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THE IMMUNOPHARMACOLOGY OF ANTIMICROBIAL DRUGS

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SUMMARY

Very little is known about the immunopharmacology of antimicrobial drugs. There are few reports in the scientific literature, and no mention of this subject can be found in recent editions of standard pharmacology textbooks. It is important to understand the immunopharmacology of antimicrobial drugs because immunomodulation by these drugs can affect the outcome of the infection being treated. Recovery from serious infections generally requires the participation of a reasonably intact immune system, even when appropriate and potent antimicrobial drugs have been prescribed. In such clinical situations, suppression of immunity can be detrimental to recovery while enhancement of immunity can contribute to recovery. This consideration is even more critical when the patients concerned are already immunocompromised by cancer or other debilitating diseases, or by anti-cancer or immunosuppressive therapy.

A systematic approach to the testing for the immunopharmacological properties of antimicrobial drugs was adopted in the present studies. The results of an in-vitro screening programme showed that the tetracyclines, miconazole, amphotericin B, the antimalarials and diaminopyrimidines have an effect on mitogen-induced human lymphocyte proliferative responses, whereas the penicillins, macrolides, aminoglycosides, cephalosporins and sulphonamides have little or no effect. In-vivo studies confirmed the immunosuppressive potential of tetracyclines, miconazole and amphotericin B, but not the antimalarials.

Of particular interest was the discovery that pyrimethamine has immunopotentiating properties. There is current interest in such agents because of the potential for use in immunotherapy of cancer and other diseases where the immunological responses are inadequate, as well as their potential for use as probes to study immunological processes.

The results of the present studies suggest that caution should be exercised in selecting antimicrobial drugs for clinical use, especially in immunocompromised patients. The extensive and indiscriminate use of antimicrobial drugs by the medical community should be discouraged,not only because of toxic and allergic complications, the induction of resistant strains of micro-organisms, and the financial burden on the community and individual, but also because the immunosuppressive potential of some antimicrobial drugs can predispose to susceptibility to infection, birth defects, cancer, ageing and cardiovascular diseases, although the last three possibilities have not yet been realized, largely because epidemiological studies to date have not addressed themselvesdirectly to the problem.

Further studies are required along a broad front in order to understand better the immunopharmacology of antimicrobial drugs, their sites and mechanisms of action, their interactions with each other and other classes of drugs, their clinical effects especially in complex clinical situations, and their long term complications.