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COMBINATIONS OF ANTIMICROBIAL DRUGS

The indiscriminate use of antimicrobial drugs has been much condemned. There are several important disadvantages and dangers. The use of combinations of these drugs introduces additional problems and risks, among which is an increase in the incidence of adverse reactions and in sensitization.

The possible indications for combined use of these drugs have been stated by Jawetz.[1] In certain patients who are extremely ill with infection of unknown cause, it might be advisable to use more than one antimicrobial drug, while every effort is being made to establish the correct diagnosis. In mixed infections a combination of drugs aimed at a complex flora may be more effective than a single drug. Infections of the skin, wounds, body cavities, and of the cardiovascular, respiratory and urinary systems, may necessitate this form of attack. In certain infections where resistant organisms develop, an additional drug may delay the emergence of resistant strains. This has been well established in the chemotherapy of tuberculosis, but it may apply also to other chronic infections. The administration of a combination of drugs may in certain instances decrease adverse reactions, since each of the administered drugs may be given in a smaller dose below the level of adverse reaction. There are occasions when one drug may enhance the action of another on a particular microorganism; one of the best examples of such 'synergism' is the use of penicillin with streptomycin in bacterial endocarditis due to *Strept. faecalis*. Desirable combinations of drugs have to be established or suggested by appropriate laboratory methods.

The mechanism involved in synergism is not properly understood at present. One drug may be more effective on one type of microorganism, and the other on the remainder of the microbial population; or one drug may block microbial replication incompletely and the second drug then produce bactericidal effects. Thus the bactericidal action of penicillin on *Streptococcus viridans* is enhanced by the presence of streptomycin. The possibility of a second drug actually diminishing the effectiveness of the drug with which it is given in combination is also to be borne in mind. Fortunately, in clinical practice this is not a frequent occurrence, but there are a few documented examples of 'antagonism'. Penicillin and chlortetracycline (Aureomycin) were found to cure fewer patients with pneumococcal meningitis than when penicillin was used alone. There are other examples of such antibiotic antagonism. The mechanism must be the result of sequential action whereby the interfering drug reduces the activity of that metabolic pathway that would have been inhibited by the bactericidal drug. An interfering agent such as tetracycline acts primarily as an inhibitor of protein synthesis and antagonizes penicillin, which acts as an inhibitor of mucopeptide synthesis by the cell wall. It may be that protein synthesis must proceed actively for active mucopeptide synthesis to occur, and so inhibitors of protein synthesis antagonize inhibitors of mucopeptide synthesis.

The results of *in vitro* tests have correlated very poorly with the clinical results;[2] a mixture of antimicrobial drugs is superior to a single agent only in a few instances. It is remarkable that there has been such readiness and enthusiasm to accept claims made for mixtures of antimicrobial drugs. Particularly condemned have been the 'fixed dose' forms. This use of drugs does not offer the physician discretion in the choice of components or of the ratios in which they are used. 'The use of such "fixed dose" antibiotic mixtures and the manner in which they are being exploited represent a major backward step in the management of infections.'[3] Inadequate treatment is encouraged because there is the tendency to use the same total dose of mixture as of a single agent. Also, a false sense of security is created when in fact a narrower rather than a wider coverage is supplied. Antibiotics should generally be selected individually, each for its own value, and administered in the proper dose for the intended purpose.

1. Jawetz, E. (1967): Pharmacology for Physicians, **1**, 1.
2. Dowling, H. F. (1957): Postgrad. Med., **22**, 428.
3. Goodman, L. S. and Gilman, A. (1965): *The Pharmacological Basis of Therapeutics*. New York: Macmillan.

THE RACIAL INCIDENCE OF TESTICULAR TUMOURS*

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It is generally accepted that tumours of the testis of the seminoma/teratoma type are uncommon in non-White patients. Dixon and Moore[1] state that only 1·5% of these tumours in their series occurred in non-Whites, although the population at risk contained up to 8·5% non-Whites. Kochler *et al.*,[2] in a series of 1,127 testicular tumours collected from a population which contained 50% Negroes, found only 17 cases (1·5%) in the non-White group. Cohen and Tomskey[3] found only 5 cases (8·9%) in Negroes, out of 56 tumours, and all of these were in undescended testes.

Groote Schuur Hospital, Cape Town, admits patients from 3 racial groups: White, Bantu and a group of mixed blood known as Cape Coloured. It was thought worth while to study the racial incidence of testicular tumours within this population to discover whether it followed the same trends as elsewhere.

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