ANTIBIOTICS IN ORTHOPAEDICS

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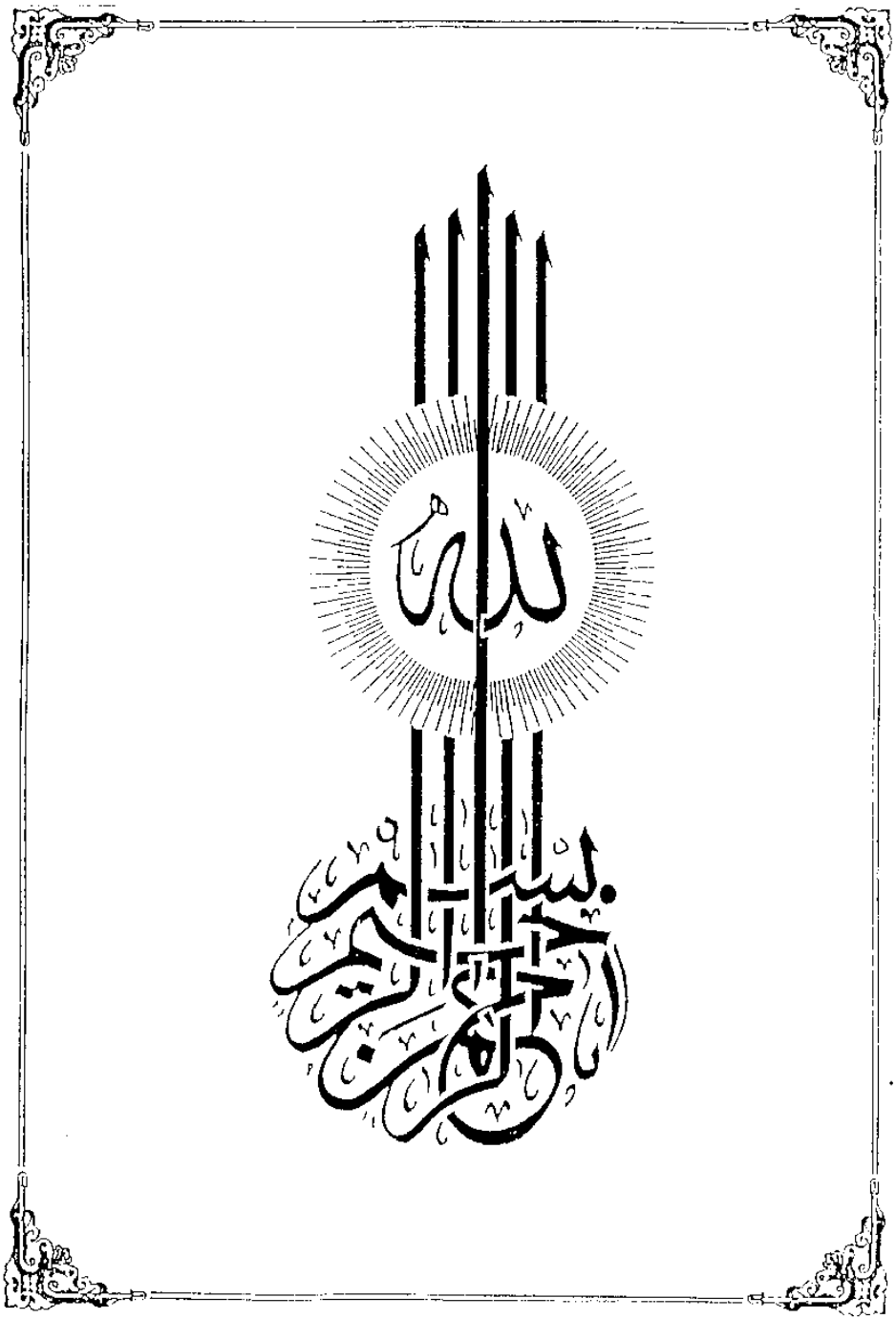
AIM OF THE WORK

" The aim of this work is to throw some light on the role played by antibiotics in orthopaedic " .



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CONTENTS

DEFINITION OF ANTIBIOTICS

The word of " antibiosis " was coined by Vuillemin in 1889 to denote antagonism between living creature in general, but the noun " antibiotic " was first used by (Waksman,1942) and later by (Waksman and Lechevalier , 1962) which gives him the right to redefine it and his definition confines it to substances produced by microorganisms antagonistic to the growth or life in high dilution (Garrod , Lambert and O'Grody , 1975) .

The advent of synthetic methods has however resulted in a modification of this definition and an atibiotic now refers to a substance (produced wholly or partially by chemical synthesis) which in low concentration inhibit the growth of other microorganisms (Hugo , 1977) .

Two years later (Winner , 1979) proposed that antibiotics are chemotherapeutic agents which are derived from living organisms such as moulds , nowadays the term antibiotic therapy and chemotherapy are used almost interchangeably, so the entire range of chemotherapeutic and antibiotic drugs are referred to as antibiotics .

Antibiotics are substances that are obtained from microorganisms and are able , even in high dilutions to inhibit

or kill other microorganisms , chemotherapeutic substances have similar activity in high dilutions but they are obtained by chemical processes rather than derived from biological sources , benzyl-penicillin is an antibiotic and sulphonamides are chemotherapeutic agents , this simple distinction has been complicated by two facts , firstly an antibiotic with a simple chemical formula such as chloramphinicol may be easier to produce chemically than to obtain by fermentations , secondly , many substances now in use , are derived initially from fermentation and are then chemically modified to increase activity or modify the behaviour in vivo , these semisynthetic substances are therefore partly antibiotics , partly chemotherapeutic consequently their nomenclature is rather impricise " the term antimicrobial agent " cover all substances whether naturally occuring , synthesized or semisynthetic , but despite its broad meaning is still not very precise as it includes other substances such as disinfectants . In other words , antibiotic is now often used as a trivial name to cover all substances except disinfectants obtained from microorganisms , synthetic or semisynthetic and are able to inhibit or kill other micoorganisms (Topley and Wilson , 1984) .

THE DEVELOPMENT OF CHEMOTHERAPY

Folk remedies against infestation with protozoa such as amaebae (ipecachuana) and malaria (quinine bark) had been used for centuries before a more scientific approach to chemotherapy was instituted by Paul Ehrlich . He investigated a series of organic arsenical compounds in order to find one which was far more active on the infesting organisms than upon the host i.e. had a high therapeutic index . This culminated in the discovery of salvarsan which was highly active against tr. pallidum and other spirochaetes .

The first publication on the use of penicillin was on its value as a selective agent to isolate H. influenzae from sputum (Fleming , 1929) and over a decade elapsed before the therapeutic use in man was established (Chain , et al., 1940) , many other antibiotics were subsequently isolated by screening mould for antibiotics production (Schotz and Waksman , 1944) , isolated streptomycin from streptomyces griseus and this was found to be active against myco-tuberculosis .

Before the introduction of penicillin , the sulphonamides were used against a wide range of illness but they are less potent than the antibiotics , so that the dose must be

larger with a concemitantly greater risk of side effects (Fisher and George Achristic , 1973) .

BACTERIOLOGY OF BONE AND JOINT INFECTIONS

(A) BACTERIOLOGY OF BONE INFECTIONS :

Sir James Hawie has said " chemotherapy without bacteriology is guess work"(Avery , 1980) .

- SPECTRUM OF ANTIBIOTICS :

(Craig and Stitzel , 1982) stated that antibiotics are often referred as either narrow or broad spectrum agents, tetracycline and chloramphenicol are examples of broad or extended spectrum antibiotics that is why are active against both Gram-positive and Gram-negative bacteria , penicillin G is active primarily against gram-positive bacteria and is classified as a narrow spectrum antibiotic while (Topley and Wilson's , 1984) stated that antibiotics can be divided into three main categories :

I. Antibiotics active against Gram-positive organisms for example , Benzyl penicillin and related acid stable penicillins , erythromycin , lincomycin , fusidic acid , rifampicin,

vancomycin and bacitracin .

II . Antibiotics active mainly against Gram-negative rods for example , ampicillin and related compounds , ureido-penicillins, mecillinam , temocillin , and aminoglycosides antibiotics (streptomycin , neomycin , kanamycin and gentamicin) .

III . Broad spectrum antibiotics : include trimethoprime , cephalosporins and related compounds Beta-lactamase inhibitors [clavulanic acid and sublactam] , tetracyclines and chloramphenicol , antituberculous drugs include ethambutol , cycloserine , isoniazid , para-amino salycilic acid and thio semicarbazones . Cephalosporins especially cephradine was chosen as a prophylactic antibiotic in bone surgery for the following reasons , it has a broad spectrum effect against most Gram-positivie microorganisms , including staphylococcus aureus and many of Gram-negative microorganisms which may contaminate the area of operation (Lacey and Stokes , 1977 ; Parsons , 1978) .

The mean inhibitory concentration for cephradine against staphylococcus aureus as reported by (Neiss , 1973) is 0.3 mg per littre and the mean bactericidal concentration is 1.5 mg per littre , cephradine acts against the bacteria by interferring with synthesis of the cell wall and is more

resistant than cephaloridine , cephazolin , cephalothin and methicillin to the B-lactamases produced by the bacteria, cephradine has very low protein binding and most of it is available in the unbound form , therefore it can reach the tissue fluid more easily (Selwys , 1976) . So , one gram of cephradine given intramuscularly will have an antibiotic effect sufficient to prevent infection during operation (Wicks , et al. , 1981) . Cefamandole along with cefoxtin and cefuroxime comprise what have been referred to as the second generation of cephalosporins , these newer cephalosporins are resistant to degradation by beta-lactamase enzymes of gram-negative organisms . Cefamandol's spectrum of activity against gram-positive organisms is comparable to that of cephalothin , it is active against staphylococcus aureus and staphylococcus epidermides , streptococcus pneumonia and B-haemolytic streptococcus , in vitro cefamandole is more active than cephlothin against the gram-negative bacilli , including escherichia coli , klebsiella pneumonia , proteus mirabulis and haemophilus influenzae . Neither cefamandole nor cephlothin is active against pseudomonas . Both cefamandole and cephlothin are broadly active against most of the principal anaerobic bacilli including clostridium. (Schurman , Hirshman and Buston , 1980) stated that cephradine , cephalothin and cefamandole should be regarded as of equivalent value in the treatment of staphylococcal

infection , but cefamandole is preferable for prophylaxis because , it is essentially as effective as cephalothin against staphylococcus and is more effective against a large variety of gram-negative bacteria and anaerobic bacteria , moreover cefamandole achieves higher bone and joint concentrations when compared to cephradine or cephalothin at the same dose .

Also the serum levels of cefamandole are higher and remains high for a longer time than the serum levels of cephalothin , however cefamandole is more expensive , so the final costs to the patient is modest .

All of the cephalosporins reach fairly high concentration in serum , synovial fluid and bone tissues (Gristing , et al. , 1983) . A staphylococcus aureus has remained the most common organism isolated in acute osteomyelitis and septic arthritis (Gilmour , 1962 ; Green , 1967 ; Blockey and Watson , 1970 ; Anderson , et al. , 1980 ; Col et al., 1982) .

Early fears of the development of resistance to cephalosporins and cloxacillin were unfounded and staphylococcus aureus remains consistently sensitive to these drugs

(Rountree and Vickery , 1973) .

Gram-negative infections are usually more serious than other infections and almost always require removal of all foreign material , the patient with a gram-negative infection of the hip usually , must undergo , a girdle stone arthroplasty , a procedure that may result in permanent pain and limited movement . After the prothesis and all of the cement is removed , the deep seated infection may persist leading in some instances to amputation or to septicaemia and death . Bacteria in late infections colonize and propagate in cryptic fashion are difficult to identify and are resistant to conventional modes of therapy (Gristina , et al. , 1983) .

So in order to estimate the therapeutic activity of an antibiotic treatment regimen in bone infection , one important assumption is to know the pathogens and their susceptibility , the bacteriological diagnosis can be preceeded through blood cultures which ideally collected just as the temperature of the patient starts to rise , are the rule of the microbial diagnosis of acute osteomyelitis , the numbers of positive blood cultures in chronic osteomyelitis are much less than with acute osteomyelitis (Shanson , 1983) .

The sources of biopsies from infected bone may be discharged pus , a part of excised wound and infected sinus , the pus and part of an excised wound are preferred for examination rather than swab samples of such materials , because the swab specimen will dry out to a greater or a lesser extent and some pathogenes eg. strept. pyogens may not survive , also the number of media employed in examining such specimens implies a reducing inoculum over several plates and tnbes of culture media (Gillies and Dodds , 1979) .

This type of specimen (excised wound) is not available from patients with acute osteomyelitis who have closed lesions , unless a surgeon exceptionally decides to perform a bone biopsy or drainage of the infected bone lesions (Shanson , 1982) .

If the lesion is deep-seated and drainage through a sinus as in chronic osteomyelitis then the entire inner dressing should be sent to the laboratory in a sterile wide jar (Gillies and Dodds , 1979) .

But (Dingeldein , et al., 1983) stated that cultures from the sinus tract disagree in 50% or even more with cultures from operative material , therefore sinus tract swabs

should not be used in bacteriological diagnosis,culture of faeces and urine for salmonella should be carried out in chronic osteomyelitis patients who have no microbial diagnosis (Shanson , 1982) .

(B) BACTERIOLOGY OF JOINT INFECTIONS :

The most common causative organism of acute septic arthritis in all age groups is staphylococcus aureus , many other organisms have been isolated from septic joints as streptococcus pyogens , streptococcus pneumonia , escherichia coli , proteus , salmonella (Mortin , Merril and Lammot , 1968) , clostridium welchii (Torg and Barret , 1970) , also neisseria , staphylococcus albus , aerobacter meningococcus , bacteroids and paracolon .

Nelson and Koontz (1966) and Almquist (1970) suggested that :

In infants under six months of age , the most likely organisms were staphylococci or gram negative enteric pathogenes , between six months and two years of age , staphylococci or haemophilus influenzae and over two years of age ,