

Book Review

Antibiotics in Medicine. *Brit. med. Bull.*, **16**, (1960)

The January edition of the British Medical Bulletin deals with the subject of antibiotics in medicine, and comprises a series of articles written by some of the most eminent authorities in this field in the United Kingdom. Whilst the antibiotic era has brought with it great benefits to mankind, it has also produced problems, such as bacterial resistance, sensitization phenomena, superinfection, blood dyscrasias, toxicity to vital organs, and other untoward effects resulting from chemotherapy. Much of this has stemmed from incomplete understanding by those concerned with their administration, and from the undoubted over-use and abuse of this most valuable contribution to medicine.

The British Medical Bulletin has attempted to crystallize the opinions and views of the experts in Britain, and represents the best review of the field thus far produced. Much care and planning have been given to this symposium but, as Garrod points out, anything that takes some time to be written and printed is likely to be out of date before it is published. However, apart from the latest development in the penicillin field—namely the synthetic isolation of 6-aminopenicillanic acid, and the production of α -phenoxyethyl penicillin, which is now being used clinically—nothing of importance has been omitted.

The review commences with the chemistry and classification of the antibiotics, fittingly enough from Oxford, where penicillin was first used on a patient. This article, by Abraham and Newton, is extremely well compiled, and, as most antibiotics are derived from amino acids, acetate and simple sugars, so they are chemically classified. Although so much work has been done, we still know little of the mode of action of antibiotics, and such knowledge would lead to a more rational approach to therapy. The metabolic pathways of these substances are being actively studied, and with further developments in tissue culture and research on the biochemistry of the living cell, we are beginning to come to grips with the problem. Dr. Gale of the M.R.C. considers some of these points under the heading: 'The nature and selective toxicity of antibiotics'.

The development of resistant strains has become a vital issue especially in hospitals, where today the incidence of penicillin-resistant staphylococci is well over 70 per cent. This problem is considered by Dr. Pollock, who has done much research on this matter. The mechanism still remains obscure and the solution is hampered by lack of knowledge of the biochemical processes at work, although, obviously, mutations and enzymic systems are involved. From the therapeutic aspect this resistance is very serious. In a recent article in the British Medical Journal by Murdoch *et al.* from the Royal Infirmary Edinburgh—another contributor to this

symposium—an interesting observation was made. In a series of chronic bronchitics receiving oxytetracycline on a continuous regime of 1 g daily for 6 months every year for two years, compared with a similar group on placebo, at the end of the study the number of patients with resistant *Staphylococcus aureus* in the sputa was the same in the active as in the control group. This very important observation may indicate that bacteria do not develop resistance as a result of therapy but are present in the hospital environment from which patients may be infected on entering hospital.

Garrod and Scowen from St. Bartholomew's consider the principles of the therapeutic use of antibiotics. Correct use of these drugs requires some understanding of the bacteriological principles involved. Many physicians do not appreciate this but there is no doubt that the bacteriologist and physician work more closely today than ever before. The first sentence in this article is interesting, namely that the first decision to be made is whether antibiotic treatment is necessary at all. These authors deal with antibiotic assays in body fluids, a subject that has come increasingly under scrutiny, with emphasis on blood levels and their relation to clinical efficacy. However, some antibiotics which give relatively low serum levels give high tissue levels, which may well be more important. It is very much easier to assay serum levels of antibiotics than tissue levels, and it is not necessarily true that the higher serum levels give the better clinical result, providing the antibiotic reaches the inhibiting concentration.

J. C. Gould, who has published much on the *Staphylococcus* deals very adequately with the laboratory control of antibiotic therapy, and describes in detail the various forms of sensitivity testing. The pharmacology of antibiotics is presented by Professors Robson and Buttle, who deal with those commonly in use, and also the antifungal and polypeptide antibiotics. Methods of administration, absorption and excretion, and distribution patterns are fully considered. However, much remains to be learned of the mechanisms and sites of absorption of antibiotics—so important in relation to oral therapy. Some brief consideration is given by these authors to antibiotics in malignant disease. Combined therapy may well be one important approach in the future. It is established in tuberculosis and bacterial endocarditis. Dr. Lacey considers the rationale and management of such therapy.

Professor Bywaters and Mr. G. W. Taylor examine the preventive use of antibiotics in medicine and surgery respectively. With regard to the former, toxicity and resistance are serious considerations. In the surgical field there has certainly been indiscriminate use of antibiotics as a prophylaxis against post-operative infection. Mr. Taylor states that antibiotics should not be used prophylactically in clean surgical procedures. They may, in fact, cause serious complications and also fail to reduce the incidence of infection. It is doubtful if sterilisation of the gut with antibiotics, such as neomycin, is a wise procedure. In burns, thigh amputations in ischaemic disease, where foreign bodies are present, and in cardiac and neuro-surgery, prophylaxis may be desirable.

The clinical applications of the antibiotics reported in this review are mainly confined to the chemotherapy of tuberculosis and bacterial endocarditis. Professor Crofton deals with tuberculosis by dividing the patients into those sensitive to streptomycin, PAS and INAH, and those who are not. In his experience, if the standard drugs are used properly, drug-resistant organisms should emerge very rarely, and the object of combining these drugs is to prevent such emergence; a logical approach. The M.R.C. has already established the best combinations of different pairs of the standard drugs, which the author calls 'good chemotherapy'. Viomycin, tetracyclines, pyrazinamide and cycloserine may be employed for resistant cases, although the last two may be very toxic drugs when used at therapeutic levels. High doses of tetracyclines in combination with viomycin greatly reduce the emergence of viomycin-resistant strains. Certainly in the field of tuberculosis the impact of antituberculous drugs has been tremendous. As far as bacterial endocarditis is concerned, Dr. Dormer describes the infecting organisms which may be responsible, and discusses treatment. This should be a deliberately chosen and well planned campaign. Penicillin and streptomycin as combined therapy are recommended.

Professor Dunlop and Dr. Murdoch from the Edinburgh school describe in considerable detail the dangers of antibiotic treatment. This is a balanced and well conceived article. All the antibiotics in common use today are looked at in the light of toxicity and side effects. Penicillin appears to produce the highest incidence of severe and fatal anaphylactoid reactions. This is a reflection on the indiscriminate usage of this valuable weapon in the last decade by the medical profession. Despite such reactions, penicillin is still the most widely used antibiotic today, although the broad-spectrum antibiotics appear to be replacing it. Certainly this is so in hospitals. The tetracyclines do not produce allergy or neurotoxicity, but superinfection with virulent *Staphylococcus aureus* is a potential hazard. This is a very rare hazard in actual practice, and this group of antibiotics, with their wide range of effectiveness and low toxicity, are the best of the antibiotics available today. It would seem more logical to prescribe them as a first line of attack and to revert to other antibiotics should they fail. This is, despite their cost, a more natural approach to therapy, where the organism has not been identified and its sensitivity to antibiotics established. As is right, these authors condemn the widespread and often empirical prescription of antibiotics, largely because of their potentially dangerous side effects.

Dr. Lowbury of the M.R.C. discusses the clinical problems of drug resistance, with, of course, emphasis on the *Staphylococcus*. The chief hope for this problem is the discovery of new antibiotics, of which several have recently become available, for example vancomycin, kanamycin, ristocetin and, more recently, cephalosporin. Professor Cruickshank, Fleming's successor at the Wright-Fleming Institute and now in Edinburgh, describes in some detail the laboratory uses of antibiotics under the headings: 'Selective Culture Media', 'Antibiotic-Sensitivity Patterns',

'Bacterial Growth and Variation' and 'Isolation of Viruses'. Finally, Dr. Campbell of Glaxo Laboratories looks at the search for newer antibiotics, and describes some of the screening methods employed. Griseofulvin C, an antifungal antibiotic, is considered in some detail.

This edition of the British Medical Bulletin is an extremely valuable contribution. Whilst it is a review itself, and tells us nothing new, it marshalls the facts and opinions in one publication in a more concise manner than ever before. For all those physicians and scientists concerned with antibiotics, this excellent review is essential reading.

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