the Privy Council is about to make an order to put the fee into effect. A situation might therefore arise in which defaulters' names could be erased from the *Register*. Any Government faced with a disruption of the medical services by an intraprofessional dispute affecting the public interest would be bound to act, and this action might well be not only to pay for the G.M.C. itself but also make it a part of the Government machine. The dangers of this to a profession already employed by the State in a National Health Service are too obvious to need stressing. What is also obvious, but is so important that it cannot be stressed too much, is the urgent need for the medical profession to come to terms with itself and to secure its own future. Here the B.M.A. must take the lead, because it can claim through its membership to represent the profession. The Representative Body has asked for an immediate review jointly by the B.M.A. and the G.M.C. of the G.M.C.'s functions and composition. Fortunately the Representative Body has also paved the way for this, for it decided to ask doctors to make a single contribution to the G.M.C. in the financial year 1970-1 to help it through its financial crisis. Provided that doctors do this, it will remove the urgency from the need for the annual retention fee and give time for thought.

Inevitably discussion on the composition and functions of the G.M.C. has been linked with the debate on the retention fee, and further confused by the questioning of the propriety of the Council's action in disregarding Association policy as made by the Representative Body. As a result the B.M.A.'s demand for a majority of the G.M.C. to consist of members directly elected by the profession has been nailed to the mast without the full-scale consideration that such a far-reaching reform requires. The demand is that what has hitherto been not far removed from an autocracy should assume the trappings of democracy. As the B.M.A. itself has sometimes found, democracy can be inconvenient, despite its unexceptionable credentials. The G.M.C. throughout its long history has served the profession well. Largely owing to it a British doctor can echo in paraphrase the old Roman boast and proudly proclaim *civis medicus sum!* Any plans to democratize the G.M.C. must take into account that in it repose the ethics, education—the integrity—of the profession, and that it should not be subjected to the fluctuating and conflicting pressures of medico-politics.

[1] *British Medical Journal Supplement*, 1969, **4**, 5.
[2] *British Medical Journal*, 1966, **1**, 1164.

Laevo-dopa for Parkinsonism

So often has the treatment of chronic neurological diseases been disappointing that the promise of effective treatment of Parkinsonism by laevo-dopa was initially treated with understandable reserve. But the pioneer reports of W. Birkmeyer and O. Hornykiewicz[1] and G. C. Cotzias and his colleagues[2] have now been confirmed by several clinical trials.[3–6] Many patients have had their disabilities alleviated by L-dopa. From the evidence so far collected it is now possible to carry on the story from previous discussion in these columns and outline the role of L-dopa as it is seen at present.[7 8]

Patients with atypical syndromes of Parkinsonism—such as those with striato-nigral degeneration or Jakob-Creutzfeldt's disease—responds poorly to L-dopa. Of the rest it seems impossible to predict the eventual clinical response. Studies of patients with idiopathic,[6] post-encephalitic,[4] and disease of mixed origin[9] have failed to show reliable clinical or biochemical indications of the response to be expected. A recent trial suggests[10] that degree of improvement tended to be inversely related to age of patient, duration of illness, and severity of disease, but this conclusion does not accord with the results of trials based on larger numbers of patients.

With minor variations of detail the general principles of giving the drug are agreed. At first 0·25–1·0 g. is given in three or four divided doses after meals. The daily dose is then increased by a further 0·5 to 1·0 g. at intervals of three to four days. These increments are continued until intolerable side-effects are provoked or a total daily dose of about 8 g. is attained. Cotzias and his colleagues[11] maintain—and there have been no studies to contradict them—that if the maximum tolerated dose is approached at a much slower rate and with smaller increments of 50 mg. many of the initial side-effects can be avoided or reduced. When the daily dose giving most improvement and least sign of intoxication is reached, it may have to be redistributed in the day according to fluctuations in the individual's requirements.

Most patients are content to take their drugs four times a day. Some prefer to take them two-hourly to obtain smoother benefit, whereas others who develop akinetic crises at particular times of the day learn by experience what regimen is best. Diurnal or postprandial fluctuations in response may occur and can often be ameliorated by these changes. Intelligent and otherwise healthy patients can have suitable regimens devised on an outpatient basis. But if side-effects are troublesome, or the patient and his relatives are unable to cope with the principles of administration, L-dopa is best started in hospital. Thereafter it is necessary to review the patient's requirements regularly. Several observers have commented that it is premature to define an optimal dose or maximal clinical benefit until at least six months' treatment has been given.[9 12] There is no necessity to alter satisfactory prescriptions of anticholinergic drugs, but monoamine-oxidase inhibitors, reserpine, phenothiazines, and pyridoxine should not be given. These drugs may negate the beneficial effects of L-dopa.

About one-third of the patients so far reported on have failed to benefit from L-dopa. Intolerable side-effects (gastrointestinal disturbance, hypotension, induced involuntary movements, and mental disturbances) are the main reasons for failure of therapy. Some patients have shown no clinical improvement after taking 4 to 8 g. of the drug daily for several weeks. The relief gained by the remaining two-thirds has varied from slight to spectacular. Initial improvement may be entirely subjective—increased vigour and wellbeing, greater

[1] Birkmayer, W., and Hornykiewicz, O., *Wiener Klinische Wochenschrift*, 1961, **73**, 787.
[2] Cotzias, G. C., van Woert, M. H., and Schiffer, L. M., *New England Journal of Medicine*, 1967, **276**, 374.
[3] Yahr, M. D., Duvoisin, R. C., Hoehn, M. M., Schear, M. J., and Barrett, R.E., *Transactions of the American Neurological Association*, 1968, **93**, 56.
[4] Calne, D. B., Stern, G. M., Laurence, D. R., Sharkey, J., and Armitage, P., *Lancet*, 1969, **1**, 744.
[5] Godwin-Austen, R. B., Tomlinson, E. B., Frears, C. C., and Kok, H. W., *Lancet*, 1969, **2**, 165.
[6] Calne, D. B., Spiers, A. S. D., Stern, G. M., Laurence, D. R., and Armitage, P., *Lancet*, 1969, **2**, 973.
[7] *British Medical Journal*, 1967, **2**, 783.
[8] *British Medical Journal*, 1969, **2**, 202.
[9] Yahr, M. D., Duvoisin, R. C., Schear, M. J., Barrett, R. E., and Hoehn, M. M., *Archives of Neurology*, 1969, **21**, 343.
[10] Peaston, M. J. T., and Bianchine, J. R., *British Medical Journal*, 1970, **1**, 400.
[11] Cotzias, G. C., Papavasiliou, P. S., and Gellene, R., *New England Journal of Medicine*, 1969, **280**, 337?
[12] Mawdsley, C., *British Medical Journal*, 1970, **1**, 331.

clarity of thought and memory, and a general feeling of increased mobility. Soon unequivocal and sustained evidence of benefit may become apparent. A long immobile facies may become animated, a sparkle returns to the eye, and the gait, posture, dexterity of the hands, speech, and balance may all improve. Particularly convincing is a renewed ability to perform movements which have been lost for several years such as rising from a chair or a lavatory seat and turning over in bed. This renaissance may extend to tasks such as shaving, typing, knitting, playing the piano, and even completing the football pools. An early physical sign of response is that silent dentures, hitherto fitted snugly in an immobile face, rattle freely. In exceptional cases patients confined to bed and wheelchair have walked independently. More commonly those whose activities were restricted to the house have shown such improvement in gait, balance, and confidence that they have resumed almost normal physical activities. In other instances men unemployed because of their disabilities have resumed their former occupations. Patients and their relatives have been known to comment that the development of the disease seemed to have been retraced backwards for several years while the dose of L-dopa was augmented.

All the many types of Parkinsonian disabilities may respond, including the classical features of rigidity, tremor, and akinesia, but it is in the last that the greatest benefit may be seen. Dysphagia, dysarthria, salivation, handwriting, and even seborrhoea may benefit; tremor may not improve early but often does later. The well-known discrepancy between physical signs and functional incapacity in Parkinsonism often persists when the patient has responded successfully to L-dopa. A modest improvement in conventional physical signs is often surpassed by the improvement in general motor performance as exemplified by washing, feeding, dressing, cooking, sewing, and the pursuit of normal interests and activities.

The main side-effects are anorexia, nausea, vomiting, hypotension, dyskinesias, nightmares, disturbed sleep, and psychiatric upsets. The haematological abnormalities which were reported when the racemic mixture of D L-dopa in doses of up to 16 g. daily was given have not been found in patients taking the laevo-isomer. Gastrointestinal symptoms tend to occur within the first few days of treatment and may last up to an hour. These side-effects are usually greater when the drug is taken on an empty stomach and when the dose exceeds 1·5 g. Taking the drug after each meal may be helpful; rarely it may be necessary to give 50 mg. of cyclizine half an hour before the dose of L-dopa, but tolerance frequently occurs. There is a general tendency for the blood pressure to fall without change in pulse rate, as noted by Dr. D. B. Calne and his colleagues in their paper at page 474 of the *B.M.J.* this week. In many patients this drop is unaccompanied by symptoms; in a minority changes of posture may be followed by lightheadedness and dizziness. Elastic stockings may be helpful, and the administration of 2 g. of sodium chloride daily has been recommended. The hypotensive effect tends to decrease with time and can probably be minimized, as can nausea and vomiting, by a slower increase in dosage of the drug.

Involuntary movements and grimaces will occur when the dose is high enough, and these induced dyskinesias constitute the commonest reason for limitation of treatment. They cease when the drug is stopped and usually do not recur when, after cessation, it is reintroduced at 0·5–1·0 g. less per day. Some patients treated over many months have developed dyskinesias on a dosage which had previously produced no side-effects; a reduction in dosage may lead to their cessation without decrease of beneficial effect. But for some patients the margin between a toxic and a beneficial dose is too small to be of any value; reluctantly they have been forced to stop treatment despite initial benefit.

Restlessness, apprehension, and agitation of varying degree have been reported. Hallucinations, nightmares, and vivid dreams—a lecturer in European history described with pleasure the contents of a prolonged nocturnal discussion with Bismark—have been described in a minority, as has toxic delirium and frank psychosis. All these behavioural disturbances have reverted to normal when the drug has been stopped. Most of the trials of L-dopa have been restricted to patients with normal electrocardiograms. But some of the published reports suggest that cardiac disturbances may result from it—for example, paroxysmal tachycardia, reversible atrial fibrillation and atrio-ventricular conduction block, and myocardial infarction. Further studies are necessary to establish whether these abnormalities can be related to treatment or were mere coincidence. Patients with Parkinsonism tend to have lower blood pressures than normal, and the hypotension and increased vigour caused by L-dopa in a patient with ischaemic heart disease might prove a serious hazard. Though a history of angina can sometimes be elicited from a patient, the increasing immobility of his disease tends to remove this symptom; a covert state of cardiac ischaemia could be provoked by treatment. Until these particular hazards are clarified by further experience it would be unwise to give L-dopa indiscriminately to patients with cardiac ischaemia or arrhythmias. But apart from these possible heart complications all the side-effects of L-dopa are dose-dependent and reversible. This drug is proving to be a remarkably effective treatment of Parkinsonism.

Failure to Control Venereal Disease

Last year the International Union against the Venereal Diseases and Treponematoses[1] [2] recommended governments of member organizations to review their venereal disease services and to make any necessary financial provisions for them as a matter of great urgency in view of the serious world situation. In addition to increases in the numbers of known cases in most countries many women with asymptomatic, undiagnosed, sexually transmitted disease are seen at gynaecological, antenatal, cervical cytology, family planning, and student health clinics. Some women with asymptomatic disease can be regarded as belonging to a high-risk group, and factors leading to their identification have been discussed by C. B. S. Schofield[3].

Over the last ten years in the United Kingdom there has been no expansion of either staff or premises despite a great increase in the volume of patients attending. During this time the increase of new cases at most clinics has been two- to three-fold. In some cities the numbers have grown dramatically, notably in the Greater London area, where are seen almost half the total cases in the whole of England and Wales; nearly 50% of these cases go to the clinics of one of the four metropolitan regions.

Of patients attending clinics only about 25% have legally defined venereal diseases—that is, syphilis, gonorrhoea, and

[1] International Union against the Venereal Diseases and Treponematoses, *Medical Officer*, 1969, **122**, 45.
[2] International Union against the Venereal Diseases and Treponematoses Bulletin, *British Journal of Venereal Diseases*, 1970. In press.
[3] Schofield, C. B. S., *Lancet*, 1969, **2**, 1182.
[4] National Health Service (Venereal Diseases) Regulations, 1968 (S.I. 1624).