antibacterial drugs, can be recognized. The first comprises animal models used to assess antibacterial efficacy in vivo in relation to activity in vitro. The second comprises animal models of human disease that are employed to predict therapeutic efficacy in man. The fundamental difference between the two kinds of model is often forgotten. The first of these categories has been used to study the way in which pharmacokinetics modulate the intrinsic antibacterial efficacy (Mattie, 1981). An example of this type is the thigh infection model in mice, where a known number of bacteria is injected into a thigh muscle, and some time later the bacteria are counted in the homogenized muscle tissue. These bacterial counts can serve to establish an accurate dose-effect relationship, for instance as a basis for the comparison of different antibiotics in vivo, or, if pharmacokinetics are taken into account, with the activity in vitro (Kunst & Mattie, 1978; Mattie & Van der Voet, 1981). The cited experiments showed that there is yet no scientific basis for reliable prediction of clinical efficacy, solely in terms of human pharmacokinetics and arbitrary in-vitro parameters such as the MIC. In the same model the contribution of host resistance factors, such as granulocytes, proved to be quantitatively related to the contribution of the antibacterial drugs. It was shown, for instance, that in granulocytopenia the dose of aminoglycosides must be doubled to achieve the same effect as in normal animals (Van der Voet, Mattie & Van Furth, in press).

Lastly, animal models of human disease suffer from a fundamental limitation of interpretability. If it may be assumed that the intrinsic antibacterial effect is identical in animals and in man, and even that bacterial growth kinetics are similar in both species, it is nevertheless certain that the pharmacokinetics differ widely and probably host resistance factors as well. This means that the time course of an infection under treatment will always be different in animals and in man. A good example is the endocarditis model in rabbits (Petersdorf, Pelletier & Durack, 1977). This model has proved to be very useful for qualitative predictions concerning the antibacterial treatment of endocarditis. If, however, the results are interpreted in terms of dosage regimens, the above mentioned objections should be kept in mind.

In conclusion, it may be said that the difficulty associated with animal models lies less in the performance of the experiments than in the interpretation of the results in a clinically relevant way. If, however, the limitations of interpretation, which always hold for animal experiments are properly respected, there is good reason to extend and improve the use of animal models in the field of antibacterial drugs, as a basis for carefully planned clinical research.

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each of the published series the treatment of bone and joint infections predominated, with occasional cases of systemic fungal infection, endocarditis, and other deep seated infections (Frame, 1982). Outpatient intravenous antibiotic therapy is being increasingly used (in our institution we now treat sixty to seventy patients per year in this way) and this rapid growth may be related to economic and social factors.

The outpatient intravenous antibiotic programme shares similarities with a number of other 'new' outpatient programmes, such as total parenteral nutrition, outpatient intravenous chemotherapy, continuous ambulatory peritoneal dialysis, home haemodialysis and self-administration of antihaeomophilic globulin. In each of these therapies common issues have to be addressed, such as patient selection, education and follow-up. All demand a team approach with careful integration of a number of hospital services, as well as increased responsibility on the patient's part for self-care.

In the outpatient intravenous antibiotic programme the typical patient is a young adult with osteomyelitis, who has had two weeks of intravenous antibiotic therapy in the hospital, all appropriate surgical procedures, and is clinically improving. The patient, and whenever possible another member of the family, is taught the technique of intravenous antibiotic self-administration by a specially trained nurse. The antibiotics are prepackaged in Viaflex infusion 'mini' bags (Baxter Travenol Laboratories, Morton Grove, Illinois, U.S.A.) and the antibiotic is usually administered via a peripheral intravenous cannula with a heparin lock device. In most instances antibiotics are given on a three- to five-times-a-day regimen, and are timed so as to ensure a good night's sleep. When the patient has successfully completed the educational process, arrangements are made for discharge. Patients receive a prepackaged 48–72 h supply of antibiotics, together with equipment appropriate for intravenous drug administration. Written instructions are provided of what to do in the event of drug infiltration, cannula-associated phlebitis, or other emergency. Patients return to the outpatient department every 48–72 h to change the cannula site, and collect additional supplies of antibiotics. Penicillins and cephalosporins are the antibiotics most frequently used. We have favoured, where appropriate, drugs with relatively long half-lives, as this reduces the number of drug administrations, and thus both the cost and the potential for technical problems.

Patients ages have ranged from two months to 92 years (mean 34 years), and about 25% have been less than 15 years. The duration of outpatient intravenous treatment has ranged from one to 79 days, with a mean of 14 days. Laboratory tests are tailored to the antibiotic being administered but all patients have routine laboratory tests done weekly. No significant problems have been encountered. Most patients have the first 7–14 days of the antibiotic therapy in the hospital, and as they are invariably discharged on the same drug, allergic complications have been infrequent. Compliance has been excellent, and there have been no serious problems associated with intravenous therapy per se.

Cost savings of outpatient, when compared with inpatient, treatment are enormous. We currently estimate a saving of about $5000 per patient treated on our outpatient intravenous antibiotic programme. However, not all insurers, including the U.S. Federal Government's Medicare Program, have firmly grasped the enormous cost savings. Thus, all too frequently, inpatient treatments are, from an insurance standpoint, somewhat better covered than outpatient regimens. However, newly formulated regulations in the U.S. will favour increased usage of outpatient therapy.

Could this approach be applied to the financially-strapped National Health Service? Theoretically, costly hospitalizations solely for intravenous therapy would be circumvented, and hospital beds made available for sicker patients. In order to instigate such a programme a number of problems have to be surmounted, not the least of which is acceptance by the medical and allied professions of the availability and feasibility of such a programme. One might also ask, 'do patients in the United States have too much intravenous therapy? Could many of these patients be treated with oral drugs?' These questions have been addressed indirectly in the paediatric literature citing experience in the treatment of septic arthritis and osteomyelitis with oral therapy (Nelson, 1978). However, this approach too requires careful patient selection, compliance and follow-up.

We treat patients with osteomyelitis (both haematogenous and contiguous), and most patients be treated with oral drugs? These questions have been addressed indirectly in the paediatric literature citing experience in the treatment of septic arthritis and osteomyelitis with oral therapy (Nelson, 1978). However, this approach too requires careful patient selection, compliance and follow-up. We treat patients with osteomyelitis (both haematogenous and contiguous), and most patients with endocarditis, with intravenous drugs for three to six weeks. We feel that such therapy is appropriate and not a misuse of resources.
Our greatest initial concern was the safety issue. We believe that the care with which patients are selected and taught ensures safety. As a generalization, patients in the U.K. receive fewer intravenous drugs than their U.S. counterparts. These differences may be related to styles of practice, inasmuch as in the U.S.A. intravenous therapy is easily accomplished without requiring the presence of a registered nurse or a physician during drug administration. In the U.K. hospital policy may require a physician to administer the first dose of an intravenous antibiotic.

The direct financial benefits of outpatient treatment have already been stated. Additionally, there are the indirect benefits occasioned by the ability to return to work or school, and the intangible benefits of alleviating boredom, worry, and separation from the family. Outpatient intravenous therapy of all kinds could become a reality in the United Kingdom, but to do so one would have to overcome the national disinclination for intravenous drug administration, and organize programmes in regional centres with teams of interested physicians, nurses and pharmacists.

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