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ASPECTS OF TREATMENT*

An antibiotic policy for surgical patients

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Summary

This paper offers guidance on antibiotic usage in surgical patients. A policy is outlined rather than the comprehensive coverage of every surgical situation. The principles of antibiotic prescribing are given. The antibiotics available and their routes of administration are reviewed. Indications for the prophylactic and therapeutic use of antibiotics are discussed. Factors causing the failure of antibiotic therapy are considered in brief.

Introduction

Antibiotics from their inception have been regarded as safe drugs of wide application, and consequently they are often misused. The incidence of resistant strains, infection by opportunist organisms, and allergy are increasing, thus undermining the value of these important drugs. These trends will be reversed only by the judicious and informed use of antibiotics. It is essential, therefore, that every surgeon should have a knowledge of the particular properties of the various antibiotics available, their spectra of activity, mode of action, and side effects.

Management of antibiotic therapy

General principles There must be clear clinical indications for the initiation of antibiotic therapy, and these should be listed in the patient's notes. Advice on the use of antibiotics and their management may be obtained from the microbiologist, too often a neglected member of the clinical team. It is mandatory that specimens should be taken before antibiotic treatment is started, for even trivial exposure may prevent the isolation of relevant organisms. Samples of pus or exudate are preferable to swabs as the bacterial yield is often more informative. Swabs should be taken with the correct technique and the appropriate site sampled, preferably by the house officer. Once antibiotic treatment has been decided upon it should be started with the minimum delay. The most frequently required antibiotics should be readily available, preferably on the ward.

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Prescribing antibiotics In general, antibiotics should be prescribed for an initial period of five days. The prescription must indicate the hourly interval between doses in all cases. The antibiotics should be changed only with the guidance of laboratory reports or when there has been no clinical response, and sharp substitution of one antibiotic for another should be avoided. It is safer to add rather than substitute antibiotics in an existing regimen, especially in an acutely ill patient when the infecting organism is unknown. The antibiotics prescribed should be reviewed at regular intervals of, say, 48 h, 5 d, and 10 d in the light of clinical results and laboratory reports, remembering that the patient is the best indication of therapeutic response.

Many antibiotics are excreted through the kidneys and some—for example, kanamycin, gentamicin, and cephaloridine—may be nephrotoxic. If there is evidence of renal dysfunction or nephrotoxic antibiotics are used plasma electrolyte and creatinine levels should be measured regularly. In renal failure antibiotics need not be withheld, but closer monitoring of serum antibiotic concentrations and modified dosages are required and tetracycline, chloramphenicol, and nitrofurantoin must not be used[1].

The tetracyclines, erythromycin, rifampicin, and chloramphenicol are potentially hepatotoxic and should be avoided in patients with liver disease.

The dosage advised by the manufacturer should be adhered to unless excretion is reduced. Lower dosage may encourage development of resistant strains and delay resolution. In severe infection there is a role for increased dosage, and the effect of probenecid in reducing renal tubular excretion of penicillins and some cephalosporins is useful.

Choice of antibiotics The different properties of the many antibiotics now available make it essential to have precise reasons for using a particular one. These should include: (1) the range and type of antibacterial activity; (2) the place of the antibiotic in the epidemiology of bacterial resistance and the dangers of eliciting resistance to it; (3) side effects; and (4) ease of administration.

The descending order of choice should be: bactericidal before bacteriostatic, narrow-spectrum single antibiotic before broad-spectrum antibiotic, and lastly a combination of antibiotics. Bactericidal antibiotics must be used in septicaemia, osteomyelitis, and pyelonephritis, in debilitated patients, and, if possible, in the very young and old. Table I lists the bactericidal and bacteriostatic antibiotics.

Bacterial resistance has developed to each antibiotic innovation. The tendency to prescribe unnecessarily the newer antibiotics, which may have a restricted place in therapy, is to be resisted. Table II indicates our order of preference of antibiotics and our choice of broad-spectrum antibiotics. Second- and third-line drugs should be used only in place of first-line drugs when recognized indications for this substitution exist. Erythro-

TABLE I *Mode of action of antibiotics*

Bactericidal	*Bacteriostatic*
Penicillins	Tetracycline
Benzylpenicillin	Erythromycin
Ampicillin	Lincomycin/Clindamycin
Cloxacillin	Sulphonamides
Carbenicillin	Chloramphenicol
Cephalosporins	
Cephaloridine	
Cephalothin	
Cephalexin	
Co-trimoxazole	
Aminoglycosides	
Kanamycin	
Gentamicin	
Tobramycin	
Colistin	
Fusidic acid	

TABLE II *Order of choice of antibiotics*

First line	*Second line*	*Third line*
Benzylpenicillin	Erythromycin	*Aminoglycosides
*Ampicillin/Amoxycillin	Lincomycin/Clindamycin	Carbenicillin
Cloxacillin/Flucloxacillin	*Cephalosporins	Fusidic acid
Sulphonamides	Tetracyclines	Colistin
Co-trimoxazole		Chloramphenicol

*Broad-spectrum antibiotics of choice

mycin may be used in penicillin-allergic patients for sensitive Gram-positive organisms. Lincomycin or clindamycin may be used for resistant staphylococci and are the drugs of choice for bacteroides and several other anaerobic infections. Their ability to penetrate tissues should be made use of in osteomyelitis and inaccessible infections due to staphylococci. Patients treated with these antibiotics should be watched for diarrhoea and pseudomembraneous colitis. Cephalosporins may be used for broad-spectrum cover in penicillin-sensitive patients and for klebsiella or resistant *Escherichia coli* and proteus infections, but should be avoided in renal failure. Cephaloridine must not be used with diuretics. Aminoglycosides should be reserved for broad-spectrum cover of serious infections of unknown aetiology and for resistant organisms. Of these, gentamicin remains the drug of choice at the present time. It is essential to ensure that adequate doses of this antibiotic are given and that in cases with renal dysfunction serum levels are monitored both to maintain appropriate concentrations and to prevent ototoxicity. Carbenicillin should be reserved for resistant organisms and is particularly valuable for pseudomonas infections in combination with gentamicin. Fusidic acid is active against resistant staphylococci and penetrates bone well. Colistin should be reserved for resistant Gram-negative organisms.

Benzylpenicillin remains the drug of choice for penicillin-sensitive staphylococcal infections, clostridial infections, Group A haemolytic streptococcal infections, pneumococcal pneumonia, and actinomycosis. It is, however, a narrow-spectrum antibiotic and cannot be expected to provide wide cover against unidentified infections, even in high doses. Streptomycin and rifampicin should be reserved for antituberculosis therapy. Chloramphenicol should be avoided, being the only antibiotic with fatal directly toxic properties. Tetracyclines have several limitations, being (1) bacteriostatic, (2) contraindicated in neonates, children, and pregnancy and in renal or hepatic dysfunction, (3) unsuitable in combination with penicillin or cephalosporins.

Antibiotic combinations may be used in surgical practice (1) to provide broad-spectrum cover for serious infections when the causative organism is unknown, (2) in life-threatening infections where possible errors in early sensitivity tests and delayed response need to be guarded against, (3) where antibiotics of different properties are used together to provide more complete bacterial eradication (for example, cloxacillin with fusidic acid or lincomycin in osteomyelitis, where the last two drugs more effectively penetrate bone), (4) to provide a synergistic effect (for example, carbenicillin and gentamicin against pseudomonas), (5) for infections due to more than one organism.

Bacteriostatic drugs should not be combined with the penicillins or cephalosporins, which act only on growing organisms. Combinations are usually unnecessary when the infecting organism and its sensitivities are known.

Routes of administration Many antibiotics are poorly absorbed from the gut, particularly in the presence of food. If this route is used they should be given half an hour before a meal and the newer, better absorbed forms of certain antibiotics—for example, amoxycillin, flucloxacillin, and clindamycin—prescribed. Only parenteral therapy assures complete absorption and the attainment of high peak blood levels. Antibiotics should be solubilized in normal saline and be given immediately. In general they should not be added to other materials or mixed together[2]. For serious infections, where there is evidence of blood invasion or specific organ involvement, a bolus injection into the tubing of an intravenous infusion over 5 min is the preferred route of administration (though lincomycin must be given in 100 ml of dextrose saline or normal saline over 1 h). Continuous intravenous infusion of antibiotics is not recommended because the serum concentrations obtained may be inadequate, some antibiotics deteriorate when held in solution at room temperature[3], and more nursing attention may be required. Full asepsis is necessary whenever an intravenous infusion is set up, and drip sites should be protected from infection and examined frequently. Cannulae should be changed regularly and, when removed, cultured for bacteria and fungi[4].

The use of topical antibiotics should be discouraged. Penetration of antibiotics to the site of bacterial growth is poor and the development of both skin sensitivity and bacterial resistance is encouraged. The patient's bed-clothes and environment become polluted with antibiotic, exposing the hospital flora to the drug, with the subsequent selection of resistant strains[5]. Only neomycin, sulphonamides, and chloramphenicol should be considered for topical use. Other antibiotics, in particular gentamicin and fusidic acid, should be restricted to the systemic route, where their use may be life-saving and devoid of alternatives.

Prophylaxis

There is greater scope for antibiotic abuse in prophylaxis than in treatment. Prophylaxis is most likely to be successful when the objective is protection against a known organism. Antibiotic prophylaxis, however, may lead to higher rather than lower rates of infection[6,7], with emergence of resistant organisms.

Clostridial infection Benzylpenicillin should be given intramuscularly one hour before surgery to all patients undergoing above-knee amputations. A povidone–iodine compress applied to the site of amputation for 15 min before operation is advocated[8] as prophylaxis against *Clostridium welchii* contaminating the thigh. Benzylpenicillin should also be given in all cases of extensive trauma, especially if surgical debridement is delayed.

Bacterial endocarditis Patients with mechanical defects of the heart should be given prophylactic antibiotic cover, particularly against *Streptococcus viridans* for operations in the mouth and against a wider variety of other organisms for operations elsewhere. Benzylpenicillin or a broad-spectrum antibiotic such as cephaloridine should be given intramuscularly one hour before surgery so that peak levels are present in the blood at the time of the operation. If a patient with rheumatic fever is already taking penicillin, lincomycin should be given. Prophylaxis should continue for 2 d after the procedure.

Bowel preparation It is generally agreed that the mechanical clearance of the large bowel before resection is important and that intestinal antibacterials reduce the colonic flora. There is, however, no ideal regimen

and little agreement as to the best antibacterial. The choice of phthalylsulphathiazole, neomycin, or kanamycin depends mainly on time available and personal choice. Staphylococcal superinfection is more likely if antibiotics are used.

Postoperative antibiotics are probably unnecessary except when there is doubt regarding intestinal viability at the anastomotic site, for there is good experimental evidence to show that antibiotics prevent ischaemic gut becoming gangrenous[9].

Chest infections Antibiotic prophylaxis appears to be valueless except perhaps in chronic bronchitics undergoing upper abdominal surgery[10]. Chest infections should be treated before surgery whenever possible.

Insertion of prostheses The value of prophylactic parenteral antibiotics when inserting prostheses in orthopaedic, vascular, or cardiac surgery is unproven. Rigorous asepsis and meticulous technique in appropriate surroundings are the main defence against infection. If systemic antibiotics are used a combination which is effective against staphylococci and the common Gram-negative organisms is indicated—for example, cloxacillin and gentamicin or cloxacillin and cephaloridine. There is evidence that antibiotics applied locally at the site of operation may reduce late infection[11].

Burns Benzylpenicillin or erythromycin prophylaxis against clostridial and streptococcal infections is indicated in all severely burned patients. Other antibiotics should be reserved for the treatment of subsequent infections. Rigorous control of cross-infection is vital, and swabs of the anterior nares, throat, and perineum should be taken from all patients on admission, for autoinfection is also common. Topical chemoprophylaxis with silver sulphadiazine, silver nitrate, or Sulfamylon (mafenide acetate) all reduce infection, but all have their disadvantages[12].

Wound infections Penicillin[13], ampicillin[14], tetracycline[15], and cephaloridine[16] have all been shown to reduce wound infection after surgery when instilled into the wound. Short-term systemic prophylaxis with cephaloridine[17,18] and gentamicin and lincomycin in combination[19] is also effective provided the first dose is given just before the operation. The emergence of resistant bacteria usually follows systemic antibiotic therapy, but the widespread use of topical antibiotics is responsible for the resistance of some organisms[20]. For these reasons the use of systemic antibiotics to prevent wound infection would appear unjustified and their topical use unwise. A dry powder form of povidone–iodine (Disadine DP) has been shown to prevent wound infection and is now an alternative to topical antibiotics[21-23].

Therapeutic indications

Minor sepsis Systemic antibiotics are not indicated in superficial staphylococcal infections unless the lesion is in the mask area or the patient debilitated. Fusidic acid gel has, however, been shown to speed healing when injected into curetted abscess cavities[24]. There is evidence that systemic antibiotics allow anorectal abscesses to heal by primary intention following incision, curettage, and closure[25]

Postoperative chest infections Many postoperative chest infections are due to multiple small areas of atelectasis and resolve within 24–48 h with physiotherapy and expectoration of sputum. Antibiotics are indicated only if fever and purulent sputum persist or there is evidence of pneumonia. If bacteriological results are not available a broad-spectrum antibiotic should be given—for example, ampicillin or co-trimoxazole. For oral administration amoxycillin is better

absorbed and reaches higher concentrations in sputum than ampicillin[26]. Treatment may be changed in the light of subsequent reports if there has been no response.

Intraperitoneal sepsis Systemic antibiotics are not beneficial in appendicitis, provided the organ is removed before perforation. When perforation has occurred broad-spectrum antibiotics prevent the development of intraperitoneal complications but have no effect on wound sepsis[27]. Antibiotics are often unnecessary in the treatment of an appendix mass. The treatment of a pelvic abscess is drainage.

In acute cholecystitis antibiotics are necessary only if there is marked tenderness or the patient develops ascending cholangitis, in which case surgery is also indicated. In acute pancreatitis antibiotics should be saved for infective complications.

Antibiotic therapy is indicated whenever surgery and the intrinsic defence of the peritoneum are unable to prevent the progression of intraperitoneal sepsis. Unnecessary antibiotic treatment, however, may prolong sepsis and confuse the clinical picture. Systemic antibiotics are invaluable in generalized peritonitis but only as an adjunct to surgery. A combination of gentamicin and lincomycin will protect against most gut organisms except *Strep. faecalis.* If there is evidence of infection with clostridia, Group A haemolytic streptococci, or a sensitive staphylococcus benzylpenicillin should be added. High doses of carbenicillin should be used with gentamicin in pseudomonas infections. Surgical treatment should include peritoneal toilet, and noxythiolin lavage may be of value[28]. The intraperitoneal administration of antibiotics is advocated by some, but the aminoglycosides are contraindicated, for when used intraperitoneally they have interacted with ether, cyclopropane, and several muscle relaxants, causing neuromuscular blockade with resulting apnoea and death[29].

Septicaemia Before antibiotics are given it is imperative that blood cultures be taken. The choice of antibiotics is helped by clinical clues—a rigor after urinary tract instrumentation is likely to be due to a coliform infection and after biliary or intestinal surgery to an infection with gut organisms. Previous microbiological reports on urine or draining fluids may indicate the causative organism. In the absence of clues initial treatment should cover all likely causative organisms. Gentamicin is effective against staphylococci, coliforms, and pseudomonas but not against streptococci or clostridia; a combination of this drug with a broad-spectrum penicillin or a cephalosporin provides wide cover. If the patient has recently undergone intestinal or gynaecological surgery, especially a septic abortion, lincomycin should be given to protect against bacteroides infection. If a resistant staphylococcus is suspected cloxacillin is indicated.

Acute osteomyelitis Blood cultures should be taken before any treatment is started, and other foci of infection should be sought. The patient should be given a combination of parenteral cloxacillin and fusidic acid or cloxacillin and lincomycin, as the majority of infections are due to staphylococci, a number of which are penicillinase-producing. Exploration and drainage is indicated in patients with a history of over 48 h and in those with a shorter history if the infection does not rapidly subside. Antibiotic therapy should be altered in the light of subsequent laboratory reports and in all cases treatment should continue for 4–6 weeks.

Urinary tract infection Antibacterial treatment of urinary tract infection can be guided by isolation of the organism from the urine. Many antibacterials are excreted

by the kidney and reach high levels in the urine, but it must be ensured that the urinary pH is appropriate—for example, alkaline for sulphonamides, penicillin, and aminoglycosides and acid for nitrofurantoin and mandelamine. There is no place for tetracycline in urinary tract infections in hospital practice and it is contraindicated in cases of renal dysfunction. Nitrofurantoin is inactive against proteus owing to the ability of this organism to render urine alkaline. Follow-up urine cultures are mandatory and patients with recurrent infections require thorough investigation.

Acute cystitis may be treated with co-trimoxazole or ampicillin and other antibiotics substituted according to laboratory reports. Patients with acute pyelonephritis require a bactericidal antibiotic which achieves adequate serum and urinary levels. Ampicillin, co-trimoxazole, or cephalexin may be given, but if there is evidence of bacteraemia or septicaemia parenteral antibiotics, including the aminoglycosides, are indicated. Urinary tract infections should be treated before any urological procedure is undertaken. If this is not possible the patient should be covered by the appropriate antibiotic at the time of operation. Antibiotics are not, however, indicated as a cover for routine catheterization.

We do not have space to discuss the management of recurrent urinary tract infections, chronic prostatitis, or the paraplegic bladder.

Reasons for failure of antibiotic therapy

The failure of antibiotic therapy is usually due to clinical factors but occasionally may be caused by errors in the laboratory[30]. A poorly taken swab may yield feasible but irrelevant organisms and a specimen of sputum may represent only upper respiratory tract secretions. In the laboratory an atypical colony or a secondary organism may be picked for sensitivity testing or the results of the tests may be wrongly read.

Clinically, the antibiotic may not reach the site of infection in sufficient concentration because of inadequate, irregular, or missed doses. The wrong route of administration may be used or the site of infection be inaccessible. Delay in starting therapy may make elimination of the infection more difficult. Failure to review the antibiotics prescribed in the light of laboratory results and the clinical response may conceal the emergence of a resistant organism or a new infection or hide a mistaken diagnosis of bacterial infection. Other causes of fever may require consideration. Finally, the patient may need supportive therapy to boost the defences against infection.

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