health care and of improving efficiency. Bravely and rightly the editors put these questions, even though their answers are less than wholly satisfactory. So far as equity is concerned the NHS does appear to be moving in the right direction. The geographical distribution of resources, prompted by the much criticised RAWP formula, is becoming more even, if very slowly. Indeed the performance of the NHS is rather better than the editors concede: they ignore the evidence that equity in terms of access to primary health care has been achieved even allowing for differences in need among social classes, though of course qualitative differences in the care received may still persist.[2] But the evidence about efficiency, reviewed in *Health Care UK 1984*, is more ambiguous. If costs per case are declining, and if lengths of stay are falling, does this mean that standards of care are being reduced or that efficiency is increasing? Like the government's own massive tome on performance indicators[3] this compendium is better at prompting speculation than in providing an answer on issues such as these, even though it invokes the help of a variety of specialist contributors who provide background papers on some of the topics covered.

Presumably *Health Care UK 1984* is designed to become an annual event, and indeed much of its usefulness would be lost if the information were not to be brought up to date regularly. Its value lies not only in making a vast mass of data readily accessible but also in providing a moving picture of trends and developments. The main advantage, however, that the editors have brought to the production of their first issue—the fact that, free from all institutional entanglements in the NHS, they have been able to take risks in interpreting the data—may turn out to be a perishable commodity. There will always be a place for a compendium of existing data which brings official statistics and academic research to a wider audience. But in the long run it is the quality of analysis which matters. If the notion of evaluating the performance of the NHS—or of health care policies in the wider sense—remains elusive, it is largely because the conceptual groundwork has not been done[4]—a weakness which undermines the government's own performance indicators exercise as much as it affects this attempt at audit.

The existence of this intellectual vacuum is a formidable indictment of the Department of Health and Social Security's research policies over the decades and of the Medical Research Council's health services research programme in recent years. In retrospect the government's failure to adopt the recommendation of the Royal Commission on the National Health Service for the creation of an Institute of Health Services Research seems even more puzzling now than it did at the time.[5] Perhaps the DHSS's new Health Services Supervisory Board—established in the wake of the Griffiths report[6]—will set up the kind of institution needed to develop both the conceptual framework and the tools required if health care policies are to be properly evaluated. Certainly it is difficult to see how the board can carry out its job effectively in the absence of such an analysis of performance: it would be a company board without a balance sheet. In the mean time, however, its members will have to make do with *Health Care UK 1984* and, for the time being at least, they could do a great deal worse.

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Combinations of β lactam antibiotics

Combinations of antibiotics are often used in treating serious infections, particularly when the infecting organism is not known and when the range of possible pathogens is very wide. Two antibiotics may provide increased broad spectrum cover and may give a synergistic effect against the infecting organism.[1] One such combination widely used is a β lactam antibiotic plus an aminoglycoside, and synergy between these two classes of antibiotics may readily be shown in the laboratory. Almost certainly this in vitro effect is translated into clinical benefit for the patient.[2]

Nevertheless, aminoglycoside toxicity may be a serious problem with such treatment. These antibiotics are often given to seriously ill patients who may have poor renal function and to immunocompromised patients who may receive prolonged or repeated courses of treatment. In such circumstances an alternative line is to give two β lactam antibiotics together—for example, an antipseudomonal penicillin plus a β-lactamase stable, broad spectrum cephalosporin. A theoretical result of such a combination is an interaction between β lactams. Is this possibility likely to be of clinical importance?

Laboratory studies of the effects of combinations of β lactams on large numbers of bacterial isolates have shown mostly indifference or merely an additive effect. Occasionally, however, synergy or antagonism has been seen.[3-6] At least two mechanisms may explain synergy. Firstly, different compounds may act at different target sites—the penicillin binding proteins in the bacterial cell wall—and sequentially interfere with synthesis of the cell wall. For example, mecillinam is synergistic with a range of other β lactams, including benzylpenicillin, ampicillin, carbenicillin, cephalothin, and cephazolin.[7 8] Mecillinam acts mainly at penicillin binding protein two, while the other agents act mainly at one and three. Unfortunately, most β lactams act at penicillin binding proteins one and three,[9] so that this type of synergy is uncommon. Nevertheless, Grunberg *et al* showed that the interaction occurred in vivo in experimental infections in mice.[8]

A second and more common mechanism of synergy is due to the inhibition of bacterial β-lactamases by some β lactam antibiotics. Three requirements have been defined for synergistic action between β lactams against a given micro-organism[3]: firstly, the organism should produce β-lactamase; secondly, the β-lactamase must be capable of hydrolysing one of the agents (that is, that the organism must be resistant to that agent by virtue of β-lactamase production); and, finally, the other agent must be stable to and inhibit the β-lactamase concerned. Certain types of β-lactamase may be inhibited by many β lactams, including cloxacillin, nafcillin, carbenicillin,

cefoxitin, latamoxef (moxalactam), and thienamycin, as well as the "specialist" β-lactamase inhibitors clavulanic acid and sulbactam.[10-13] Given the above criteria the occurrence of synergy between β lactams should be predictable, and Farrar and Newsome showed that in general this is the case,[11] though some expected effects do not always occur.[10]

Little clinical work has been reported with synergistic combinations of β lactams, though Sabath and his coworkers treated 17 episodes of "complicated" urinary tract infection with synergistic combinations of penicillins with cure or appreciable improvement in 71%.[14]

Antagonism between β lactam antibiotics may readily be shown in the laboratory. Many strains of Gram negative bacilli possess inducible β-lactamases. Such strains produce small amounts of β-lactamase in the uninduced state, but in the presence of an inducing agent (for example, certain β lactam antibiotics) they vastly increase their production of β-lactamase and so become resistant to a wide range of penicillins and cephalosporins. When the inducing agent is removed production of the enzyme reverts to the uninduced low rate. Induction of β-lactamase by the antagonising antibiotic is one explanation of the antagonism of penicillins and cephalosporins by other β lactams.[15-19]

Once induced, production of β-lactamases may have two possible effects. Firstly, the antagonised drug may be hydrolysed by the enzyme and thereby rendered inactive. Alternatively, even if the antagonised agent is not susceptible to hydrolysis by β-lactamase it may still be bound by the enzyme, thus preventing access to the target penicillin binding proteins. This has been termed the barrier or sponge effect. Both of these effects occur in the laboratory.[20-22]

Under what conditions is antagonism between two β lactams most likely to occur? Firstly, one agent must be a good inducer of β-lactamase. Many of the newer β-lactamase stable cephalosporins are good inducers—indeed, it may be this very property of high stability that makes them good inducers.[22 23] The organism concerned must possess an inducible β-lactamase capable of hydrolysing or binding to the antagonised drug. Organisms which commonly possess these inducible enzymes include *Pseudomonas aeruginosa*, species of *Enterobacter*, *Serratia marcescens*, and indole positive *Proteus*[21 22]—all organisms often implicated in outbreaks of hospital infection. Nor is induced, reversible resistance the only anxiety: stably resistant organisms have been isolated from patients treated with many of the newer cephalosporins, and this resistance has led to failure of treatment.[22 24-26] Probably resistance to even the new, highly β-lactamase stable cephalosporins could become widespread if these agents are used too readily.

The relevance of antagonism between β lactams has mainly been studied in animals. Goering and his colleagues showed that the dose of cephamandole or carbenicillin required to protect half the mice infected with a strain of *Enterobacter cloacae* was substantially increased in the presence of cefoxitin.[27] This antagonism was not due to the selection of a subpopulation of resistant organisms. The resistance was reversible and dependent on the presence of cefoxitin. Cultures from mice treated with cephamandole alone, however, yielded *E cloacae* permanently resistant to cephamandole in 87% of the animals treated. Cefoxitin also antagonised the protective effect of carbenicillin in mice infected with *Ps aeruginosa*.[27]

Unfortunately, far fewer studies have examined the clinical efficacy of treatment with two β lactams than have studied combinations of aminoglycoside plus β lactam. Three randomised studies which have compared these two types of combination have shown similar cure rates in all groups of patients.[28-30] Only one of these studies looked at the effect of synergistic combinations on cure rates, and the authors were unable to draw a conclusion owing to the small numbers.[28] No study looked at the effect of antagonism.

Thus, though synergy or antagonism between β lactams may occur, the final effect depends very much on the particular combination used and the characteristics of the organism concerned. Since antagonism between penicillins and cephalosporins may have clinical importance, and since treatment is often started before the infecting organism is known, β lactam combinations are best avoided until clinical trials have shown a definite advantage over a single β lactam or a β lactam plus an aminoglycoside. Furthermore, the third generation cephalosporins should be used with discretion, since some bacteria can be induced to become resistant to all of them.

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Self help

"One of my clients has a daughter with Pierre Robin's syndrome and would like to be put in contact with other parents in similar circumstances"—letter in "Health Visitors' Association Journal"[1]

Over half a million self help groups are said to exist in the United States,[2] and when the *Sunday Times* published its first edition of the *Self Help Directory* in 1975 it sold out and has since run to three editions.[3] The recently founded College of Health offers to its subscribers "information services on self help groups," as well as other benefits for the £10 membership, and the 1983 *GP Guide* includes 17 pages of addresses of self help organisations for family doctors' reference.[4] The monthly *Mother and Baby Magazine* regularly publishes a page of 62 addresses to which its readers can apply for help and support (from the Association for Improvement of Maternity Services to the Vegetarian Society of the United Kingdom) and the agony aunts of the popular women's magazines are thought to deal with 10 000 letters a week from readers who want more information about their illnesses and treatment.[5]

Clearly the public has a vast appetite for information about illness. The conclusion must be that because we live in a literate society communication by the written word is ever more necessary to supplement what has been said by word of mouth: the doctor's consultation alone is not enough. Doctor-patient contacts may be too brief to satisfy all the questions that need answering, patients may want to feel self reliant,[6] have a second opinion,[5] solve a common problem through mutual aid,[6] or exchange information and support to alleviate feelings of isolation brought about by illness or disaster in the family. These are not unreasonable aspirations.

Can a family doctor who has not actually had a diabetic child in his own family understand and anticipate all the day to day problems of management that the diagnosis will bring to the parents? Or can he provide lifelong emotional support for the parents of a baby with Down's syndrome? Or can he cope from personal experience with the ever recurrent problems of the alcoholic, the gambler, the paraplegic, or patients with multiple sclerosis, mastectomy, or eczema? The general practitioner may well be the constant provider of primary medical care, but in contemporary society he can be neither omniscient nor omnipotent with regard to all its ills.

For many people a self help organisation may offer a special lifeline, a companion, comfort, a source of practical help, and an easing of the burden that is not provided by any other source of medical or social care.[6] It may provide people with their only opportunity to stand on their own feet and be independent from what they see as stigmatising help from the many arms of the welfare state.[6] This sort of help may be seen as a "welcome alternative to the expensive services of paid professionals" if it provides effective support for those with particular socioeconomic problems—the single parent, the carer for elderly relatives, the homeless, and the relatives of patients with physical and mental handicaps.[6]

Organisations of this kind are developing rapidly—and not on the initiative of the medical professions. One recent survey showed that only 18% of the people concerned had heard of their self help organisation through their doctor or health visitor; most had learnt of the help available through word of mouth, newspaper, magazine, statutory organisation, or the Citizen's Advice Bureau.[6]

Most, if not all, mutual aid organisations and most local groups provide a similar range of activities for their members: leaflets, booklets, magazines, newsletters, and reading lists, meetings and social occasions—all of which help to provide mutual support and exchange of information. Direct services may be available to help with practical problems. Some organisations collect funds for research, while others are active in political work to improve statutory services and stimulate the greater understanding of members' needs.[6]

Mutual aid organisations need be neither feared nor viewed with suspicion by the medical establishment—indeed, without their help many of our patients would be the poorer served and medical as well as social research much less well endowed. Many local authorities employ community workers to liaise with and advise local voluntary organisations. Experienced health visitors and medical social workers build up contacts with those organisations that have provided effective help. The British Red Cross Society, the Citizen's Advice Bureau, and the Women's Royal Voluntary Service may all refer requests for help to the appropriate self help organisation. From Action Against Allergy to Women's National Cancer Control Campaign and from Age Concern to Women's Aid, the alphabetical lists available in the various directories encompass diseases and disorders from asthma to thalassaemia and from anorexia to tetraplegia.[3 4 7–14] Their leaflets are obtainable for the surgery or outpatient waiting area display, their staff are often of inestimable help to our patients, and their services, information, guidance, and support are an essential complement to what the doctor can provide.

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