Current Practice

PRACTICAL NEUROLOGY

Parkinsonism

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Parkinsonism must be one of the commonest of the chronic disabling disorders of the central nervous system. Since it is not a notifiable disease and it is rarely a cause of death there is little epidemiological information, but recent studies in the United Kingdom and Europe suggest a prevalence of about 100 per 100,000 of the population, and in North America about 50,000 new cases are diagnosed each year. In the majority of patients the age onset of symptoms is 50–65 years, and with the expectation of more people living longer the incidence of Parkinsonism will probably increase.

It is customary to attempt to classify patients according to cause. Currently, postencephalitic Parkinsonism accounts for only a minority of patients. In this group diagnosis poses few problems ; a previous attack of encephalitis, onset of Parkinsonism at an earlier age, oculogyric crises, tics and compulsive habits, bizarre gaits and grotesque postures, and marked seborrhoea constitute a distinctive diagnostic profile. Though Parkinsonism may develop shortly after an attack of encephalitis it is worth recalling that the latent interval may be longer than two decades. When Parkinsonism develops in an arteriopath with sclerotic retinal vessels, ischaemic heart disease, or claudication it is customary to designate it as arteriosclerotic. Predominantly tremulous Parkinsonism occurring in the elderly is coined paralysis agitans. Drug-induced Parkinsonism is occurring more frequently ; psychotropic agents of the phenothiazine group are particularly suspect. However, it must be admitted that in practice it may be difficult to distinguish postencephalitic, paralysis agitans, arteriosclerotic, and presumed degenerative types. A clear-cut history of previous encephalitis may be lacking in a young Parkinsonian patient, transitional types often occur, and the precise cause may be obscure.

Diagnosis

The recognition of advanced Parkinsonism, with its characteristic facies, tremor, posture, and gait, is usually instant and rarely presents diagnostic difficulties. However, some of the early symptoms may be deceptively vague and non-specific. Cramps often occur in the legs before frank rigidity is evidenced. Undue fatigability, lack of energy and drive, may be misinterpreted as evidence of depression. Difficulty in turning over in bed or hesitancy in arising from a chair do not immediately suggest Parkinsonism. Inability to perform repetitive tasks such as typing, knitting, or stirring may be the presenting complaint before tremor and rigidity are conspicuous. Disorders of balance frequently occur, and, apart from the better-known manifestations of festination or retropulsion, patients may notice that they tend to keel away to one side when sitting unsupported, as on a bench. One patient who had swum regularly for many years recalled that one of his earliest symptoms was a humiliating inability to maintain his swimming posture, so that he slowly submerged. Alimentary disorders, including difficulty in chewing, dysphagia, frequent heartburn, and constipation, occur more frequently in Parkinsonian subjects than in controls. Without stopping treatment it is often difficult to decide whether these upsets are primary manifestations of dysfunction of basal ganglia and vagal nuclei or side-effects of drugs.

It is common knowledge that the severity of all Parkinsonian disabilities may vary greatly from moment to moment and that emotional factors may influence the extent of disabilities. For example, tremor invariably disappears during deep sleep, and a tranquil state of mind may considerably damp down movements ; conversely, emotional distress and embarrassment may dramatically intensify the disturbance. Many patients describe how sudden surprises may effect curious changes in their condition ; one woman felt she was rendered rigid and immobile by the unexpected ring of a telephone. Psychiatric complications are common in Parkinsonism, but clinical assessment should not be unduly influenced by facial immobility and lack of expression. Many patients, including those with the most phlegmatic and equable of temperaments, become demoralized by their wretched disabilities and disfigurements, and severe depression with suicidal hazards may occur. It has been claimed that quite apart from the changes of intellect, retarded thought processes, and lack of concentration, which may be attributed to an organically determined dementia, certain Parkinsonian patients show egocentric traits with a tendency to undue querulousness and exacting hypochondriacism.

Physical Signs

Among the helpful physical signs which may help in the confirmation of a doubtful clinical diagnosis may be mentioned impaired associated movements of the upper limbs when walking, decrement and subsequently disintegration of performance in repetitive movements, such as attempting rhythmically to open and shut the fist, a positive glabellar tap—an inability to inhibit the blink reflex when the bridge of the nose is tapped—and the demonstration of rigidity or cogwheeling at a joint during active contralateral movements. Rather than dwell in detail on the numerous clinical manifestations of Parkinsonism —slowness and delay in initiating voluntary movements, the many varieties of speech disturbance, disorders of handwriting and salivation, the commonly observed ocular defects, including impairment of convergence and upward conjugate gaze, wide palpebral fissures, and infrequent blinking—the remainder of this article will be concerned with current modes of therapy.

Treatment

Most of the currently prescribed drugs are anticholinergic compounds. Their use stems from an early clinical observation

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that belladonna conferred some relief. Naturally occurring alkaloids, such as tincture of belladonna, are now rarely prescribed, but a host of synthetic analogues are available. The general principle is to introduce one drug at a time, beginning with a small dose thrice daily after meals and gradually increasing the amount until optimum relief is obtained or toxic effects become intolerable. This empirical task of adjusting dosage and drug in the hope of establishing a beneficial regimen is often exacting and frustrating; few patients claim dramatic and sustained relief from Parkinsonian disabilities, whereas undesirable side-effects are all too frequent. Despite sceptical comments which entirely relate amelioration of disabilities to prescriber's enthusiasm, there can be little doubt that some patients experience useful improvement of tremor and rigidity and show unequivocal relapse when their drugs are stopped abruptly.

Visual hallucinations, toxic confusional states, impaired visual accommodation, and excessive dryness of the mouth often cause patients to reduce or stop their medication without their physician's acquiescence. Rather than persisting with drugs of doubtful efficacy, and even in the patient who is apparently gaining satisfactory relief despite minor toxic effects, it may be worth while gradually weaning treatment from time to time to ensure that the recipient agrees with his donor.

Thrice daily doses of benzhexol 2 mg., orphenadrine 50 mg., benztropine 0·5 mg., ethopropazine 50 mg., and cycrimine 2·5 mg. are approximately equivalent initiating regimens of commonly used drugs. Combinations of drugs at subtoxic levels have been favoured, but there is no agreement on optimum groups, and certainly little justification for giving more than two drugs at the same time. When increments are made very slowly many patients, particularly those with postencephalitic Parkinsonism, may tolerate remarkably large doses of drugs, but it still remains important to ensure that such heroic measures are desirable and justifiable. Should severe intoxication with the centrally active anticholinergic agents occur, confusional agitation, hallucinations, stupor, and ataxia may be promptly reversed by 1–2 mg. of physostigmine salicylate administered parenterally. Dextroamphetamine, 5–10 mg. twice daily, is occasionally helpful to hypokinetic patients, and antidepressant drugs are often indicated in the management of this disease.

L-Dopa

Recently considerable attention in the medical and lay press has been directed to L-dopa (laevo-dihydroxyphenylalanine), a naturally occurring amino-acid. It is well established that dopamine is present in large amounts in parts of the basal ganglia, particularly the striatum and the substantia nigra, and that the concentration of dopamine in these areas in Parkinsonian patients is significantly reduced. Further, drugs which may cause Parkinsonism such as the phenothiazines, reserpine, and methyldopa are known to interfere with dopamine synthesis and activity within the brain. Dopamine given by mouth does not reach the central nervous system, but oral dopa, the immediate precursor of dopamine, crosses the blood-brain barrier. Initial therapeutic trials gave conflicting results, and it was not until 1967 that Cotzias and his colleagues showed that substantial improvement occurred in many patients when large doses of dopa were given. Tremor, cogwheeling, rigidity, loss of associated movements, and gait were all ameliorated. However, induced involuntary movements, nausea, and vomiting were seen in certain patients, and four developed reversible granulocytopenia during treatment. Bone marrow examination revealed intracellular vacuoles in cells of the myeloid series. The haematological disturbances which occurred when the racemic mixture was given have not been found when the laevo-isomer was used in doses of 2·0–8·0 g. daily.

The beneficial effects of L-dopa in many Parkinsonian patients has now been confirmed in other controlled trials, but several problems—of which safety and efficacy during chronic administration are paramount—remain to be elucidated. For example, it has become apparent that postencephalitic patients can tolerate only small doses of L-dopa, and that they are particularly vulnerable to induced hyperkinesias. Tremor does not yield particularly well to L-dopa, but there may be a striking overall improvement in motor performance. This includes the classical disorders of swallowing, speech, balance, and gait, but also extends to many Parkinsonian deficits which cannot be entirely attributed to tremor or rigidity. Patients note the improvement in difficulty with buttons, shoelaces, shaving, household tasks, bathing, and many other similar obstacles to independent existence. These benefits may be idiosyncratic and occasionally spectacular, such as a renewed ability to play the piano, knit, or complete football pools after an interval of several years. A general feeling of euphoria and wellbeing often occurs, which may be understandably reactive but might reflect a direct central influence of L-dopa upon mood. Not all patients can tolerate this drug and significant improvement is by no means general. At the time of writing L-dopa is expensive and it is not generally available in the United Kingdom. It is hoped that in the near future a pure and safe preparation will be available for more detailed clinical assessments. For the moment medical treatment must be restricted to the anticholinergic drugs.

Surgery

There is now considerable agreement on the role of stereotaxic surgery in the relief of Parkinsonian disabilities. Severe tremor often responds dramatically to successfully placed lesions in the ventrolateral nucleus of the thalamus, and the younger patients with predominantly unilateral tremor often gain gratifying relief. When tremor is generalized bilateral operations may be required, and here there is a small but definite hazard of exacerbating other Parkinsonian disabilities such as impaired balance and speech. Rigidity may also yield satisfactorily to surgery, but again bilateral operations are often necessary. Regrettably, the great number of Parkinsonian patients are frail and elderly and are not ideal subjects for surgery. Marked immobility, severe disorders of gait and balance, bulbar symptoms, and evidence of intellectual deterioration are further contraindications to surgical treatment. Even the best results are essentially palliative and do not alter the natural history of the underlying and usually progressive pathological process.

Each patient poses an individual problem in management, and practical advice from rubber-tipped walking-sticks to strategically placed aids to daily living may be much appreciated. Short and intensive courses of physiotherapy rather than sporadic visits scattered over many months may be of great help in restoring confidence after minor setbacks. Patients should be encouraged to persist with their activities as long as possible, despite the anxiety often engendered in their relatives, and prolonged bed rest during transient minor illnesses should be avoided.