regional capabilities, especially when dealing with sources of technology and finance.

United Nations agencies are increasingly under pressure from developing countries, not only to help them develop more efficient strategies, but also to assist in developing a multisectoral approach to the solutions. In December 1976, a task force of United Nations agencies (WHO, UNIDO, UNCTAD, UNDP, UNICEF and UNAPEC) began working 'to provide a coordinated response by the United Nations system to the needs of the developing countries in the pharmaceutical sector'.

WHO, together with other United Nations agencies, is participating in a project entitled 'Economic and Technical Cooperation among Developing Countries in the Pharmaceutical Sector', the executing agency being the Government of Guyana. This project is unique in its nature and approach.

WHO has initiated, within its drug policies and management programme, an action programme on essential drugs, which is a comprehensive response to the unbalanced economic and technological situation between developed and developing countries in the pharmaceutical sector. This programme forms part of the strategy for implementing the aim of health for all by the year 2000.

In short, pharmaceuticals is one of the components of the health sector where a move has been made towards achieving the objectives of the New International Economic Order. This is true as regards the development of appropriate technology (drawing up lists of essential drugs and improving their utilization), the transfer of such technology (concerning the production and control of essential drugs), and better trade (through bulk purchasing agreements and strengthening the bargaining power of developing countries). In this field there has been both technical cooperation among developing countries (preparing consolidated lists of essential drugs, regional and subregional cooperation on drug quality control arrangements) and economic cooperation among developing countries (trade and financial agreements and price information and transfer agreements).

The activities in pharmaceuticals, although oriented to health, are multisectoral in nature, with implications that are of social, economic and technological relevance, and these activities may perhaps serve as examples for sectors other than health. It is for the developing countries themselves to decide on such matters as which drugs they need and in what quantities, the precise way in which they are to be utilized, how they are to be supplied, and where and how drug quality is to be controlled. What is needed now is the transfer of resources to help developing countries to establish their own pharmaceutical supply systems appropriate to their needs.

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Cost effectiveness of prophylaxis of venous thromboembolism

Venous thromboembolism is a common complication of surgical operations. It frequently arises in patients in whom other risk factors are present. These include advanced age, obesity, malignant disease, cardiac failure, a previous history of venous disorders, immobilization, the use of oestrogen-containing oral contraceptive preparations, and trauma to the pelvic region or lower extremities.

It is estimated (Coon *et al.* 1973) that in the United States, each year, some quarter of a million new cases of deep vein thrombosis (DVT) become clinically apparent and that up to 200 000 deaths occur due primarily to pulmonary embolism (PE). An estimated 7 million people suffer from stasis changes following venous thrombosis and perhaps half a million of these have frank venous ulceration. Early studies by Morrell *et al.* (1963) from Oxford suggest that the incidence of venous thromboembolism is increasing, and that the increase is not just a manifestation of greater awareness resulting from improved diagnostic methods.

A recent report (Salzman & Davies 1980) from the Department of Surgery at Harvard Medical School has attempted to analyse the cost and effectiveness of several methods of prevention in patients at risk of developing venous thromboembolism.

In the introduction, the authors point out that the literature on the prophylaxis of venous thromboembolism is legion and that the results of apparently similar studies may often be conflicting and, therefore, confusing to the practitioner. The relatively recent advent of investigations such as ^{125}I-fibrinogen scanning of the legs, ascending phlebography, Doppler ultrasound and impedance plethysmography, ventilation/perfusion lung scanning and pulmonary angiography, has improved diagnostic accuracy. Detection of venous thromboembolism by these

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means should lead to treatment earlier in the disease's natural history, with probable subsequent reduction of both morbidity and mortality. Thus in trials of prophylactic regimes, where such tests are employed for the diagnosis of thromboembolism, the results obtained will necessarily represent not only the effectiveness of prophylaxis but also the benefits accrued from the diagnostic method itself.

Such results, therefore, may not be directly translated into routine practice, where clinical examination is often the only diagnostic method available.

In an effort to compensate for these apparent discrepancies, a cost-benefit analysis has been constructed for the commonly used methods of prophylaxis. It encompasses results in patients in whom several physical and therapeutic prophylactic regimes were used, those in whom surveillance alone was employed, and those in whom no prophylaxis was offered.

The study population consists of two groups of 'at risk' patients: those undergoing general surgery, and those receiving total hip replacement. The latter group has specifically been selected to exemplify patients known to be at especially high risk. The analysis has been made by using aggregate figures, compiled from all the apparently similar published controlled studies. The method of analysis used ensures that the trials encompassing the largest numbers of patients are afforded particular attention. Such an approach to analysis in the aggregate is offered only as a working guide; it is of course tentative and subject to revision, depending on the result of future well-conducted prospective clinical trials. The reader is referred back to the original publication (Salzman & Davies 1980) for the derivation of the figures quoted below.

Since there appears to be a similar incidence of venous thromboembolism on both sides of the Atlantic, it seems pertinent to consider closely the findings of the analysis and relate it to our own practices, substituting the British cost equivalent for the US estimate. Obviously, health service economics differ considerably between the two countries, and this discrepancy means that direct comparison of the costs to each country or to each patient for each regime is not simple. Also, costs may vary from region to region within the United Kingdom; minor variations shall not seriously affect the outcome of such an analysis.

It can be predicted (Salzman & Davies 1980) that among general surgical patients over 40 years of age, undergoing abdominal operations, without the benefits of prophylaxis or surveillance, clinically obvious DVT will be detected in 3.5% of patients, and clinically obvious pulmonary embolism in 1.8%. An additional 23% will have silent (and, therefore, unrecognized) venous thrombi, and a similar percentage, asymptomatic pulmonary embolism. An estimated 10 deaths from pulmonary embolism will occur per 1000 such patients, in only 6 of which will the embolus have been clinically diagnosed before death.

Similarly, at least 18 deaths per 1000 patients undergoing total hip replacement can be expected if no form of prophylaxis or surveillance is used.

Using the costs and charges likely to be encountered by a United Kingdom teaching hospital, it is possible to estimate typical costs of complications in these patients. These would include, in patients developing deep vein thrombosis, the cost of anticoagulation and the extra period in hospital that would usually be incurred. Patients suffering pulmonary emboli would be expected to be additionally investigated with a chest X-ray, blood gases, an electrocardiogram, enzyme estimations, and probably a ventilation lung scan. The typical cost to a hospital of a deep vein thrombosis would thus be in the region of £175, whereas a pulmonary embolism would cost £350.

In addition to these typical costs, many patients might receive other investigations or treatments. For example, most patients, on suspicion of developing a deep vein thrombosis would have a phlebogram performed at an extra charge to the hospital of approximately £35–£50. ^{125}I-fibrinogen calf scanning costs about £16 for two days. Patients suspected of developing pulmonary embolism might be referred for perfusion lung scans or pulmonary angiography, at about £45 per investigation. Intensive care treatment would cost £210 per week, while a 72-hour course of streptokinase would be in excess of £350.

The cost of radiological investigation does not take into account a physician's fee or salary. These are difficult to cost in Great Britain and have been excluded from the analysis for this reason. Such figures are more readily available in the USA and were included in the original costing (Salzman & Davies 1980). The charges used in this analysis are those that might reasonably be expected to be incurred by the hospital and are as estimated by a leading health insurance company. The cost of a pulmonary embolectomy would be in excess of £1500, based on a compilation presented by Monro *et al.* (1978).

Costs of various prophylactic regimes in the United Kingdom have also been computed. These would include approximately £15 per patient for a 7-day course of low dose heparin, £4-£16 for dextran prophylaxis, depending on the regimen selected, £5.60 for external pneumatic compression of the calves, £24 for warfarin prophylaxis and 5p for 7 days prophylaxis with aspirin.

Figures derived from the literature would suggest that, if no prophylaxis is employed, 35 clinically obvious deep vein thrombi and 18 clinically obvious pulmonary emboli might be expected to be encountered per 1000 general surgical operations. Ten deaths would be expected, six from clinically obvious pulmonary embolism and 4 attributable to silent embolism. Whereas, for every 1000 total hip replacements, 120 clinically obvious DVTs may be expected and 110 clinically obvious emboli. Eighteen deaths might be expected from venous thromboembolism in this group, of which one is likely to be attributable to complications of anticoagulation. This would imply a cost to the nation of nearly £12 500 for every 1000 general surgical operations performed and nearly £60 000 for every 1000 total hip replacements, in terms of the development of DVT and pulmonary embolism, should no form of prophylaxis be used.

If ^{125}I-fibrinogen scanning were to be employed in general surgical patients, with a view to providing early detection of postoperative thrombosis, anticoagulant treatment would normally be instigated before embolism occurred. Under such circumstances, a further 235 patients per thousand would be diagnosed as having DVT, all having previously been undiagnosed. If all these patients with DVT were given routine anticoagulant therapy, the death rate due to pulmonary embolism would be reduced by 9 per thousand; one death per thousand would be expected, due to haemorrhagic complications of anticoagulation, which would have been employed in more than 27% of patients.

Unfortunately, such a reduction in mortality in general surgical patients would cost £65 000 per thousand patients with a net cost of nearly £5000 per life saved.

Experience with surveillance alone for detection of thrombosis in total hip replacement patients is too limited to allow justifiable analysis. Prohibitive cost would seem likely to preclude its use as a routine method of reducing mortality in such patients.

Prophylaxis with low-dose subcutaneous heparin or, alternatively, external pneumatic compression of the calves with inflatable boots appears highly effective in the general surgical population. The expected mortality could be reduced to fewer than 3 per 1000. The cost of such action, when compared to the overall cost of taking no preventive steps, would be in the region of £1000 per death averted in the case of low-dose heparin, and even less if external pneumatic compression were to be used. The disadvantages of the latter method appear to relate to patient acceptability and tolerance, since it is probably mandatory to continue using the method in the postoperative period until the patient is ambulant.

Low-dose heparin does not appear as effective as other available agents for the prevention of deep vein thrombosis after total hip replacement. Its efficacy in preventing proximal thrombi, perhaps initiated by endothelial damage adjacent to the site of the operation, does not match its effectiveness in general surgical patients. Four lives per thousand hip replacements may be expected to be saved, at a cost of £4000 per death averted. The use of heparin in conjunction with other agents, such as dihydroergotamine, requires further assessment, as does pneumatic calf compression in total hip replacement patients.

The cumulative figures suggest that dextran is likely to be less effective than either low-dose heparin or pneumatic calf compression in general surgical patients, besides being more costly. Dextran is considerably cheaper in the UK than in the USA, approaching low-dose heparin in cost, but the apparent discrepancy in effectiveness remains.

Neither aspirin nor warfarin appears to have a part to play in routine prophylaxis in the general surgical population, the former because of the contradictory literature regarding its use, and the latter because of the unacceptable frequency of haemorrhagic side effects compared with the benefit in terms of preventing thrombosis.

Dextran, warfarin and aspirin all appear able to reduce significantly the number of fatal pulmonary emboli in patients undergoing total hip replacement. The cost of their use is trivial compared to the number of lives saved and to the cost of treating thromboembolic complications which would otherwise be encountered. Dextran appears equivalent in cost to warfarin in the United Kingdom. The use of either of these two agents saves about 10 lives per 1000 hip replacements and reduces the cost in terms of venous thromboembolism by about half. Dextran prophylaxis is probably associated less often with haemorrhagic side-effects than is warfarin; with the latter agent, nearly one-half of the expected deaths will be attributable to the haemorrhagic side effects of the drug itself. However, in these patients, at very high risk of thromboembolism, the inevitable increase in bleeding that accompanies the use of warfarin is probably offset by its superior antithrombotic efficacy.

Aspirin appears to be most effective in male patients, in whom it has been shown to be efficacious after hip replacement (Harris *et al.* 1977). The basis for the sex difference in its antithrombotic activity is unknown. It is the least expensive of the prophylactic agents and involves costs as little as one-third of those incurred when no prophylaxis is used. The rate of fatal pulmonary emboli occurring with aspirin appears to be extremely low.

The conclusions from such an analysis are made in the face of incomplete understanding of the problem of preventing venous thromboembolism. It would appear that low-dose heparin or external pneumatic calf compression are the methods of choice for prophylaxis in the general surgical patient over the age of 40, whereas warfarin or antiplatelet agents may be indicated in patients undergoing total hip replacement. These recommendations are not necessarily final and are open to change as the result of future studies. The most suitable prophylactic regimes for other patient groups remain to be determined.

Consideration of cost effectiveness, as distinguished from efficacy alone, is relevant in the United Kingdom, as well as in the USA. Prophylaxis against venous thromboembolism should be employed more widely; it is a cost effective form of preventive medicine.

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What should be done about schizophrenia?

Schizophrenia remains one of the most intractable of all problems facing patients, their relatives and the health services. The neuroleptic drugs, starting with chlorpromazine and leading up to the present long-acting depot preparations, have had an enormous impact on the disease. Without them the policy of emptying the long-stay mental hospitals could not even have been contemplated. But anyone who is a member of or close to a family in which there is a neuroleptic-treated schizophrenic is fully aware that such drugs are far from providing a full answer. Complete normality is almost never obtained, and the side effects can be distressing and severe. Rarely does one see a drug-treated schizophrenic fulfilling the potential apparent when he or she was, say, in the mid-teens. If employment is possible, the type of work is often menial, trivial and insecure. Particularly disturbing at present is the spectre of tardive dyskinesia, a side effect of treatment which is exceedingly distressing, which invariably initially worsens on drug withdrawal, and which in many may never be fully reversed. There is still much argument about how many drug-treated schizophrenics develop tardive dyskinesia, and how reversible it is, but there is little dispute that a serious crisis in psychiatric treatment is looming.

In the face of these problems, what is to be done? A complete solution would probably – though not necessarily – require full understanding of the aetiology of the disease, a topic about which there is no agreement. Some believe that schizophrenia develops in the context of a particular type of family structure, some that it requires a particular type of social environment, some that it is caused by a biochemical defect, and some that is does not exist. Many find partial validity in most of the available hypotheses and recommend a mixed approach to treatment. The average well-adjusted British psychiatrist might therefore recommend judicious use of drugs coupled with an emphasis on social measures to regulate the patient's environment both in and out of the home. Unfortunately for the schizophrenic and his or her family, the outcome is too often thoroughly unsatisfactory. The improvement achieved by the drugs is limited, severe strains are placed on the family attempting to provide a suitable environment for a person whose susceptibility to stress may be utterly unreasonable, and the social and community services are inappropriate or do not exist.

In the mental health community the Schizophrenia Association of Great Britain (SAGB) strikes what to many seems a strident and discordant note. The SAGB is an organization of lay people, largely relatives and friends of schizophrenics and schizophrenics themselves. They have dared to challenge the well-balanced views of the mental health experts by coming out unequivocally in favour of the view that schizophrenia is a disease which has a biochemical cause, and which therefore will have a biochemical solution. They will have nothing to do with the family and social views of the causation of schizophrenia. They argue that by far the most urgent priority is to fund research to find the biochemical cause of the disease, since that will almost certainly lead to a genuine cure. They have little time for the multifactorial concepts of the establishment, except in the sense that schizophrenia may have a number of different

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