New Drugs

Beta-blockers and sympathomimetics

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The availability of some 10 different beta-adrenoceptor blockers testifies to the success of these agents in modern therapeutics. Many of the newer members of this group do not represent a fundamental advance over the more established members, but in certain clinical settings they may offer distinct advantages. Combinations of beta-blockers with diuretics and a beta-blocker

a role for beta-blockers in the secondary prevention of myocardial infarction and sudden death in patients with coronary heart disease.

Adrenoceptors are classified into two groups, alpha (primarily stimulation) and beta (primarily relaxation) (figure). Alpha-blockers are discussed elsewhere in this series. Beta-blockers

Effects of stimulation of the sympathetic system.

with a weak alpha-blocking effect (labetalol) are now also available. Some of the original beta-blockers with short elimination half lives have now been reformulated to allow once or twice daily dosages. The place of beta-blockers in such diverse conditions as thyrotoxicosis and glaucoma has now become clearer, and the results of several recent studies have suggested

may differ both in their pharmacokinetics and in their profile of activity and adverse effects but they all share the ability to antagonise beta-sympathetic stimulation competitively, whether it is of endogenous or exogenous origin. In general, as their efficacy in the management of hypertension and ischaemic heart disease is comparable the choice of drug is determined particularly by the above factors and by cost, patient acceptability, and ease of administration. In many patients several agents may be equally suitable; the prescriber should then choose the one with which he is most familiar.

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Pharmacokinetics

Some general comments will simplify interpretation of the diverse kinetics of these drugs as listed in the table. Beta-blockers that are highly lipid soluble (propranolol, oxprenolol, meto-

Characteristics of available β -blockers

Name (proprietary name)	ISA	MSA	Route of elimination and general comments	Elimination half life (h)	Usual daily dosage (mg)
Non-cardioselective					
Propranolol (Inderal, Angilol, Apsolol, Berkolol)	—	+	Hepatic: pronounced presystemic elimination	2-6	80-480
Labetalol (Trandate)	—	+	Hepatic: pronounced presystemic elimination, α -blocking activity also	3-4	300-2400
Nadolol (Corgard)	—	—	Renal (100% unchanged). Reduce dose in renal failure	16-24	80-240
Oxprenolol (Trasicor, Apsolox)	+	+	Hepatic: pronounced presystemic elimination	2	120-480
Pindolol (Visken)	+	+/-	Renal (about 40% unchanged) and some hepatic metabolism. Reduce dose in renal failure	4	7.5-45
Sotalol (Beta-Cardone, Sotacor)	—	—	Renal. Reduce dose in renal failure	15-17	160-480
Timolol (Betim, Blocadren)	+	-/-	Hepatic primarily. About 20% excreted unchanged in urine	4-6	10-60
Cardioselective					
Atenolol (Tenormin)	—	—	Renal. Reduce dose in renal failure	6-9	50-100
Metoprolol (Betaloc, Lopresor)	—	+/-	Hepatic: pronounced presystemic elimination	3-4	100-400
Acebutolol (Sectral)	+	+	Renal and hepatic metabolism. Not cardioselective at higher doses	6	400-800
Practolol (Eraldin)	+	+	Renal. Use restricted to intravenous administration (5 mg) for arrhythmias. Reduce dose in renal failure	8-12	—

ISA = Intrinsic sympathomimetic activity. MSA = Membrane stabilising (local anaesthetic) activity.

prolol) are well absorbed but extensively metabolised in the liver, which results in a short half life. In comparison with the 100% availability of the drug to the systemic circulation when given intravenously only 30-50% of the drug reaches the systemic circulation after oral administration—that is, 50-70% is extracted on passage through the liver (presystemic elimination or first pass effect). The extent of this hepatic metabolism is subject to several factors including genetic control, age (decreased metabolism in elderly patients), smoking (increases metabolism), concurrent drugs that inhibit metabolism such as cimetidine or induce it such as phenytoin and phenobarbitone, and food (increases oral bioavailability). Consequently, there is considerable variation in steady state plasma concentrations (about 10-fold) of these drugs in any group of individuals given the same dosage. When consistent beta-blockade is required—for instance, in angina and hyperthyroidism—dosage must be carefully titrated as the requirement of individual patients varies considerably. Furthermore, in liver disease one would expect a decreased clearance of these drugs. This, however, is usually important only when there is extensive liver damage.

Water soluble beta-blockers such as atenolol, nadolol, and sotalol are less well absorbed and are more slowly eliminated primarily by the kidney. The resultant long half life makes once daily dosage practical. These drugs, however, accumulate in patients with renal insufficiency, and dosage needs to be reduced—for instance, by half if creatinine clearance is less than 30 ml/min. The beta-blockers excreted by both renal and hepatic routes (pindolol, timolol, and acebutolol) are theoretically less likely to accumulate in renal or hepatic disease as alternative routes of elimination exist. A reduced dosage is usually necessary only in severe renal failure (creatinine clearance under 10 ml/min) where the clearance of metabolised beta-blockers including propranolol is also reduced. Propranolol is the most highly protein bound (about 90%) member of this group of drugs, and with the exception of inflammatory disorders that increase the binding of propranolol (by increasing acute phase reactant acid glycoproteins) these drugs are not subject to clinically important alterations in protein binding.

Recently, several shorter acting beta-blockers (metoprolol, oxprenolol, and propranolol) have been formulated as sustained release preparations in an attempt to provide adequate blood concentrations throughout a 24 hour period and allow once daily dosage. With these preparations peak blood concentrations do not occur for three to six hours after dosage, and there is a prolonged elimination half life (metoprolol about five hours; oxprenolol about six hours; and propranolol about 10 hours). Preliminary observations suggest that a high degree of beta-blockade is not consistently achieved with oxprenolol or metoprolol, and some patients require twice daily dosage of the sus-

tained release formulation. In angina a dosage once daily of long acting propranolol is equivalent to 40 mg four times daily. If an adequate response is seen with conventional formulations there is little benefit, apart from the chance of improved compliance and fewer side effects in some patients, in switching to the sustained release formulations as they are considerably more expensive. This is particularly so in hypertension when the hypotensive effect is not related to plasma concentrations and when drug effect is longer lasting than blood concentrations. Indeed most patients respond satisfactorily to once or twice daily dosage of conventional preparations. In contrast, in angina, where concentrations are related to efficacy, three or four times daily dosage of conventional preparations is usually necessary. The role of sustained release preparations of beta-blockers in angina is not yet clear.

Pharmacodynamics

All beta-blockers are equally effective in producing beta-blockade. They must therefore be categorised on the basis of their additional properties. By far the most important of these is receptor selectivity. Non-selective beta-blockers (table) antagonise the action of catecholamines at all beta-receptors (β_1 and β_2) and so have widespread effects throughout the body (figure). Some beta-blockers are relatively selective and block predominantly the effects of catecholamines on the β_1 receptors that are primarily located in the heart (hence cardio-selective) but also to a lesser extent at the juxtaglomerular apparatus (modulating renin release) and in adipose tissue where release of free fatty acids is stimulated. Cardioselective agents are, therefore, less likely to produce unwanted effects that may occur in some susceptible individuals as a consequence of blockade of β_2 -receptors—bronchospasm, intermittent claudication, cold hands and feet, and delayed gluconeogenic response to hypoglycaemia. It must be emphasised, however, that because cardio-selectivity is relative to the effects on β_1 -receptors high doses of drugs such as atenolol and metoprolol also cause some degree of β_2 -blockade and may therefore precipitate bronchospasm in some patients with obstructive airways disease. Acebutolol is the least cardioselective member of this group because one of its metabolites is active at both β_1 -receptors and β_2 -receptors.

The theoretical therapeutic potential of such properties as intrinsic sympathomimetic activity (ISA or partial agonist activity) and membrane stabilising activity (local anaesthetic effect) which should reduce the cardiodepressant action and increase the antiarrhythmic efficacy respectively has not been satisfactorily established in clinical practice. Nevertheless, in patients with poor cardiac reserve in whom reduction of the

compensatory sympathetic drive is of potential harm a drug with intrinsic sympathomimetic activity is commonly chosen. If heart failure is likely with a beta-blocker it is usually seen shortly after starting treatment rather than when dosage is increased during chronic treatment. Drugs with intrinsic sympathomimetic activity do not, in general, produce as great a degree of reduction in heart rate and are less suitable for conditions in which there is evidence of excessive sympathetic activity such as thyrotoxicosis. On the other hand, patients with idiopathic orthostatic hypotension who have decreased sympathetic activity may benefit from the high intrinsic sympathomimetic activity of pindolol.

A membrane stabilising effect (class I antiarrhythmic effect antagonising fast depolarisation) is seen only with blood concentrations that are considerably higher than those usually encountered in clinical practice. Sotalol appears to have class III (prolongation of the myocardial cell action potential) antiarrhythmic activity. There has been no clear demonstration that these properties enhance the clinical benefits of these drugs. The use of beta-blockers to treat arrhythmias is considered in a later article.

Adverse effects

As indicated above many of the unwanted effects of beta-blockade—for example, bronchospasm, heart failure, and cold hands and feet—are simply expected but undesirable pharmacological effects. The exclusion of patients at particular risk and the choice of a cardioselective agent when appropriate means that most patients given a beta-blocker will be able to tolerate these drugs. Bradycardia of 50-60 beats/min is not uncommon and in the absence of symptoms, such as cerebrovascular insufficiency or atrioventricular block, is not an indication for withdrawal. Postural hypotension or impaired sexual function is uncommon, although with labetalol, particularly in high dosage, postural hypotension may be a problem because of concurrent alpha-blockade, and this may limit its usefulness. Pronounced sympathetic stimulation—for instance, in phaeochromocytoma, clonidine withdrawal, or insulin hypoglycaemia in the presence of non-selective blockers—leads to unopposed alpha-stimulation resulting in diastolic hypertension. While beta-blockers alone are unsuitable for phaeochromocytoma and clonidine withdrawal, in the hypoglycaemia-prone diabetic blockade of beta₂-receptors also in part delays recovery by blocking gluconeogenesis, making a cardioselective agent the drug of choice. Precipitation or aggravation of Raynaud's phenomenon due to blockade of peripheral beta₂-vasodilatory receptors with consequently unopposed alpha-mediated vasoconstriction may also in part result from a beta₁-mediated reduction in cardiac output. Fatigue, depression, vivid dreams, insomnia, or drowsiness are more commonly seen with drugs that penetrate the brain and cerebrospinal fluid (propranolol, oxprenolol, metoprolol, pindolol) and may be relieved by switching to atenolol, nadolol, or sotalol. A few patients develop diarrhoea, nausea, or rash. The oculomucocutaneous syndrome (rash, dry eyes, sclerosing peritonitis) seems to have been specific to practolol, and use of this drug is now restricted to acute parenteral administration in hospital.

Stopping treatment suddenly after chronic use is associated with evidence of a withdrawal syndrome (tachycardia, hypertension, agitation). Although this occurs in fewer than 5% of patients, it may be particularly troublesome in patients with ischaemic heart disease, as worsening angina and myocardial infarct have occasionally been reported. A gradual withdrawal of treatment over some weeks is therefore advised for these patients.

Use of beta-blockers

All beta-blockers are effective in the management of hypertension and angina; drug choice is therefore dependent on the factors outlined above. When there is a risk of inducing cardiac

failure or bronchospasm dosage should be introduced cautiously and the patient's response reviewed within a few days. In uncomplicated angina or hypertension treatment may begin with the lower doses given in the table and as recommended in the *British National Formulary*. In hypertension a full effect may not be seen for some weeks, so dosage increments should be at least two weeks apart. The important mechanism(s) responsible for the hypotensive effect of these drugs is not clear, although various ones have been suggested (reduced cardiac output and renin release, central or vascular effect). Labetalol is of equal efficacy to other beta-blockers and has the advantage of acting rapidly when given intravenously because of its additional alpha-blocking properties (see later article). Increasing the dosage above the upper levels shown in the table—for example, above 480 mg propranolol—usually gains only a modest further reduction in blood pressure and at the expense of much more trouble from side effects, particularly fatigue. The addition of a diuretic (and if need be a vasodilator) is therefore a better approach to resistant hypertension and will lead to good blood pressure control in up to 90% of patients. Combined beta-blocker-diuretic preparations are expensive and are often reserved for patients who have difficulty in complying with the standard formulations.

In angina pectoris dosage must be titrated according to the clinical response. This is particularly important for drugs that show a wide variation in blood concentrations after a given dose, as efficacy is partly related to concentration. Formal assessment of beta-blockade is not practical for routine clinical use, but serial measurement of pulse rate will indicate patient compliance. Beta-blockers with intrinsic sympathomimetic activity will produce a lesser reduction in heart rate. Frequent dosage (three or four times daily) is required with drugs that have a short—for instance, under six hours—half life. If break through pain occurs by the end of an interval between doses a sustained release formulation or longer acting beta-blocker should be considered in addition to increasing the dosage. Although some of the side effects such as decreased contractility and bradycardia may be cumulative, calcium antagonists (see later article) may, with benefit, be added to beta-blockers. Calcium antagonists are particularly useful in patients with variant angina in whom beta-blockers may occasionally exacerbate coronary artery spasm.

One of the most interesting recent developments is the use of beta-blockers to reduce the incidence of sudden death and reinfarction during the first year of recovery from myocardial infarction. Propranolol, practolol, timolol, and metoprolol have all been shown to reduce mortality by about one quarter. It seems that benefit is seen when the drug is started at any time between five and 28 days after the infarct and may be obvious by as early as three months of starting treatment. There is no consistent trend to suggest which group (by age, site of infarct, complications, etc) benefits most. Starting beta-blockers at the time of infarct has not yet been consistently shown to reduce mortality. Fewer than half of patients with infarcts studied in the trials were suitable candidates for beta-blockade. The only property common to all of these agents is beta-blockade. When the results of all the beta-blocker secondary prevention trials in myocardial infarction are considered together, and especially as side effects in most studies have been minimal, many believe that there is now a strong case for advocating the use of beta-blockers in patients who have survived a myocardial infarction, irrespective of whether or not they suffer from angina. How long such treatment should continue is not clear, although most benefit appears to accrue in the first year.

The use of beta-blockers in several other conditions has recently been clarified. In thyrotoxicosis, where the metabolism of lipid soluble drugs such as propranolol and metoprolol is increased, larger doses than conventionally used (160 mg/day of propranolol) may be necessary in some patients if adequate beta-blockade is to be achieved. This is particularly important when patients are prepared for surgery with these drugs. Propranolol, and to a lesser extent cardioselective beta-blockers, are effective in the prophylaxis of migraine in about 50-60% of patients, but the mechanism of action is probably complex.

Propranolol has recently been shown to reduce the incidence of gastrointestinal haemorrhage considerably in patients with mild liver cirrhosis by reducing liver blood flow (due to the fall in cardiac output and possibly also to an effect on splanchnic vessels). It is not, however, useful in acute bleeding and should be used with caution in patients with severe liver disease. Essential tremor is mediated through beta-receptors, and in addition to their use in this condition non-selective beta-blockers have proved useful in the management of stress associated tremor—for instance, in musicians. Beta-blockers reduce intraocular pressure by decreasing the secretion of aqueous humour, and timolol given twice daily as eyedrops has now been shown in long term studies to control intraocular pressure satisfactorily in over 70% of patients with chronic simple glaucoma. It should be remembered that because of absorption of the drug from the eye some systemic effects of beta-blockade may occur and caution should therefore be exercised in patients liable to heart failure or bronchospasm.

Sympathomimetics

DOPAMINE

Dopamine, in addition to being the immediate precursor of noradrenaline, acts on a series of specific receptors within the brain and vascular system. Outside the central nervous system dopamine acts both directly on beta₁-receptors of the heart and indirectly by releasing noradrenaline, producing primarily alpha-adrenergic effects. In addition, it acts directly on dopamine receptors in the myocardium to increase contractility and cardiac output and in the renal, mesenteric, and coronary vessels causing vasodilatation. Because of these multiple actions, variable haemodynamic consequences may be expected, depending on the dosage used. Low doses (1–5 µg/kg/min) stimulate dopamine receptors, thus increasing renal blood flow, glomerular filtration rate, and sodium excretion with little or no effect on cardiac output. Nausea and vomiting may result from stimulation of central dopamine receptors. With dosage in the region of 5–10 µg/kg/min the beta-stimulant effect becomes more pronounced with an increase in myocardial contractility, stroke volume, and cardiac output without much alteration in peripheral resistance, blood pressure, or heart rate. Infusion rates of 10–20 µg/kg/min produce more pronounced alpha effects with a rise in peripheral resistance and blood pressure and a fall in renal blood flow. Excessive beta-stimulation produces an increase in heart rate and cardiac arrhythmias that limits the use of dopamine in patients with tachyarrhythmias.

Dopamine (Inotropin) is inactive when taken by mouth and has a half life of two minutes when given intravenously. Metabolism will be impaired in patients receiving monoamine oxidase inhibitors. Extravasation produces local vasoconstriction, sloughing, and skin necrosis and is treated by local infiltration of the alpha-blocker phentolamine. Starting with 2 µg/kg/min, dopamine dosage is increased every 15–30 minutes until therapeutic or undesirable effects are encountered. A gradual withdrawal is recommended as hypotension and anuria has followed abrupt withdrawal. Dopamine is used in low output states such as cardiogenic and septic shock and cardiac failure.

Beta₁-stimulants

The availability of dopamine and more selective beta₁-stimulants has superseded the use of isoprenaline as an inotropic agent. Prenalterol (Hyprenan, Varbian) is useful in patients requiring inotropic support, particularly after cardiac surgery and in cardiogenic shock. Unlike dobutamine, prenalterol has little chronotropic activity and increases myocardial contractility without appreciably increasing heart rate or causing arrhythmias. Recent studies in patients with chronic congestive heart failure have also shown that it may improve myocardial contractility both at rest and on exercise.

As a pure beta₁-agonist that is devoid of the alpha-adrenergic effects seen with dopamine, prenalterol has potential in the treatment of unwanted beta-adrenergic blocker effects. In cases of deliberate self poisoning with a beta-blocker large doses of prenalterol (2–5 mg) may be required to antagonise the unwanted effects.

At present, prenalterol is available for clinical use only in a parenteral form but an oral preparation is under study. The plasma half life is 120 minutes, and excretion occurs mainly via the kidneys with more than half the drug being recovered unchanged in the urine. It is given at a rate of 0.5 mg per minute, at first with titration based on clinical effect. The current maximum recommended dosage is 20 mg. While there is increasing evidence that it does not precipitate or worsen cardiac ischaemic pain or arrhythmias it should be avoided in patients with serious ventricular arrhythmias. If pronounced hypertension or tachycardia is produced this may be counteracted by a beta-blocker. Symptoms of beta-stimulation such as tremulousness have been encountered but are rarely important.

Dobutamine (Dobutrex) is a synthetic derivative of isoprenaline that acts directly on beta₁-receptors with a greater inotropic than chronotropic effect and has little effect on peripheral vessels, except in high doses where tachycardia and hypertension (or hypotension occasionally) may occur. It does not act on dopamine receptors. Dobutamine is given by intravenous infusion and is rapidly metabolised in the liver with an elimination half life of two minutes. The dosage, 2.5 to 10 µg/kg/min, is adjusted according to the response. It is claimed to have a lower incidence of arrhythmias compared with isoprenaline. Comparative studies have shown a similar increase in contractility with fewer adverse haemodynamic effects. Dobutamine seems to be useful in cardiogenic shock (pump failure due to myocardial infarction or heart surgery) and in heart failure (where it may be preferable to dopamine), particularly if uncomplicated by severe hypotension.

Beta₂-stimulants

The use of beta₂-stimulants in obstructive airways disease is considered in *Drugs in Respiratory Disorders*. Experience with beta₂-stimulants in resistant heart failure to reduce afterload is limited and experimental; hypotension and tachycardia are major side effects. Beta₂-stimulants are also used to relax uterine muscle in an attempt to arrest preterm labour. Ritodrine is relatively selective for beta₂-receptors and isoxsuprine, orciprenaline, salbutamol, and terbutaline have also been used. These drugs are given first by intravenous infusion with dosage titration until uterine contractions have stopped. They all cause maternal tachycardia and to a lesser extent anxiety, flushing, tremor, nausea, and diastolic hypotension. A rise in blood sugar concentrations and ketoacidosis have been reported, particularly when corticosteroids are given concomitantly to induce fetal lung maturation. Placental transfer of the drug may cause fetal tachycardia. The effect of these agents on perinatal morbidity and mortality is not yet clear.

Bibliography

- Anonymous. The arrest of preterm labour. *Drug Ther Bull* 1980;18:34-6.
- A general discussion of β-stimulants including criteria for use and unwanted effects which concludes that they suppress labour in up to two thirds of patients.
- Feely J, Forrest A, Gunn A, Hamilton W, Stevenson IH, Crooks J. Propranolol dosage in thyrotoxicosis. *J Clin Endocrinol Metab* 1980;51:658-61.
- Clinical study reporting that the variability in response may be related to drug concentrations and when propranolol is used alone to prepare patients for surgery larger doses are necessary in younger and more severely toxic patients.
- Frishman WH. β-Adrenoceptor antagonists: new drugs and new indications. *N Engl J Med* 1981;305:500-6.
- A brief outline of the pharmacological differences in the widely used β-blockers, with a consideration of their use in glaucoma and migraine.

Hampton JR. Should every survivor of a heart attack be given a beta-blocker? Evidence from clinical trials. *Br Med J* 1982;285:33-6.

A detailed critique of the available data followed by the views of a clinical pharmacologist (A Breckenridge pp 37-8) and some overall conclusions (G Rose pp 39-40).

Hitchings RA. Beta-blockers in the treatment of chronic simple glaucoma. *Br Med J* 1982;285:84-5.

An up to date editorial that concludes that timolol maleate is a major advance in the medical management of this condition.

Lebrech D, Poynard T, Hillon P, Benhamou J-P. Propranolol for prevention of recurrent gastrointestinal bleeding in patients with cirrhosis: a controlled study. *N Engl J Med* 1981;305:1371-4.

Of 74 patients 96% who were randomly assigned to propranolol were free from recurrent bleeding at one year compared with 50% of patients treated with placebo.

Loeb HS, Bredakis J, Gunnar RM. Superiority of dobutamine over dopamine for augmentation of cardiac output in patients with chronic low output cardiac failure. *Circulation* 1977;55:375-81.

The acute haemodynamic effects were compared in 13 patients (cardiomyopathy, ischaemic heart disease) receiving digitalis and diuretics.

Man In 'T Veld AJ, Schalekamp MA. Pindolol acts as beta-adrenoceptor agonist in orthostatic hypotension: therapeutic implications. *Br Med J* 1981;282:929-31.

Description of successful treatment in three patients.

Norwegian multicentre study group. Timolol-induced reduction in mortality and reinfarction in patients surviving acute myocardial infarction. *N Engl J Med* 1981;304:801-7.

A well conducted secondary prevention trial.

Petrie JC, Jeffers TA, Robb OJ, Scott AK, Webster J. Atenolol, sustained-release oxprenolol, and long-acting propranolol in hypertension. *Br Med J* 1980;280:1573-4.

Once daily sustained-release oxprenolol was inferior to the others in producing satisfactory control of blood pressure over 24 hours.

Sonnenblick EH, Frishman WH, Le Jemtel TH. Dobutamine: a new synthetic cardioactive sympathetic amine. *N Engl J Med* 1979;300:17-22.

A consideration of adrenergic inotropic agents and the use of dobutamine, including comparative studies, in congestive heart failure and myocardial infarction with pump failure.

Letters to a Young Doctor

Overseas doctors

PHILIP RHODES

Many overseas doctors do well in the National Health Service. About one fifth of all principals in general practice were born overseas. About a tenth of all consultants are not natives of the United Kingdom or Eire. This success story, however, hides a serious problem. Unfortunately, many doctors from overseas have come to Britain for training and have been bitterly disappointed by their experiences. They have not been as well cared for educationally as they should have been. This has now been widely recognised, and honest, serious attempts are being made to set matters right. Nevertheless, it still cannot be guaranteed that foreign doctors will get a fair deal and do what they wish to do.

Most overseas doctors come to Britain to obtain a different experience from that in their own countries, to get a higher diploma of one of the royal colleges or faculties, to get some more experience after that, and then to return home. This is laudable, and many who work in the NHS sincerely wish to help. They genuinely think that in so doing they are making a valuable contribution to medical care elsewhere, especially in developing countries. A country such as Britain, which has advanced medical services, should help to train doctors so that they can return home better educated to deal with health care problems. In fact about 85% of all overseas doctors return to their own countries after a time in the NHS.

Overseas doctors should be warned that teachers in Britain cannot (with rare exceptions) teach in a way that is fully appropriate for a foreign country. Countries differ so much in their cultural attitudes, language, medical resources, politics, and other things that affect medical practice. All that may be done in the NHS is to teach British ways, skills, and attitudes.

With these taken in and understood the overseas doctor may return home to modify them and use them in a culture that he understands. He cannot normally transplant a British system to his own country, nor would he wish to. Rather, he must select out of the British system what he thinks is best and most suited to where he works. What is especially hoped for is that British medical standards may be so high that they may be used as a paradigm elsewhere. If doctors go home determined to raise the standards of practice, perhaps on the model of British medicine if that is thought applicable, then British medicine will have made a useful and lasting contribution to the medical weal. In many cases this high ideal has been attained, but in far too many others there has been failure. The reason for the failure of some overseas doctors to get what they want and need out of the NHS is not always to be laid at the door of the NHS. It is in the hope of minimising correctable errors that this article is written.

What to do before coming to Britain

Do not resign your job at home or move to Britain until you have done a lot of preliminary work by post. Much time and anguish may be saved if you do this. You may get some information about Britain and the NHS from the British Embassy or the British Council. But the best place to write to is the National Advice Centre, 7 Marylebone Road, London NW1 5HA, which advises and helps overseas doctors specifically and is independent of the government. It cannot arrange jobs for you, but by its advice it can give you an idea of how the system works and therefore of how to use it to your best advantage. The National Advice Centre may also be contacted if you are already in Britain. Interviews with counsellors may be arranged and information about educational courses and diplomas may be obtained. The BMA's commonwealth and international medical advisory bureau also provides advice for overseas doctors. If you are already in the NHS, however, you may seek advice

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