibiotic resistance pattern in the population in which the infection is acquired, and by an assessment of the relative efficacy and toxicity of the drugs available. In Britain the initial choice will probably lie between one of the β-lactamase resistant semi-synthetic penicillins such as flucloxacillin, fucidin, erythromycin, gentamicin, clindamycin or a cephalosporin, either alone or in combination. In addition, in a community-acquired infection with strains sensitive to benzyl penicillin this should be given for its unsurpassed efficacy against those strains of staphylococci which remain sensitive to it. Occasionally resistance patterns may dictate the use of more toxic drugs such as vancomycin.

Resistance to the β-lactamase resistant penicillins started rising shortly after their introduction methicillin-resistance reaching 4.1% of over 7000 cultures received from all over the U.K. for phage typing at the Central Public Health Laboratory in 1969 (Parker & Hewitt, 1970). The size of the problem varies with locality and in Newcastle in 1970 58% of 201 isolates were found to be resistant (Hale & Selkon, 1970). Fortunately resistance to this group of penicillins has not become the widespread problem that such figures threatened, although Europe has fared less well in this respect than the United States (Mayhall, Medoff & Marn, 1976). Recently a new form of penicillin resistance, 'methicillin tolerance', has been described and implicated in treatment failures with cell wall antibiotics (Sabath, Wheeler, Laverdiere, Blazevic & Wilkinson, 1977). There is, however, some scepticism as to its importance in producing such failures and its clinical relevance is as yet poorly defined (Lacey, 1977). Amongst the other drugs, resistance to the cephalosporins is frequently found in association with methicillin resistance and cephaloridine should be avoided because of its susceptibility to staphylococcal penicillins (Whitehead, 1973; Wise, 1973). Resistance to fucidin, erythromycin and clindamycin develops rapidly when these drugs are used singly and they are therefore usually given in combination to preserve their usefulness (Brumfitt & Percival, 1971). Until recently resistance to gentamicin was seen rarely, but a number of reports have appeared describing resistance emerging in association with its widespread topical usage. Perhaps of particular concern is that some of these strains have also been resistant to a large number of other antibiotics (Shanson, Kensit & Duke, 1976; Klimeck & Quinthioni, 1977; Wyatt, Ferguson, Wilson & McCormick, 1977). In
the face of the potential danger of such multi-resistant organisms it is evident that all hospitals should have clear guide-lines on the use of antibiotics together with efficient means for the prevention of cross infection.

Ranked in descending order of potency against most strains of staphylococci in vitro these drugs run in the order: fucidin and gentamicin (equal potency), erythromycin, cloxacillin, cephalothin, with clindamycin varying in the ranking from just above erythromycin to below cephalothin (Garrod, Lambert & O'Grady, 1973). Given this choice of antibiotics most clinicians would probably prefer to avoid using gentamicin or clindamycin in view of their possible toxic side effects, and furthermore gentamicin may be ineffective in clinical infections with staphylococci of proven in vitro sensitivity (Klimek & Quintonhioni, 1977). Recently, however, Steigbigel, Greenman & Remington (1975) showed that a combination of benzyl penicillin and gentamicin produced a higher survival rate in mice with experimental staphylococcal infection than did either drug alone. Some centres have subsequently added gentamicin to the β-lactamase resistant penicillins they were using as routine antistaphylococcal therapy, but do not report whether this has conferred any benefit on their results (Musher & McKenzie, 1977). Cephalothin may be considered either when the patient is allergic to penicillin or when the organism is resistant to methicillin. Unfortunately there is some cross allergenicity between penicillin and cephalosporins and a frequent association between methicillin resistance and cephalosporin resistance. Erythromycin or fucidin may therefore be better alternatives under these circumstances.

A mortality of the order of 30 to 50% has been reported in patients with staphylococcal pneumonia treated with β-lactamase resistant penicillins alone (Klein & Finland, 1963). Jensen & Lassen (1969) used a combination of fucidin and either methicillin or benzyl penicillin in the few cases where sensitivity to the latter was present. In 86 cases of staphylococcal pneumonia the overall mortality was 40%, but after exclusion of those cases in whom the staphylococcus was thought to be a non-contributory factor this figure corrects to 21%. In addition there was a clinical impression that the response to the two antibiotics given together was more rapid than that seen after penicillin given alone. However, there are numerous pitfalls in comparing results of treatment in unmatched groups of patients with various underlying diseases, and although a combination of a β-lactamase resistant penicillin with fucidin has since been used extensively and successfully in a variety of staphylococcal infections, to date there is no clear clinical evidence that it is superior to a penicillin alone in pneumonia due to methicillin sensitive staphylococci. Furthermore antagonism has been demonstrated between fucidin and penicillin for up to 48 h in vitro (Jensen, 1970; O'Grady & Greenwood, 1973) and although the importance of this in vivo is questioned it is notable that the majority of Jensen & Lassen's patients who died as a consequence of their staphylococcal infections did so within 24 h. Theoretically, therefore, in a fulminating staphylococcal pneumonia a combination of a β-lactamase resistant penicillin and erythromycin may be more effective in the critical early phase of the illness, and there is evidence that there is synergy between these two drugs from studies of their effect in experimental staphylococcal infections in mice (Steigbigel, Greenman & Remington, 1975).

In conclusion a combination such as flucloxacillin and fucidin is comparatively non-toxic, of proven efficacy in staphylococcal infections, and provides some safeguard against the possibility of methicillin resistance in the infecting organism. On the other hand a combination of flucloxacillin and erythromycin has some theoretical advantages backed by limited experimental support, but has not been adequately studied in the clinical context. In view of the appallingly high mortality still seen in staphylococcal pneumonia it is apparent that such studies should be instituted.

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References


Factors affecting antimicrobial agents in an anaerobic abscess

The optimal treatment of anaerobic infections includes the selection of an appropriate antibiotic and the surgical drainage of purulent collections (Finegold et al., 1975). The surgical dictum that 'pus must be drained' has been known for centuries but drainage alone is not adequate because in the pre-antibiotic era one-third of the patients died of the infection despite surgical therapy. The need for this dual therapeutic approach is dictated by the pathological characteristic of these infections which is tissue destruction, usually progressing to discrete abscesses. Recent studies have shown that the environment in an anaerobic abscess is hostile to action of white cells and the activity of many antibiotics. It is important to have some knowledge of white cell function as well as antimicrobial activity.

A decrease in polymorphonuclear leukocyte (PMN) function under anaerobic conditions has been documented (Mandell, 1974). This most likely results from the lack of an oxygen dependent metabolic burst which is important in phagocytosis and bacterial killing by PMNs (Babior, 1978). Because anaerobic abscesses are devoid of oxygen, the PMN is at a disadvantage. Additionally, inhibition of PMN phagocytosis of aerobic bacteria by certain anaerobic organisms has been documented (Mandell, 1974). This has been known for centuries but drainage alone is not adequate because in the pre-antibiotic era one-third of the patients died of the infection despite surgical therapy. The need for this dual therapeutic approach is dictated by the pathological characteristic of these infections which is tissue destruction, usually progressing to discrete abscesses. Recent studies have shown that the environment in an anaerobic abscess is hostile to action of white cells and the activity of many antibiotics. It is important to have some knowledge of white cell function as well as antimicrobial activity.

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