

MEDICINES IN THE 1990's a technological forecast



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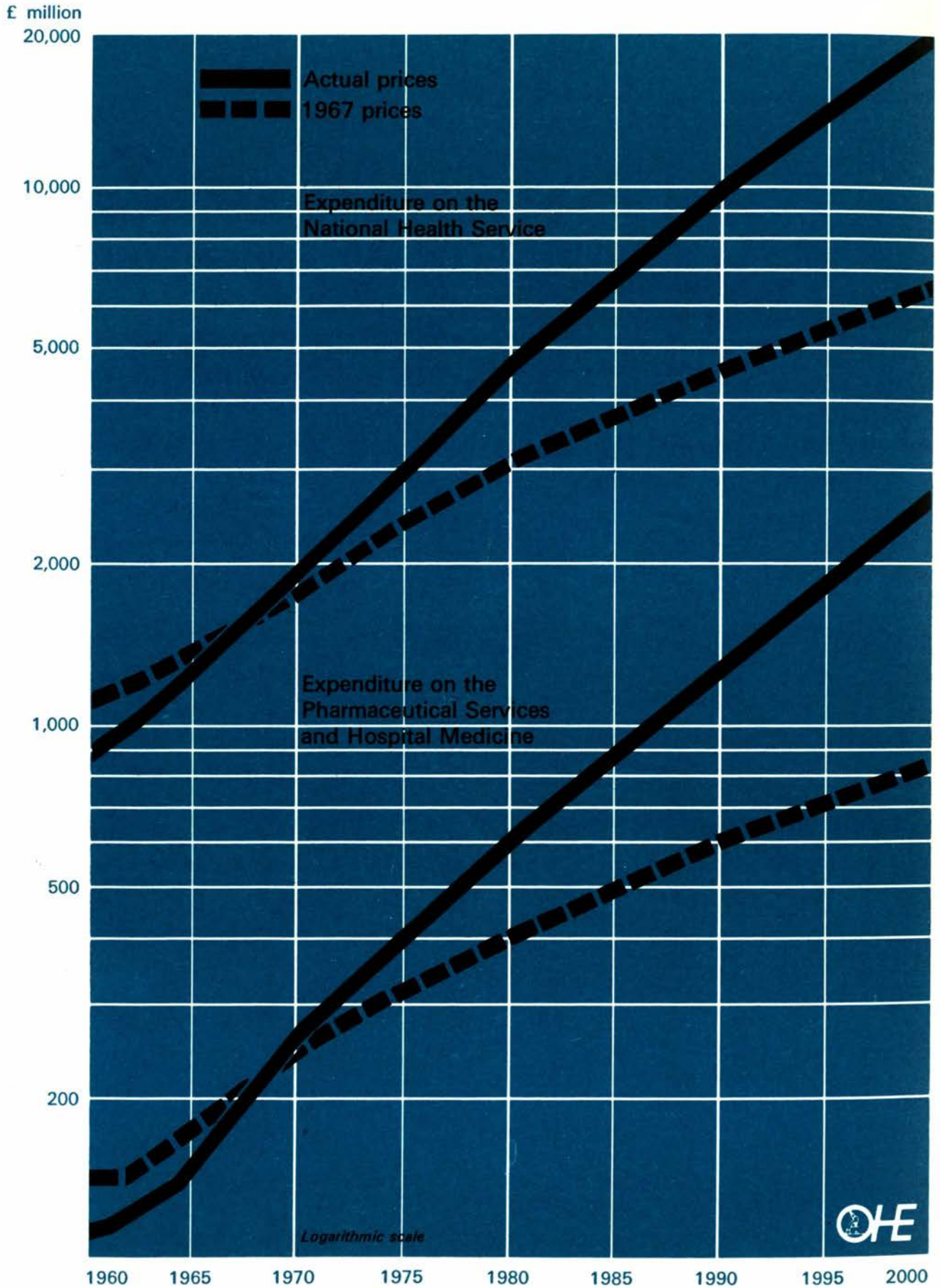
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Estimated expenditure on the National Health Service and the Pharmaceutical Services and Hospital Medicine, U.K., 1960 to 2000



By 1990, the total cost of the National Health Service will probably have reached about £10,000 million of which about £1,300 million will be for medicines prescribed by general practitioners and hospital doctors. (Figure I). At 1968 prices the corresponding figures would be about £4,500 million and £600 million. These calculations are based on the assumption that the Health Service (or its successor) will slowly continue to increase its share of the steadily rising national income. Its proportion rose from 4·04 per cent in 1958 to 5·12 per cent in 1967 and we predict that as society becomes more affluent it will continue upwards to 7·5 per cent in 1990. Pharmaceuticals are expected to maintain their steady share of total health service expenditure of about 13 per cent.*

This technological forecast predicts the progress which may be expected by that time. It also forecasts related changes in the pharmaceutical industry and in the practice of medicine. It is primarily a medical forecast and therefore drew mainly on medical expertise; perhaps on reflection it is regrettable that it did not draw more on other professions also.

The forecast was produced by a modification of what is called the 'Delphi' technique. The panel of experts listed in Appendix II volunteered to make forecasts on those of the subjects from the checklist in Appendix III on which they had special knowledge. The individual forecasts under each heading were then consolidated with the inclusion of conflicting forecasts when these arose. The resulting draft was sent out for comment to all the experts. In general this produced a rather satisfying result. Half a dozen or so of the original forecasts were each picked out as being technically invalid by a number of experts, and were, therefore, rejected. Many of the comments either clarified or developed the forecasts. The only difficulty arose in cases where entirely new forecasts or completely opposite opinions were offered by single individuals at this second stage; some – particularly the more off-beat suggestions – were left out because it was impracticable for them to be scrutinised by the other experts in yet a further round of consultation. Finally, the whole forecast was read by the OHE Editorial Board, and a number of points clarified in the light of their comments.

The resulting forecast is inevitably somewhat uneven. In places there is considerable detail while elsewhere it is in very general terms. Although most of the forecasts refer primarily to Britain, it was necessary in predicting, for example, the structure of the industry and its relationships with government to view the situation internationally. Some of the forecasts are dramatic, others mundane. But

despite this a clear and interesting picture emerges on many aspects of the progress and problems which can be expected. If it does no more, this booklet will remind those who read it of the benefits to society which can be hoped for if scientific and technical resources can successfully be applied in the health field. Above all, it highlights some of the sociological problems which may arise as pharmacology moves into new fields.

In making the forecast, contributors have, of course, made certain basic assumptions. First, that there will be continued national and international economic growth at roughly the same rates as over the past two decades. Second, that there will be reasonable political stability and that the basic social and economic structure of the Western world will not change fundamentally; however much the organisation of the National Health Service in Britain may change, health will continue to be regarded largely as a community responsibility. As is clear in the detailed discussion which follows, it has been assumed that the fruits of medical and pharmaceutical research will continue to be enjoyed internationally; thus the vast resources for health research in the United States will continue, as in the past, to supplement our own achievements in Europe. It has also been assumed that the necessary scientific manpower will be available internationally for the expanded research facilities both in the universities and in industry. Obviously all these assumptions depend on very much wider considerations than would fall within the scope of this forecast and no attempt is made to justify them.

Finally, I would like to thank all those who have helped in preparing this forecast for the time and effort which they have given to it. Their having helped does not, of course, commit them individually to any of the views expressed; but without their collective work the forecast would have been impossible.

GEORGE TEELING-SMITH

*The detailed bases of the calculations on which these predictions are made are given in Appendix I.

forecasts on disease headings

a Bacterial infections

In bacterial infections there are likely to be many small changes but few big ones over the next 20 years. However, by the 1980s there should have been significant progress in the control of chronic recurring infections such as those associated with progressive deterioration in bronchitis and renal disease. (Chronic bronchitis itself is not a bacterial disease, although it is normally associated with intermittent bacterial infections).

The range of available antibiotics will continue to increase. They are likely to be cheaper and more convenient and also in many cases more specific. The first such products should have been fully evaluated and entering clinical practice by the early 1970s. Subsequently, the search for new anti-bacterial substances should become progressively less empirical, more research being directed first to discovering the mechanisms of bacterial infection and then to neutralizing them. This should lead to a new generation of antibacterial substances by the 1980s.

However, in progressive recurrent infections factors other than the actual infection are important, and this will be increasingly recognised. Environmental control in particular is important. The pollution control and 'clean air' policies now being implemented are not expected to be completed until 1990; their benefits will be evident by then but will not be fully realised until the 21st Century. On smoking, fully effective cigarette filters may be available by the mid-1970s, but public resistance will probably prevent their compulsory introduction for another decade. There are other factors also; it will be increasingly important to study the infection in the context of the patient's circumstances: for example, the susceptibility of the elderly to bacterial infection.

Progress is likely to come in two main stages. First, a better understanding of the natural history of chronic infections, more prompt and precise use of currently available antibiotics and present pollution control should start to bring a significant reduction in the numbers suffering progressive deterioration from recurrent infections by the mid-1970s. This period of several years will be required for existing knowledge and available techniques to be applied more generally and for the long-term dangers arising from acute infections to be generally recognised. The benefits in terms of fewer persons becoming 'respiratory cripples' and fewer people requiring renal dialysis or kidney transplants will be felt by the late 1970s and the 1980s. By that time progressive pyelonephritis in the under 20s, for example, may have been arrested.

The second stage of progress will come with the introduction of more specific antibacterial sub-

stances, resulting from research at present under way. Education on the use of these new compounds will start in the 1970s and they will start to bring benefits by the first half of the 1980s. Screening and early diagnosis will also play an important part in this second stage. Routine methods of screening high risk groups (for example, pregnant women for renal infection) should be efficient enough to make them economic by the mid-1970s. By these means early diagnosis and control of urinary infections, for example, will be routine by the 1980s. There will also be progress in identifying additional high risk groups from the individuals' life histories.

Antibiotics will be discovered that are effective against the present resistant organisms such as *Proteus* and *Pseudomonas*, which are important in both renal and respiratory infections. There will also be a better understanding of the process of intracellular survival of bacteria, and of the biochemical bases of harmful hypersensitivity and of autoimmune processes which accompany long-term persistence of bacteria and their products in the tissues. This may affect the therapy of a number of diseases not at present recognised as bacterial in origin. Substances may also be developed which enhance man's natural resistance to infection generally.

So far the greatest progress has been against obviously virulent bacteria; other organisms, which cause less dramatic episodes of disease and which may attack only those who are already debilitated, are likely to yield to therapy in the next two decades. The health benefits which can be achieved by rearing experimental animals in an entirely germ-free environment have already been measured. It is possible that similar benefits will be achieved for man when ways have been found of controlling mildly pathogenic organisms.

The problem of antibiotic resistance is likely to become greater but to be kept within reasonable limits by a better understanding and by specific measures to combat it. From the mid-1970s onwards, antibiotics will increasingly be used in association with antibiograms. In hospitals there will be an overall strategy for the use of antibiotics to limit the risks of cross infection. It has already been indicated that new antibiotics are likely to be more precise and will be used in specific indications, some, for example, only in animals and some only against particular organisms in man. There will also be improvements in public health policy to prevent transfer of organisms between species and to speed up the identification ('typing') of the pathogens responsible for outbreaks of infection. These measures are likely to be introduced as a result of an early increase in the incidence – and particularly awareness – of gastro-enteritis caused by resistant bacteria. This better understanding, the more precise use of antibiotics, their wider range and the

stricter public health measures will prevent any disasters due to antibiotic resistance in the next 20 years.

An interesting development in the field of bacterial disease may be the production of vaccines against the sexually transmitted diseases. These would probably have a greater social effect (in association with oral contraceptives) than they would have medical effect.

b Virus infections

Practically all progress against virus infections has so far come from the development and use of vaccines. Progress in the next five to ten years is likely to consist of further developments in the same field. During the 1970s, however, effective antiviral drugs are likely to be available, at first for use prophylactically and later therapeutically. By 1980, it is probable that ways will have been found to stimulate the body's own production of interferon, although it is not yet clear whether this will be of value in the prevention or in the therapy of virus infections. However, using this basic approach, 'broad spectrum' anti-viral compounds safe enough to use against minor infections will probably be available by 1990. Resistance to antiviral compounds will by then have begun to emerge as a problem similar to that of antibiotic resistance.

With the vaccines, measles is likely to be eradicated within five years. In the same period vaccination against rubella may be routine. During the 1970s a safe and effective mumps vaccine should be available. At the same time influenza vaccination may have been added to routine child immunisation programmes, although it is questionable whether the public will be persuaded to accept the repeated re-vaccination needed to ensure immunity. Improved inactivated vaccines are likely to be available in the early 1970s and safe attenuated vaccines by 1980. A drawback with 'flu vaccine will still be that it will often not contain the appropriate non-resident strains of virus. Consequently, prophylactic chemotherapy may also be used at the approach of an epidemic.

With other respiratory infections, effective vaccination against rhinoviruses is much more difficult because of the large numbers of different serotypes. There is however a possibility of multiple oral vaccines being developed which would be accepted by a public which has always cried out for some answer to the problem of the common cold.

Within five to ten years there should be attenuated vaccines to prevent the syncytial virus infections which cause bronchitis in very young children. To develop such vaccines, it will first be necessary to develop 'laboratory markers' to measure the degree

of attenuation. Although much is already known about the biochemistry of virus replication little is known about the biochemistry of their virulence.

In the case of the viruses causing serum and infective hepatitis, the causal agents should have been isolated and cultured during the next five years. It is not yet clear, however, whether this will lead to the subsequent control of these diseases.

It is certain, however, that virus infections will not be controlled by vaccines alone. There are already a number of antiviral compounds which show some prophylactic action but are too weak to have any therapeutic effect. With respiratory infections, in particular, further progress is likely to come by 1975 with the development of more potent antiviral compounds. This will mean overcoming two problems. First, since (unlike the antibiotics acting on bacteria) antiviral compounds must act on the virus *within* the living cells it is difficult to find a compound which attacks the virus without interfering with the cell metabolism. This is why the first compounds are likely to have a very specific action, and to be effective against only a narrow range of viruses. Second, the peak of replication of the viruses often occurs before symptoms appear; and so, since antiviral compounds are likely to act on the replication process, therapy is much more difficult than prophylaxis. Hence, also, the therapeutic use of antiviral compounds is more likely to be of value in prolonged diseases such as hepatitis. As antiviral agents are likely to be inherently toxic, it is unlikely they would be safe enough for the treatment of minor diseases much before 1990.

By 1980, viruses may have been identified as causal agents in a number of tumours. Study of the so-called 'slow virus diseases' is now beginning. It is not clear, however, whether any effective therapy will emerge from this research.

In a related field, fungal infections may have been identified as a cause, for example, of some respiratory illness and these may be controlled by anti-fungal agents.

c Cancers

Problems in this field are rated at best as difficult, and at worst as extremely difficult. There is unanimity in the forecasts that the basic difficulties reside in the multiplicity of causes and types of cancer, in the fact that there are probably many points in the relevant cell processes where dysfunction can occur, and in the very complex nature of those processes.

The fact that experiments cannot be carried out in man provides another difficulty, especially in relation to cancers caused by viruses. Another

major difficulty in the way of advances in the field of cytotoxic cancer therapy is that of finding an agent that will both harm cancer cells and leave adjacent healthy cells untouched.

One forecast suggests that accidental observations in fields other than that of cancer are more likely to yield fruitful therapeutic results than planned cancer research; and various of the less optimistic forecasts suggest that earlier diagnosis of cancer, and skilful and highly selective combinations of surgery, radiotherapy, immunochemistry and chemotherapy will provide such improvements as are to be attained in this field by 1990. Total organ transplants are seen as one feasible answer to certain cancers: medicines will than be reserved to deal with any secondary cancers while they are still small. According to this group of conservative forecasts, there is likely to be a number of anti-cancer compounds developed, not just one 'wonder' cancer cure.

However, the more optimistic forecasts predict that by the 1980s we shall have achieved, via studies of cell metabolism and genetics, an understanding of the basic processes controlling cell division, and of how chemical, viral, and hormonal carcinogens fit into this process; and we shall have discovered various new factors that can alter the process, more particularly those that are now presumed to be responsible for cancers whose causation is obscure. Following these advances in knowledge, campaigns of prevention will be possible and ways should have been found to make such campaigns more effective than the present one against cigarette smoking. There will also be a variety of therapies for established cancer. It is suggested that by 1990 70 per cent of cancers will be controllable.

From the same group of forecasts comes the suggestion that work on the immune aspects of graft rejection, and on immune responses to certain cancers may also produce quite rapid results. Indeed, both specific and non-specific means of stimulating the body's immune responses (i.e., in this context its cancer-rejection mechanism) are foreseen by 1980.

By 1980, the same more optimistic prophets say, we shall have made some progress with possibly naturally occurring anti-cancer compounds which will be specific to particular types of tumour. It may well happen that the discovery of such new compounds will, if they are specific enough, indicate the aetiology of a particular cancer, which will lead to the development of more accurate research models, and so in time to the development of further new anti-cancer medicines, even more powerful or specific. Again, while only a few cancers will be shown to be caused by viruses, means of stimulating immunity to the antigens of the responsible viruses are foreseen as being available by 1990. And lastly from the

hopeful group comes the suggestion that fruitful work on enzymes, and in particular on asparaginase, will be carried out between 1970 and 1990.

A gloomy view expressed by some is that new cancers will emerge, possibly as fast as existing ones are dealt with, and that these new cancers will prove extremely difficult to control.

d Graft rejection and auto-immune response

The problems implicit in this topic – solutions to them being of crucial importance to progress in transplant surgery – are seen as difficult or very difficult. Indeed, one extreme view is that the body mechanisms involved are so fundamental to human survival that their suppression might even prove impossible. However, because we now have the technical ability to transplant organs, and because failure of a single organ (e.g. the heart) is a not uncommon cause of premature death, the pressures making for progress in this field will be considerable.

The main problem is agreed to be that of suppressing a harmful immune response (say, against a transplanted heart) while not affecting the body's general protective mechanisms, for example against infections. Significant progress will, it is felt, be seen by 1975, and major progress by 1985 or 1990.

An improved anti-lymphocyte serum is thought to be the first likely product of research, but improvements in tissue typing (and in banking of organs) will not be much slower. A more important advance, however, based upon a much better understanding of the basic phenomenon of rejection, will be the production of immuno-suppressive agents of enhanced specificity, which will suppress the undesired immune response while leaving unaffected the general immunological process.

Possibly of equal importance will be the development of *biological* methods of producing immunological tolerance for a specific tissue, again while leaving the general immunological process unaffected.

It is thought impossible that an animal will be bred the tissues of which will be wholly compatible with the great variety of human tissues types, but it may well come about that humans will be injected before or immediately after birth with extracts of animal tissues of the same tissue type as might later be used in giving them organ grafts. This is known to result in the suppression of the normal immune response to subsequent insertions of such tissues into the individual's body. First attempts in this direction – say, in the case of babies with severe congenital heart disease – might take place by 1975. The

tissues used would probably come from animals specially bred to provide organs mechanically suitable for use in humans. (See also Section h).

Advances may however also come from other directions – for instance, from the use of the latest communications techniques to enable tissue typing to be done extremely quickly. Again, by 1990 animal live organ banks should be well established allowing organs to be stored for sufficient time to allow effective transplantations; and a subsequent development will be to grow organs from tissue cultures taken from the patients themselves. It has already been possible to grow a frog from half a lung cell from a frog plus one gamete.

One unusual view is that the ability to graft skin and teeth readily will prove of more value in the relief of human suffering than easy heart transplantation, though as early as 1975 the latter will be used quite widely for irreversible heart disease.

e Congenital abnormalities

The greatest progress towards control of congenital abnormalities will come from a better understanding of their causes, and hence a greater ability to give 'genetic counselling' to prospective parents. Over the next twenty years epidemiological studies will identify many new causative factors, the majority of them environmental. In addition studies over several generations are likely to throw light on inbred genetic factors, such as those which cause porphyria. More accurate diagnoses of virus infections (such as rubella) during pregnancy should also increase the predictability of abnormalities. By 1980 we should see significant reductions in abnormalities due to a better understanding and easier identification of their causes. This may be supplemented by specific tests applied during pregnancy to determine whether the embryo at risk has been affected or not. This, however, presents very difficult problems.

For the abnormalities which still occur, better surgical treatment will be available for physically abnormal children, and replacement chemotherapy should be available to correct some inborn disorders of metabolism affecting brain function. It is not envisaged that any 'molecular engineering' will be feasible on a routine basis by 1990, either to correct genetic abnormalities or to produce specific characteristics in the offspring. However, by then it should be possible to determine (and hence select) the sex of offspring during pregnancy. This could be particularly valuable in veterinary medicine.

On the negative side, vigilance will be needed to avoid accidental, harmful 'molecular engineering' through the use of medicines or, for example, chemical additives to food.

f Endocrine disorders

Very sensitive immunological and physical methods for the quantitative determination of biochemicals and of enzyme activity in all parts of the body will be rapidly developed. This will make it possible to study more closely the pathogenesis of many disorders, in particular the endocrine and metabolic disorders, leading to significant progress in their control. For example, by 1975 diabetes should be completely and reliably controlled by oral agents. The treatment of other conditions, such as thyrotoxicosis and ovarian disease, should also be simplified. Advances in peptide syntheses should make peptide hormones more generally available at economic prices.

It is also possible that atherosclerosis should be considered to be of largely endocrine origin, and that advances in endocrine chemistry may contribute to its control by the 1980s.

g Neurological disorders

Up to the present relatively little research has been done in basic neuropathology and no major leads for research effort are in sight at present. However, work in this field in the future should lead to the control of diseases such as multiple sclerosis. The present experiments with L-dopa in Parkinsonism should stimulate further and fruitful research leading to advances in pharmacology in the 1970s. By 1990, 90 per cent of neurological disorders should be controlled.

For the remainder improved palliative therapy (e.g. cytotoxic compounds for use in the treatment of brain tumours by means of improved perfusion techniques, and medicines for Parkinsonism) should be available.

Also by 1990 effective *prevention* of certain neurological diseases may be possible thanks to study of the slow viruses and other agents that cause them. In addition, one forecast sees the elimination of both epilepsy and migraine as a result of pharmacological treatment and prophylaxis.

However, the next twenty years will see very little improvement in the fundamental treatment of established neurological disease – that is, where damage to the central nervous system has occurred. Various newly identified metabolic disorders will be found responsible for a few cases of mental subnormality by 1975, and advances in genetics will help towards an improved understanding of certain muscular disorders and perhaps by 1990 their prevention.

Fundamental advances will have to wait upon the twenty-first century: for example, one forecast

suggests that the use of very fine metallic filaments as prosthetic replacements for nerves, and nerve channels in the spinal chord, may be possible by 2020.

h Heart disease

By 1990 the possibility of preventing ischaemic (or coronary) heart disease by most of the currently mooted methods will at least have been thoroughly explored. The basic problem is to improve understanding of the factors governing the laying down of fats in the walls of the coronary arteries and the role played by platelets, plasminogen and thrombus formation and lysis.

In the realm of prevention of coronary heart disease five elements are considered: abnormalities of the blood lipids (fats), high blood pressure, diabetes, obesity and cigarette smoking. Other known or suggested risk factors include lack of exercise, an inherited tendency to the disease, and stress; these may be less amenable to control.

As regards blood lipids: the effectiveness of one important cholesterol-lowering medicine will be known by 1975. A definitive answer in respect of the benefits to be obtained from dietary changes affecting blood lipids will not be available before 1980, if then; and in any case there is a very strong and fairly general expectation that medicines and not dietary changes are the most likely means of prophylaxis to be adopted in respect of achieving lower blood lipid levels. By 1975 we should have medicines to decrease the body's absorption or synthesis of lipoproteins.

Whatever means of affecting blood lipids is adopted, a screening process, probably including young adults and children, will be used to identify those with abnormal blood levels.

As regards the second risk factor, a raised blood pressure, it is felt that the results of various trials will soon result in routine screening being offered: by 1980 people will probably be given a blood pressure screening every year, possibly by suitably trained technicians or even by self-measurement. And safe and effective medicines for the control of a high blood pressure will be available, perhaps given in fixed-dose regimens.

Some 5 to 10 per cent of the middle-aged men screened will be found to need blood lipid control (assuming that it does any good) and some 2 per cent of middle-aged and old people screened will need control of blood pressure; but it is estimated that in either case only 50 per cent of those needing such control will adopt and persist in measures needed to secure it. In addition, some 25 per cent of persons who have had an attack of coronary heart

disease will receive treatment aimed at reducing blood lipid levels, though the outlook in such persons will not be as good as in those who have not had an attack.

The association of diabetes with coronary heart disease (and with strokes and disease of the limb arteries) is already established, and by 1975 trials will have proved the value of anti-diabetic treatment in preventing the occurrence of these diseases in border-line diabetics. Once such proof is available, then, as with high blood lipid levels and a raised blood pressure, widespread preventive measures will be undertaken.

The treatment of obesity is already regarded as a medical task, and medicines which effectively 'burn off' excess calories without other undesirable side effects should soon be available. This approach is more likely to be effective than educational measures to improve dietary habits.

It is thought that the present evidence incriminating cigarette smoking will be stronger by 1975 and that by 1990 cigarette consumption, at least in high-risk subjects, may be at only 50 per cent of the present level. Finally, to combat stress there may be ways of controlling the heart action, when necessary, so that emotional overloading does not occur.

By 1975 new medicines should be available to increase the blood's ability to dissolve the fibrin of blood clots. On the other hand, there is probably a less promising future for anticoagulant medicines. There is disagreement as to the effect of the various preventive measures on the incidence and mortality of coronary heart disease, the forecasts ranging from 'an important fall' to no very marked change in the national coronary mortality rate despite all the methods of prevention adopted.

As regards treatment of the disease: in order to combat the very high mortality in the first hour after coronary thrombosis, it may be that a form of treatment will be developed that could be used immediately the patient is seen by his family doctor or possibly even by the patient himself as soon as he had a symptom suggesting an attack. This would give protection for some hours against the dangerous disturbances of the heart's rhythm that commonly occur in this condition; for the patient to use it himself its safety would be important because it would often be used mistakenly for minor conditions. Better blood plasma substitutes, and better pharmacological control of shock will also help in the treatment of the established disease, as will electrical pacing of the heart. These advances will come mostly from the experience gained in intensive coronary care units which will continue for some years but which may, if safe and efficient therapy can be derived, be a passing phase.

By 1990 it should be possible to predict which

people are going to have an attack of coronary thrombosis within a matter of days and to minimise their chances of dying from a sudden disturbance of heart action. Great advances should be made in cardiological diagnosis, using modified ballistograms and doppler shift studies of acceleration of the blood in the aorta. This should make it possible to carry out automated predictive studies for example at three-monthly intervals. These could indicate whether the heart was performing easily or haltingly. Even if this particular approach does not prove successful, it should bring benefits by re-orienting the medical profession to a predictive approach to heart disease.

As regards the treatment of angina pectoris (a condition allied in various ways to coronary thrombosis), more effective long-acting preparations, which might improve the blood supply to the heart muscle, and medicines designed to prevent anginal attacks while not depressing the heart muscle will both be developed by 1975.

Other new medicines forecast include some that will increase the strength of contraction of the heart muscle while not affecting the heart's rhythm adversely; and new diuretics suitable for cases resistant to present diuretics or less liable to cause a loss of potassium from the body. Myocardial infarction will probably be treated by direct injection through the skin into the heart of tissue culture extracts containing capillary blood vessel buds and growth stimulating substances making revascularization surgery unnecessary.

However, in a small proportion of the very large number of total cases surgery will still be needed. Artificial hearts should be perfected by 1990 and may replace human and animal transplants because of availability. Others believe that pig hearts will be increasingly used for heart transplantation, the specially bred pigs being 'immunised' beforehand against a rejection of their hearts by the human recipients.

Vascular diseases

The problems of vascular disease are in many ways similar to those of heart disease. Substantial progress cannot be expected until there is a better understanding of the underlying mechanisms of vascular changes and the causes of hypertension. This is likely to come within ten years. It should then be possible to use naturally occurring hypotensive agents to control hypertension. Immediate advances in vascular diseases will depend on better peripheral vascular diagnostic procedures, probably based on ultra-sonic techniques.

Another possible form of progress will be the identification of trace metals and other 'micro-

nutrients' whose absence may be responsible for vascular damage. Once these are identified, and tests have been developed to indicate their presence, replacement therapy should be possible for individuals in whom they are lacking. This may be available by 1975 or 1980. A better understanding of the general ageing process and its effect on the blood vessels should be achieved by 1990.

It is also likely that other environmental causative agents will be identified and (as with smoking at present) the challenge will be to change national habits to reduce exposure to such causes. In the immediate future surgical techniques will improve. Laser strippers, for instance, will be used. The next forward step will be in the field of vascular replacement, first with grafts from humans and then with grafts from animal banks and finally with grafts from tissue culture extracts such as a chick-embryo growth extract mixed with vascular buds which will be developed from a small piece of the patient's tissue that has been deliberately kept somewhat anoxic. Early in the 1970s 'thromboprophylaxis' should be possible by separating antithrombotic and anticoagulant properties. Specific fibrinolytic enzymes should be available to prevent thrombus formation.

There will remain the problem of identifying high risk individuals and presymptomatic cases, and getting social acceptance for large-scale 'preventive' medication in these individuals.

This need for early identification of vascular or blood changes is particularly important, first because many acute episodes of vascular disease are rapidly fatal and second because the changes which have occurred by the time symptoms appear are often irreversible. Specifically, the brain damage caused by a vascular catastrophe will still be untreatable by 1990.

The pessimistic view is that the conquest of many diseases of middle-age (and particularly coronary heart disease) will leave ever growing numbers to suffer in old age from progressively destructive vascular disorders and deterioration of their nervous system. The more optimistic view is that despite the great difficulties the causes of the vascular disorders also will be understood, and that the medical profession and the public will accept the consequent implications of early diagnosis and long-term therapy for those at risk. In this way vascular diseases could be effectively controlled by the 1990s.

With the less catastrophic vascular diseases such as intermittent claudication and migraine further progress is also expected within ten years. For the former, it is likely that compounds will be found which have a specific effect in increasing blood flow in muscle and skin. For the latter, it is likely that both preventive and symptomatic treatment will be

developed once the disease process is better understood. Much of the current research is centred on 5-hydroxytryptamine and its antagonists.

J Diseases of the connective tissue

Apart from the possibility of developing new test-tube methods by 1980 for diagnosing these diseases, of which rheumatoid arthritis is the commonest, the outlook is not regarded as promising. There are a great variety of serious basic difficulties: one is the need to understand the basic mechanics of cell membranes and cell enzymes, although these may be controllable by 1985; another is the need for a greater knowledge of the immunochemical reactions involved, and of immunoglobulin precursors (that is, of those substances that will form 'antibody' in response to the presence in the person's body of an 'antigen', the combination of the two being thought the essential element in these 'immune response' diseases).

A third difficulty, on a more down-to-earth level, is that of reproducing rheumatoid arthritis in animals by any process that could conceivably operate in man, and of deciding the relevance to the disease of any organisms that may be isolated from persons suffering from it. (Such organisms are not uncommon, and it is thought that certain of them may produce the antigens mentioned above).

Nevertheless by 1980 we may at least have clarified the role of infection in initiating and of an immune process in perpetuating rheumatoid arthritis. It is possible that medicines with a quite fundamental mode of action will be developed by that time, giving something more than a mere control of symptoms and without serious side effects. The main therapeutic problem is to develop medicines that will interfere selectively with antigen-antibody formation.

H Mental disorders

The problems involved are nearly always rated as difficult or as very difficult. At one extreme there is a forecast that little progress will have been made in relation to these diseases even by 1990: at the other an optimistic forecast of a large variety of specific remedies which will have social uses outside medicine.

There is unanimity that research on psychoses should be concentrated on the biochemistry of the changes involved. And there is a fair measure of agreement that a number of more efficient and even specific medicines should be available by the late 1970s and certainly by the 1980s.

This is considered particularly true of medicines for psychotic depressive illness. One forecast postulates more powerful antidepressants of the presently available types by 1975; mood-normalising compounds for manic-depressive states and quite new antidepressive agents by 1980; and by 1985 stabilising medicines for patients in whom these states are associated with 'environmental and personality factors'. Another forecast sees the future treatment of the milder psychoneurotic (nervous) depressions as comprising psychotherapy plus medicines plus better community care than at present. Neurosurgery may also have a part to play.

Progress towards specific medication for schizophrenia will be slower. There may be some progress by 1975 towards long-acting compounds similar to those at present available but more specific. Such medicines may need to be taken only once a month or so. But truly specific medicines for schizophrenia, and perhaps then only in certain limited fields, will not appear until the late 1980s. There will also be progress in differentiating a small number of fringe diseases from nuclear schizophrenia.

There will be a persisting reservoir of untreated schizophrenics in the community; and at the same time improved organisation of the psychiatric services will bring an increased demand for effective medicines. And in fact, 'cures' aside, symptomatic control, community care, and pharmacologically assisted psychotherapy will together provide steady progress in the control of schizophrenia.

Three types of forecast are made about organic psychoses (those due to physical changes in the brain). By 1980 there will be definite progress in the control and prevention of dementia. By 1985 there will be progress towards pharmacological control of psychoses having their origin in genetic or biochemical abnormalities. And thirdly, genetic counselling will reduce the incidence of certain types of mental subnormality, and better neonatal care will lead to the early correction of nutritional and other causal deficiencies.

A number of forecasts predict an increased incidence of neuroses (nervous disorders) during the period. In part, this could be due to the recognition that various physical diseases are essentially neurotic in origin; more generally, over-population and the spread of technology will cause a true increase in both anxiety states and neurotic depressive states.

There is a fairly widely held although by no means universally accepted belief that, in the treatment of neuroses, psychotherapy – particularly of groups – will continue to be more important than pharmacology; and there will be an increase in social acceptance of neurosis, and in the counselling and the provision of suitable jobs and accommodation for the neurotic.

However, by 1975 – or perhaps later – medicines should be available to alter mood or quell anxiety without producing the sedation or the loss of bodily co-ordination (manifesting as dizziness, etc.) produced by currently available remedies. One forecast suggests that, in addition, there will by 1980 be more specific medicines for periodic phobic or obsessional states; and by 1985 new compounds of the LSD type to facilitate psychotherapy, but with a greater range of use and fewer side effects than LSD. There is one forecast of new medicines to deal with the various bodily manifestations of anxiety.

One striking prophesy in this field is that 'it is likely that by 1990 nearly every individual will be taking psychotropic medicines either continuously or at intervals'. Other aspects of this prediction are discussed in Section dd). Another forecast suggests that psychotropic drugs to blunt curiosity and initiative will be available and there would be a hazard that they could be misused.

With only two exceptions all forecasts dealing with personality disorders manifesting in crime and aggression are pessimistic about possible progress by 1990. This is because the underlying factors – including frustration and such problems as over-population – are so extraordinarily complex.

Present knowledge of the basis of personality disorders is very small; and in particular, knowledge of the roles of nature and nurture, and of the biochemical basis of personality disorders, must be increased before any therapeutic advances will be made. There will be a search for medicines to reduce aggression and anti-social behaviour while not affecting creativity and socially purposeful activity; but the most optimistic forecasts of the likely end results are of some medicines by 1985 or 1990 suitable for use in habitual criminals, perhaps especially the aggressive psychopaths; of mood stabilisers for certain personality disorders starting in adolescence; and possibly of a medicament that will bear the same relationship to drugs of addiction such as heroin as disulfuram (Antabuse) does to alcohol. A possible long-acting antagonist to opiate drugs is also mentioned. (See also Section r). There will also have been advances in the general understanding of the sociology of crime and aggression.

l Allergic disorders

Difficulties in this field are generally rated as moderate, and certainly not as intractable. There will be steady marginal improvements in the anti-histamines and corticosteroids at present used in the treatment of allergic disorders, and desensitisation methods may be improved to the same degree.

However, more fundamental advances are likely to follow the study of the immunological reaction and

immune tolerance, and the biochemistry of the early and delayed allergic response; though in other forecasts stress is laid – as far as such fundamental research is concerned – on the study of inflammation and humoral messengers, or specifically on the characterisation of IgE (an immunoglobulin involved as antibody in the allergic response), or on the isolation of the antigens involved in allergic disease.

This fundamental research will continue until at least 1980; but in the 1980s it will have begun to bear therapeutic fruit – in the form of specific substances giving control of most allergic conditions. In addition, as regards asthma, general control measures will be improved and applied at an early age; although non-allergic varieties of the condition may still prove difficult to handle.

Technological advance will produce new allergens in the shape of foods, new medicines, and general utilities; and of course, it is envisaged that, whatever advance may be achieved in the control of allergies, the basic liability to allergic reactions will remain.

m Parasitic infections

This whole forecast applies primarily to Britain and other advanced countries, and hence no detailed forecasts were made on this subject. It was agreed, however, that the main difficulties reside in the poor socio-economic conditions affecting most of those suffering from parasitic infections. One result is that research in this field is not financially rewarding, and is, therefore, somewhat neglected.

Currently available forms of treatment, however, are regarded as fairly satisfactory; though advances are being made and will continue to be made – so that by 1975 major advances in the treatment of schistosomiasis and filariasis are likely. Correspondingly, actual control of the diseases should greatly improve, though even by 1990 these conditions will still be of some importance in emerging countries such as India. And economic improvements in the countries mainly concerned (and better eradication campaigns) will be as important as new medicines in leading to control.

n Surgery

There will be steady progress leading to considerable changes in surgery. By 1990 it should be possible to replace almost all parts of the body except the brain and spinal chord with transplants or prostheses. For example, artificial replacements should be available for aortic valves, peripheral vessels, joints and bones and probably for various

organs. Lung and liver transplants should be routine. It is likely that surgeons will have a choice of either heart transplants (human or mammalian) or replacement with an implanted artificial heart, complete with its own electrical control. It is also likely that implanted devices will be available to give functional electrical control of muscles (e.g. sphincters) in cases where physiological control has failed. The problems are largely those of miniaturisation.

There will also be advances in microsurgery and cryosurgery. In general, unphysiological operations such as gastrectomy for ulcers will give way to physiological manipulations of the autonomic nervous system and of the patient's cardiovascular and gastro-intestinal systems. Similarly, the need for cancer surgery will be reduced because of improvements in early diagnosis and in other methods of treatment (See Section c).

□ Anaesthetics

By 1975 there will be substantial improvements in short acting anaesthetics giving light anaesthesia with rapid onset and rapid recovery. Later developments may lead to recovery being as abrupt as waking from ordinary sleep. Thereafter, present chemical methods of narcosis will be largely replaced by electrical anaesthesia. This will allow the patient to remain conscious while the operation is performed, although full narcosis could also be induced electrically. There will also be improvements in the compounds available to control the patient's condition during operation, possibly on a localised basis, for example, to control secretions, muscle tone, or oxygen requirements. These advances should further reduce surgical shock and other complications of surgery.

It is also likely that the vital functions of patients undergoing operation will be automatically monitored in all cases by 1980. This could allow a single anaesthetist to handle several patients at one time.

By 1990, anaesthetics should be available to allow long-term hibernation, for periods of weeks or months. The main problem with these compounds will be their evaluation in man and measurement of their therapeutic usefulness.

ρ Fertility control

By 1975 there should be a 'male pill', a 'contraceptive' pill for taking after intercourse, a long-acting pill, and a technique for immunising against pregnancy.

Another forecast, however, suggests that contraceptive treatment will be restricted to females unless governments or supranational authorities begin to take fertility control out of the hands of individuals. It suggests too that the present type of pill will be replaced by one that has a local action in the uterus – perhaps the killing of the embryo at an early stage. Despite ethical objections this will be accepted because the dangers from it will be less than from the present pill, and it would also allow a degree of choice in the sex and other aspects of the children who were born.

Another forecast sees fertility control being applied to pests and being technically feasible by mass medication to humans by 1975. This would be by means of selective endocrine interference.

Q Process of ageing

By 1990 the ageing process will be delayed and even partially reversed, so that there will be a further increase in the average life span. There will be medical instead of cosmetic research on the skin, resulting in medicines giving a relatively youthful appearance to the aged.

ƒ Addiction

Addiction will become an increasing social problem and much more rigid methods of control are likely to be introduced to prevent the more extensive misuse of the 'hard' drugs. These will not only include the present restrictions on prescribing, but also international measures to curb the black market.

If, as seems not unlikely, it turns out that a predisposition to addiction can be inherited, then it may be possible to identify individuals at risk, and to give them preventive treatment or at least maintain them under surveillance. Also, new compounds will be developed of value in treatment of the physical and psychiatric concomitants of drug withdrawal; though it is unlikely that safe drugs that could be used as substitutes for narcotics will be discovered.

S Veterinary medicine

The most striking feature of the forecasts in this field is their specificity in comparison with the forecasts concerning human medicine. With hindsight, a probable reason for this is the regrettable omission of any specific veterinary experts from the panel of forecasters. Non-experts in a particular field are perhaps more able to reach dogmatic conclusions than those who are aware of its detailed problems.

It will be interesting to look back in 1990 and see how the following predictions compare with those in human medicine.

1 Agents will be available to control most aspects of reproduction: time and season of mating, whether or not conception shall occur, and the number of young produced. One forecast suggests major progress in this field by 1980.

2 Agents to promote growth, some of them anti-bacterial (as at present), while others will affect the absorption and metabolism in the animal body of nutrients supplied, giving greater efficiency of food conversion. Advances of the latter kind will occur as a result of fundamental biochemical and pharmacological research, perhaps in the sphere of human medicine. And their field usage will call for considerable educational and technical services.

3 Agents to modify the quality of (edible) animal tissues.

4 Identification of various minor mineral deficiencies.

5 Agents that will allow sex of offspring to be determined.

6 Much more systematic and regular prophylaxis and treatment of animal diseases, especially in young animals which are going to be more common. This will be very desirable because of the development during the period in conditions such as housing that will favour the spread of enteric and pneumonic infections. To a considerable extent the new forms of cover, especially vaccines, to be used against bacterial and virus infections will emerge from new knowledge of immune mechanisms.

7 Control of disease in very unusual species of animals, and also of diseases not at present controllable.

8 Improved control of parasitic diseases. Even today the correct use of anti-parasitic agents is more important than the development of new agents; and indeed by 1990 advanced countries will have abolished certain aspects of the host-environment relationship that are essential to the spread of many parasitic diseases.

An exception is made in the case of control of insects and ticks, which now develop resistance to agents active against them almost as fast as new agents are produced. Insects and ticks are especially important in regard to extensively grazed animals. However, a definitive solution to this problem is expected by about 1990, with a temporarily satisfactory solution every 5-10 years before then.

9 Certain diseases like bloat and infertility may really be diseases of mismanagement; but where the mismanagement is an integral part of an economic production system their control will call

for basic research and for new prophylactic and therapeutic agents.

Despite this generally optimistic picture certain veterinary products that are developed will not be used because the expense of satisfying the requirements of the various regulatory bodies will be thought to make their marketing uneconomic. This will be especially true of quite new products giving novel benefits for which there will be no existing yardstick (by means of which likely commercial benefits could be measured). The problem of tissue residues of medicaments is one common instance of the type of problem envisaged.

In addition, veterinary research is foreseen as being always to some extent in competition with human research for manpower and money.

forecasts on related changes

† Scope and organisation of research

Two main conflicting trends are foreseen. One is increasing demand by the public and the profession for further control and cure of disease and for greater safety in the use of medicines. The other is increasing pressure on pharmaceutical prices and profits restricting available funds for research and development. Real expenditure on pharmaceutical R and D would treble by 1990 if present trends are maintained, but there is some doubt, under the anticipated pressures, whether this will actually be achieved. Although to some extent these pressures may be absorbed by economies in other company expenditures, it is particularly likely that there may be some levelling off in the growth of research spending beyond 1980. In the past the proportion of companies' sales revenue devoted to research and development has been rising; this trend will be reversed.

Individual research projects will certainly continue to become more expensive, because research will become more sophisticated, because many unsolved problems are more complex than those of the past, and because higher standards in proof of efficiency and relative safety will be demanded in the future. On present trends, by the end of the Century a major research project might take 15 or 20 years. However, this would make an impossibly long cycle of innovation and would make the effective management of research impossible. Hence the factors tending to lengthen present research programmes will be at least partly offset by greater efficiency and by speeding up the technological processes themselves. The greater complexity of research will also tend to concentrate an increasing proportion of total research into the large multinational companies. It is suggested as a possibility that government might start to finance contract research in the pharmaceutical industry on a substantial scale, as it already does in the aircraft industry. It is generally agreed, however, that government directed research is inappropriate in pharmaceuticals, although it may make important contributions, for example, in biomedical engineering. More important, there could be serious political difficulties for any national government financing research in the local sector of a multinational company.

More emphasis will be put on studying the aetiology of disease, rather than seeking empirical cures. The latter will nevertheless continue to contribute important advances, and companies will need to guard against undertaking fundamental research which would be more appropriately carried out in universities. The National Health Service, necessarily with a more flexible structure than at present, will become better geared to study clinical pharmacology; 'Centres of excellence' specialising in narrow aspects of research can be expected to

emerge. There will be greater mobility of scientists especially between industry and universities. There will also be better opportunities in industry in large multidisciplinary teams – including bioengineers and electronics experts as well as biochemists, physiologists and pharmacologists. There will also be more subdivision within each of the various disciplines.

Information storage and retrieval will improve greatly and the interchange of information both between companies and between universities and industry will increase. Findings on such matters as species differences in toxicity tests will be made generally available; and by means of better processing and sifting of data scientists will again be able to keep abreast of *all* developments in their own fields though these will be narrower than in the past. Cheaper travel and better international communications will hasten the spread of research findings. A dissentient view on this subject is that better communications will hinder scientific progress, because it will encourage the dissemination of many preliminary findings which will often subsequently be reversed.

Fields likely to show rapid growth as a result of research are genetics, mental illness, the study of early diagnosis, the development of prostheses, the development of automated diagnostic aids and data storage equipment and 'function testing' to identify reserve capacity in metabolic and physiological systems. The existing tendency for 'non-medical' companies – such as electronics and engineering companies – to enter the medical research field will increase unless pharmaceutical companies are quick to diversify out of the narrow sector of medicinal chemicals.

‡ Structure of the industry

The pharmaceutical industry is already international. There are several companies that are truly multinational with production and research facilities in many countries. This trend will continue, and by 1980 may start spreading into Eastern Europe as well as throughout the developing nations of the free world. The existing multinational companies will themselves grow, and the increasing complexity of research and the demand for higher standards of proof of safety and efficiency will raise costs and thus encourage further amalgamations and takeovers. The first links will develop between British and other European companies in the 1970s; in the following decade the Japanese will start to amalgamate with overseas companies. By 1990 world-wide pharmaceutical research, production and marketing will mostly be in the hands of some one or two dozen companies. About half of these will have originated in the United States, and the

others in Britain, Switzerland, the rest of Europe and Japan. There will also be some small local companies with specialist interests or producing nothing but well-established compounds whose patents have expired.

The large international companies will develop greater political awareness, so that they may be able, for example, to exert considerable influence in the framing of national regulations for the control of medicines. National governments, in turn, might wish to obtain financial interest in the local subsidiary companies, so that close integration between government and industry could be achieved. This would be strongly resisted by the multinational companies, unless they could have confidence that governments would not interfere in management in a way that would affect their international business. The dangers of State participation as a stifling influence on competition and innovation are well recognised in the advanced countries of the Western World.

The effects of the increasingly international structure of the industry on world trade are difficult to predict. Although all countries will encourage local manufacture – and some will continue to insist on it – many will probably realise that this is incompatible with maximum economic efficiency. The extent to which Britain can remain a major pharmaceutical exporting base for the international companies will therefore depend on two factors. First, the extent to which other countries continue to accept pharmaceutical imports (rather than insisting on local manufacture). Second, the relative attractiveness of Britain as a manufacturing centre compared with other countries. In addition, some form of European Union including Britain will probably be in existence by 1990, so that perhaps by then the whole continent will be regarded as a ‘home market’.

The industry is expected to have an only moderate degree of diversification, largely because of the specialised nature of its business and its marketing situation. Possible diversifications include related chemical fields, to which pharmaceutical and pharmacological technologies are relevant such as the manufacture of artificial foods. Another is into medical electronics and automated diagnostic equipment. Usage of these and similar ‘non-pharmaceutical medical products’ will expand more rapidly than that of pharmaceuticals themselves.

Despite the recognition that no medicines are entirely safe, the development and acceptance of ‘self-medication’ will continue. This will occur particularly as the public demands the correction of yet more minor abnormalities and as the formal health services continue to have limited resources. This will represent an important growth area for the manufacturers. Finally, pharmaceutical manufacturers are likely to diversify (probably by take-

overs) into cosmetics. This will be logical as the latter become more pharmacologically active and subject to more stringent toxicological controls.

V Relationships with government

The most important development will be the increasingly international nature of pharmaceutical companies’ relationships with government. These will be most obvious in the registration of pharmaceutical products and manufacturing premises, in legislation affecting the marketing and distribution of medicines and in supervision of quality control procedures. At present different national authorities carry out separate inspections of overseas plant and require the very comprehensive data for the registration of new products to be presented in different forms. Although international Conventions on health matters will have been extended by 1990, it is unlikely that national governments will by then have accepted completely international controls – exercised, for example, by WHO – in place of their own national regulations. However, harmonisation and international co-operation should have eliminated much of the present duplication, and various countries will have developed special expertise, for example, in the appraisal of drugs of addiction or steroids or antibiotics.

There will also be harmonisation of patent laws, and it is likely that all countries, including the developing nations which will continue to be largely dependent on overseas research and knowhow, will have accepted that strong international patent protection is necessary if pharmaceutical research is to be financed from sales revenue. (The possibility of direct government contracts for research could never be more than complementary to companies’ own finance for research). There will be stricter restraints on pharmaceutical sales promotion, both in relation to content and (at least informally) on total volume. This is likely to encourage companies to seek new methods of promoting sales.

To a large extent future governmental attitudes on patents (and, to a lesser extent on sales promotion) will be governed by the industry’s effectiveness in demonstrating that its profits are not ‘unreasonable’. If it continues to be widely believed – however mistakenly – that some pharmaceutical companies are ‘too profitable’, both patents and promotion will continue to be under attack. If, however, the developments discussed below succeed in demonstrating the reasonableness of the industry’s prices and profits, the current pressures in these areas will diminish.

Social security schemes providing medical care will have become universal, in one form or another, by 1990. Thus in all countries the industry will have the

State or national agencies as their major customer for prescription medicines. These agencies will continue to exert world-wide downward pressure on pharmaceutical prices and profits, through a variety of procedures for price regulation or voluntary price restraint. In general, the large international companies will negotiate (normally through national trade associations) from a position of strength because they are the source of practically all new medicines. Some national governments might attempt in the short-term to establish an alternative source of medicines, for example through a national state-owned enterprise as is already happening in Sweden. However, a local national industry would be unable in the long-term to compete with the internationally organised and very much larger multinational companies. These companies must, however, avoid the appearance of 'profiteering' on sales to the health services, and much will depend on the skill of their negotiators in reaching price agreements. In Britain it is likely that the present voluntary basis of price negotiation will continue, and it is possible that over the next decade a general 'backlash' against the 'Prices and Incomes Board' philosophy will benefit the industry. On an international scale, there will be further study on how the 'reasonableness' of prices and profits of an innovating company should be assessed in economic terms. This is a likely area for co-operation between the industry, government and the universities.

Under the Section t on research, it was suggested that some direct government finance may supplement the research and development expenditures provided by companies themselves. This might be followed by some government involvement in research planning, although not on a formal basis requiring, for example, the 'approval' of specific projects.

At present in the industry's relations with government there is an increasing reliance by the latter on the advice of 'expert committees' on all aspects of the industry, its products and their use. Although decisions taken centrally will in the future be more soundly based as the relevant technologies develop, their inherent weaknesses will be recognised. The present feeling that 'grey areas' can be clearly divided by experts into black and white will give way to a belief that uncertainties and imperfections are inevitable and within the next two decades there will be a marked swing back to reliance on individual judgment rather than central 'expert' opinions.

W Control of adverse reactions

More rational attitudes to adverse reactions are expected to develop. A sounder epidemiological approach, with better monitoring, the development

of record linkage, and the use of computers and possibly local 'recording officers', will identify more precisely the risks of adverse reactions occurring with particular medicines. 'False' reports of adverse reactions, which have in fact arisen from other causes, will be reduced. The risks of adverse reactions will then be able to be logically balanced against the expected benefits from the use of the medicine. In addition, these improvements in the epidemiology of adverse reactions may sometimes identify differing degrees of risk for different types of patient and effects arising from the interaction of different preparations. The underlying mechanism of adverse reactions will be better understood and this will allow more accurate prediction and will reduce hazards. Some reactions may be avoided or minimised by specific additives in the medicine.

At the same time, better information will be disseminated about adverse reactions in Britain by the Medicines Commission. There will be improved co-operation and mutual understanding between governments, the professions and the pharmaceutical industry in relation to adverse reactions. Although there will be international collection of data on adverse reactions, national differences in the practice of medicine will mean that the greatest progress will come from national studies.

Despite this picture of a generally improving situation, there remains the risk that another thalidomide type of tragedy could occur. The gravest risk is that despite the precautions taken by industry and government some hazard associated with some long-term therapy may eventually be discovered, particularly as such therapy will be increasingly common in connection with the chronic and progressive diseases. The widespread harm done by the adverse reaction itself would be compounded by delays in medical progress following the imposition of further, irrational 'safety' requirements as a result of the public outcry about the disaster. However, a better public understanding of the need to balance risks against benefits in all forms of therapy might prevent this.

X Relationships with the medical profession

An improved relationship is expected in three areas. First, there will be more co-operation in basic research designed to uncover the underlying causes and the natural history of diseases. Secondly, there will be improved collaboration in clinical pharmacology and particularly in the evaluation of new medicines. Finally, and most important, there will be improvements in the provision of information to doctors about the industry's products and in the education which doctors receive in their use.

In the field of clinical pharmacology, a central body could be established to improve the standards of clinical trials and pharmacological studies, and to act as a liaison between the manufacturers and suitably qualified clinical evaluators. One forecast envisages the establishment of academic departments with graduates in medicines and such sciences as physiology, pharmacology, biochemistry and statistics. Those entering these departments for training would require specific basic qualifications, and would study on a set curriculum for a higher degree in pharmacology. The departments would combine clinical medicine, teaching and research. It is probable that the pharmaceutical industry will have to finance many of these developments. A period of clinical pharmacology or clinical evaluation may form a regular part of post-graduate medical training, possibly in appointments as 'research registrars'.

There will be much greater emphasis on pharmacology and statistical theory in the medical courses of the future, both at undergraduate and postgraduate level. This will overcome the present situation in which most doctors have received little or no training in the use of the many potent medicines developed in the past twenty years. It will, however, take another twenty years before this problem is entirely overcome, because it is only by then that doctors who have received comprehensive pharmacological training in the medical schools will predominate. At the same time, pharmaceutical sales promotion will tend to have a much greater information content, often presented in the form of discussion meetings or through audio-visual aids.

There are, however, still fears that other difficulties may arise, largely as a result of the changing nature of medical practice. The importance of the patient's own behaviour in seeking medical care (or not) in general practice will be increasingly recognised, and this may accentuate the present dichotomy between hospital and domiciliary medicine; the hospital doctor will continue to be sheltered from the patient-initiated consultation and will see only those with specific diseases referred by another doctor. If medical education continues to be centred mainly in hospital, the conflict between the concern of the general practitioner (with the behaviour and motivations of his patient) and the hospital doctor (mainly with the disease) may become more obvious. At worst, there could be a complete schism between academic medicine and practicing medicine. In this case practicing doctors and the pharmaceutical industry would become closely allied, and the academics would be separated in the professional medical organisations. Another possibility is that medical practice could be increasingly dominated by academics and that, for example, practicing doctors might be restricted to those medicines 'approved' by expert committees. It was, however,

suggested in Section v that this was unlikely.

The most favoured prediction is that community medicine will in fact be well taught in British medical schools and that there will be a sound understanding of the different needs of hospital medicine and of the doctors providing community care.

4 Retail channels of distribution

A 'three tier' system of distribution, such as already exists in some countries, is envisaged. One type of pharmacy would be concerned mainly with medicines on prescription, and might often be located in or near a health centre or group practice premises. The second would correspond in many ways to the existing pharmacy, but would concentrate primarily on the sale of non-prescription medicines, though in twenty years many might still be dispensing. (In some small towns the existing pharmacies, combining dispensing and general sale of medicines, would continue to exist indefinitely). Thirdly, again as at present, a 'free-list' of medicines – mostly well-tried traditional remedies – would be available from non-pharmaceutical outlets.

There is at present a move toward accepting the desirability of 'self-medication'. This trend will continue, hence allowing many present-day pharmacies to survive even when much of their dispensing has been transferred to pharmacies in health centres. At least in large towns the smaller number of pharmacies which are likely to be in business in twenty years time may be able to discontinue many of their non-pharmaceutical sidelines. It is likely in the future that more potent and specific medicines for self-medication will be permitted to be sold by the pharmacist but not by assistants only nominally under his supervision. By 1990, medicines on sale without prescription will probably include, for example, antibacterial substances for the treatment of common infections. New safer oral contraceptives may also be on sale from pharmacies without prescription. These more potent medicines would not be advertised to the public but would be available on the pharmacist's recommendation. Already the emphasis in pharmacists' training has shifted away from practical dispensing towards physiology and pharmacology. This trend is expected to continue in the future. It is possible that some of the medicaments for social use, discussed in Section dd, would also be available through pharmacies only. This could lead to a latter-day version of the US Drug Stores.

It will largely be a matter for the profession of pharmacy to determine how it should adapt to the increase in one-stop shopping often by motor car at

out-of-town locations. The new-style all-purpose shops could have pharmacy departments like the older department stores or the large diversified multiple chemists of the present day. If this is discouraged the public will rely increasingly on the 'free list' remedies which *will* be available in these shops, instead of the more potent preparations obtainable only from a pharmacy.

By 1990, new methods of stock control and stock replacement will have become almost commonplace. Pharmacies will be selling and dispensing only manufacturers' original packs, and the charging of one of these on the cash register will automatically adjust the stock records and result if appropriate in a replacement order being sent either to the wholesaler or the manufacturer.

Z Changes in production and quality control

Large scale production of both chemicals and pharmaceuticals will be entirely automated by 1990, being controlled by 'on line' computers. Quality control, also, will be largely automated including, for example, analyses by gas chromatography and spectroscopy. Quality control will often be carried out as a continuous process, integrated with the automated control of production. It will give a computer print-out of results and automatically adjust the production process to correct any incipient faults. Thus a more precise control of production will be possible and inevitably the gap in quality control procedures between those practiced by the very large manufacturers and those which are practicable for the very small manufacturer will widen. No amount of regulations can alter this inevitable fact.

Raw materials purchases and stock control will also be fully automated by 1990, and production planning may be aided by computer records received direct from retail outlets to indicate current demand. In many cases, by 1990 natural substances will have been replaced as raw materials by synthetic chemicals.

The importance of the physical form of the active ingredients of medicines as well as their chemical composition will be increasingly recognised. By 1975, it will be normal practice to carry out tests in humans to establish whether any minor change in formulation has affected the availability of the active ingredient.

As the molecules used become more complex, the problems of stability will increase. Different parts of the chemical structure may be found to decompose under different types of adverse condition. More significantly, previously unrecognised degradation of active ingredients will be revealed by more

sensitive methods of analysis, for example with chromatography. This will mean more rigid evaluation of packing materials, for example, to ensure that they exclude moisture or ultra-violet light. There will also be closer supervision of the additives and excipients (including flavours) used in medicines, and contamination by traces of foreign matter or micro-organisms will also be more strictly controlled.

One problem will be to ensure an even distribution as between unit doses of new very potent medicaments which will have to be administered in minute doses. On the other hand, for medicaments requiring large doses, direct compression of tablets will more and more replace the use of 'binders' and excipients.

aa Dosage forms and packaging

Many new dosage forms or packs are already technically possible – for example, a 'tamperproof' pack releasing an individual dose at the right time either under the control of its own inbuilt time mechanism or receipt of an electronic signal from the prescriber. More mundanely, there is likely to be a steady swing over the next two decades towards the dispensing of manufacturers' original packs, including strip and 'bubble packs'. Liquid preparation may come in boxes of single dose edible sachets (a cross, perhaps, between soft gelatine capsules and the cases of liqueur chocolates).

Medicinal implants will become more common, being designed to release their medicament automatically in response to the appropriate biochemical situation e.g., insulin in response to a rising blood sugar level.

Sugar-coated tablets will be replaced by film-coated tablets, and long-acting preparations will have become more common and more predictable in their action. Some compounds may emerge which are intrinsically long-acting. All tablets will be identifiable by code markings. Aerosols will be improved, and will be capable, for instance, of delivering a measured dose of a dry powder free of propellant with particle sizes small enough to penetrate the lung alveoli.

It was mentioned under the Section on adverse reactions that specific responses from particular types of patient are likely to be identified. This will also be the case for therapeutic responses, and there may be a conflict between the economic need to have long production runs under automatic control and the therapeutic need to produce a variety of specific formulations for different groups of patients. This may lead to the introduction of special blending processes by which a variety of active ingredients can be added to a standard

excipient; much as is done with some types of paint, for which the desired pigments can be purchased and added separately.

bb Range of medicines available

Medicines will continue to be discovered for the previously 'untreatable' diseases, so that whole new therapeutic groups will come into existence. There will also be more preparations to alleviate minor disorders which the public will be reluctant to tolerate. However, it will be increasingly difficult to get approval for new medicines, and this will deter manufacturers from seeking to market preparations providing only marginal improvements in therapy. The large manufacturers will no longer hope to compete in every important therapeutic group but will specialise in certain fields. Moreover, the expected decline in the total number of manufacturers will reduce the numbers of competitive products in any one field. Finally, removal from the market of obsolescent medicines – still always firm favourites of some prescribers – will remain a slow process however much the national regulatory agencies such as the FDA (and often manufacturers) would like to see it speeded up. On balance, there will probably be a fall in the numbers of prescription medicines available, although their therapeutic range will extend.

Companies will also diversify into the fields of nutritional preparations, and by 1990, into the synthetic mood modifiers, pacifiers and general 'comforters'. These may challenge the traditional role of tobacco and alcohol and offer less hazardous alternatives to drugs such as marihuana and LSD which the present younger generation – by then in their late 30s and 40s – are unlikely to have abandoned completely. (See Section dd).

cc Preventive medicine

Specific preventive measures have already been considered under individual disease headings. In general, however, there will be increasing reliance on vaccines, both as their scope is extended and as 'natural protection' diminishes when more and more of today's common infections become rare diseases. Some diseases may also be prevented by chemical or genetic interference with the life cycle of the causative organism.

There will be important developments in early diagnosis, despite current caution on the subject. New and more meaningful tests will be devised, detecting errors in the metabolic and physiological systems of the body. The computerisation of test results will greatly enhance their value, indicating changes from previous measurements in respect of

the same individual as well as deviations from the average for the community as a whole. This will lead to demands for widespread 'health screening' of apparently healthy individuals.

There will be efforts to reduce the incidence of industrial diseases, by closer supervision of working environments. There will also be continued efforts to identify and to eliminate disease-producing agents in the total environment (e.g. chemical additives to foods; invisible pollution of the atmosphere; impurities in water supplies). Many of the still unconquered diseases will be shown to have multifactorial causes, and no single environmental measure (except the elimination or 'detoxification' of cigarette smoking) will by itself significantly affect the health of the population. Health education will make a greater contribution as it is put on to a sounder scientific basis.

dd Other changes

As already mentioned, the most dramatic change envisaged is the probability that by 1990 the social use of medicines will have become accepted as legitimate. Tea, coffee, alcohol and tobacco are natural drugs whose use now is socially acceptable. Britain, like many other countries, is facing a demand that other drugs such as marihuana should be accepted on the same basis. Currently the hazards are thought to be too great, and the non-medical abuse of amphetamines lends support to this view. Nevertheless the currently acceptable 'social drugs' are by no means perfect; if the hazards of cigarette smoking had been foreseen it would never have gained its present social respectability. Furthermore, it is likely that safer and what many people would regard as socially preferable alternatives to alcohol will be found – if indeed they do not already exist.

Alarm about the misuse of amphetamines and LSD and fears about the effects of marihuana could possibly produce a hardening of attitude against the social use of new drugs. It is more likely, however, that the publicity about the dangers of tobacco and of alcohol will result in society welcoming safer alternatives. If this were so, reasonable evidence of the long-term safety of new substitutes would encourage the regulatory authorities to permit their free sale and would encourage society to accept them. There is a strong probability that by 1990 new drugs intended primarily for social purposes will be in use.

As early as 1975 compounds may be available to speed learning processes, to improve co-ordination and dexterity, to counter stress and fatigue and to enhance or modify man's perception of his surroundings. Another ten or fifteen years, however,

will elapse before such compounds are socially acceptable and their use permitted except for experimental purposes. Their social effects may, incidentally, be less profound than those of the oral contraceptive, which could greatly change society's attitude to sexual morality during the next two decades.

Another development along similar lines will be further research into specifically cosmetic medicines. Antiperspirants and deoderants, for example, are already accepted. Other safe and effective cosmetic preparations along the same lines will be developed, and the regulatory controls which will be applied routinely to all cosmetics will break down the traditional clearcut distinction between a cosmetic and a medicine for topical application – a change that will be encouraged by the likely developments in cosmetic surgery.

This broader concept of medicines will call for a widening of the present primarily pharmacological approach to their control. The Medicines Commission in Britain, for example, may in time include a sociologist or other behavioural scientist. The issues raised by the new types of preparation will create new links between the government, the pharmaceutical industry and the scientists and doctors. It is sometimes suggested that we are already unduly dependent on medicines and 'drugs': they are, however, likely to play a very much larger part in our lives in the years ahead.

Basis for statistical forecasts in figure 1

1 Expenditure on the National Health Service is assumed to rise by 0.13 per cent per year of National Income for the first 15 years after 1968. (This is equal to the average rise in U.S. health expenditure 1950-1960.) In the next 15 years it is assumed to rise at half this rate, i.e. 0.065 per cent. Thus 1998 NHS expenditure would be 7.84 per cent of National Income.

2 National Income is forecast as rising by 6.5 per cent per annum in actual prices and 3.6 per cent per annum in constant prices.

3 Expenditure on NHS pharmaceuticals is forecast as remaining a constant proportion of total expenditure on the NHS, i.e. 13.2 per cent.

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appendix 3

Check-list of headings for 'Delphi' forecast

Conquest of diseases

Estimates to nearest 5 years when significant progress may be expected. What form might progress take?
What are the main problems to be overcome: would you rate these difficult, very difficult, or extremely difficult?

- a) bacterial infections
 - i) prospects of preventing progressive disability *e.g. in bronchitis and renal infections*
 - ii) control of resistance
- b) virus infections
- c) cancers
- d) control of graft rejection and autoimmune responses
- e) congenital abnormalities *molecular biology*
- f) neurological disorders *e.g. parkinsonism*
- g) heart disease *e.g. coronary, blood lipids*
- h) vascular disease *e.g. stroke*
- i) endocrine disorders *e.g. diabetes*
- j) diseases of the connecting tissue *e.g. RA*
- k) mental disorders
 - i) psychoses and neuroses
 - ii) influence on personality crime and aggression
- l) allergic disorders *e.g. asthma*
- m) parasitic infections
- n) progress in surgery
 - i) technical
 - ii) anaesthetics, etc.
- o) veterinary medicine
- p) others

Related changes

Increases in total research effort: organisation of research

Structure of the industry

- size
- international relationships
- diversification

Relationships with government

- price control
- regulation of research, production, marketing

Control of adverse reactions and attitudes towards them

Relationship with medical and ancillary professions

Retail channels of distribution

Changes in:

- production and quality control *e.g. automation*
- dosage forms *e.g. depot dosage*
- packaging

Range of products available

- total numbers
- type

Industry's contribution to preventive medicine

- environmental control
- prophylaxis
- early diagnosis

Any other changes

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To undertake research on the economic aspects of medical care.

To investigate other health and social problems.

To collect data from other countries.

To publish results, data and conclusions relevant to the above.

The Office of Health Economics welcomes financial support and discussions of research problems with any persons or bodies interested in its work.

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