## *REFRESHER COURSE FOR GENERAL PRACTITIONERS*

# PARKINSONISM

BY

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As is true of morbidity in general, we know little of the incidence of Parkinsonism in Great Britain, but with the kind co-operation of a group of practitioners in the Leeds area it has been possible to gain an approximate idea of it.

*Incidence of Parkinsonism in Leeds and District*

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| Population surveyed | 485,903 |
| Parkinsonism (all forms) | 288 |
| Approximate incidence | 1 in 1,700 |
| Approximate total in Great Britain | 27,000 |

These figures may not be strictly accurate, but they probably represent the minimal incidence of Parkinsonism in the population. In the same survey the incidence of disseminated sclerosis was almost precisely the same—282 patients.

### Aetiology

The aetiology of Parkinsonism is probably always complex. Paralysis agitans, originally described by Parkinson in 1817, is a degenerative disorder or abiotrophy of the extrapyramidal system, particularly of the corpus striatum and substantia nigra. Recent Scandinavian work suggests that there is a genetic factor in its production, but other factors have to be considered. Parkinsonism not infrequently first appears after a single head injury or following the multiple injuries of a boxer, and all neurologists are familiar with the sudden appearance of Parkinsonism after some form of emotional stress, such as is occasioned by accidents in which there was no serious physical trauma. These factors, difficult to assess, are of considerable importance in medico-legal work, but unfortunately it is rarely possible to be quite certain whether the Parkinsonism was already present before the accident or other incident. Most neurologists will have had the experience of discovering the earliest evidence of Parkinsonism in a patient being examined for some unrelated condition, who at the time of examination has no symptoms referable to his signs. As with so many other chronic, progressive, and degenerative disorders, there is an increasing tendency to take the view that paralysis agitans may be essentially a psychosomatic disorder : there are those who claim that a disordered personality precedes the physical disease, suggesting that people of drive and ambition, contained within a rigid moral framework, may develop paralysis agitans as a result of frustration. Age is certainly an important factor, and paralysis agitans is essentially a disorder of middle and later life, the sexes being affected equally.

An approximate aetiological classification is shown in the following Table, which is an analysis of 90 personal examples.

*Aetiological Classification*

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|---|---|
| Paralysis agitans | 57% |
| Post-encephalitic | 32% |
| Arteriosclerotic | 4% |
| Syphilitic | 2% |
| Doubtful | 5% |

The commonest variety of Parkinsonism is the "idiopathic" degeneration, paralysis agitans. The second commonest is that which follows encephalitis lethargica. This curious infection, thought, though not proved, to be a virus disease, spread rapidly over the world in epidemic waves from 1917 to 1925. There is some controversy concerning its existence before or after these dates, but there is no argument that it was only during this period that the disease existed on a massive scale. A considerable number of those who did not succumb to the acute phase developed Parkinsonism immediately, but in others the syndrome appeared many years later ; the longest interval in my experience is 27 years, and presumably this is not the maximum figure. Much less commonly is Parkinsonism attributed to cerebral arteriosclerosis, with or without hypertension. Examples have also been reported as the result of carbon monoxide and of manganese poisoning. Very occasionally the syndrome arises in a patient with serological evidence of neurosyphilis.

It is by no means always easy to assign any one patient to a particular aetiological group, and indeed there are some who believe this always to be impossible ; but certain features discussed below seem to be the prerogative of the post-encephalitic state, and when these appear the diagnosis of post-encephalitic Parkinsonism can be made with confidence, even though there is no history of the acute illness ; indeed, such a history is now a rarity.

### Signs and Symptoms

All practitioners and many laymen are familiar with the picture of advanced Parkinsonism : the monotonous and failing voice, the expressionless face with lack of blinking, the general attitude of flexion, the tremor, which is usually asymmetrical, and the general absence of the small and repeated movements of the normal person. In its earliest stages, however, the diagnosis is difficult, particularly in the absence of tremor. The attention of the patient may be first attracted by an alteration in the handwriting, which becomes smaller and less legible. At this stage he will also notice difficulty in carrying out the finer and more skilled movements of the fingers, such as those in playing the piano. It is only rarely that disability is first noticed in the legs. On questioning, at any stage, the patient will realize in retrospect that there has been a general slowing down of all physical activity over the previous months. The tremor is familiar and characteristic, and it is rarely mistaken for anything else, but in the absence of tremor the disability, which is often limited to one arm, may be attributed to a wide variety of neurological disorders. It is only for the latter reason that early diagnosis is important so as to prevent the patient from being subjected to lumbar puncture and even more unpleasant investigations.

Among the earliest physical signs are those involving the eyes. These consist of blepharoclonus on lightly closing the lids, weakness or paralysis of convergence,

and infrequent or absent blinking except on tapping the glabella. This latter is perhaps the most constant and certainly the most characteristic sign. On tapping the glabella both eyelids blink in time with the tapping, whether this be slow or fast, and this blinking will continue indefinitely ; the normal person will only blink after the first few taps. For all practical purposes this physical sign is diagnostic of the Parkinsonian state.

Oculogyric crises are highly characteristic and are pathognomonic of the post-encephalitic state. They are becoming increasingly rare. During the crisis the two eyes are suddenly turned, usually upwards, though occasionally to one side. They may turn so far up that the patient cannot see at all, and they may maintain this position for minutes or hours, and in the latter case the eyes may become painful. The attacks occur with varying frequency, but at the worst may appear every day and last for several hours. They are frequently precipitated by psychological factors. These crises are often the presenting symptom of Parkinsonism, but there are always associated eye signs and frequently other evidence of Parkinsonism, though occasionally there may be no involvement of the limbs.

Rigidity is often first detectable in the neck, a place in which it is rarely sought. After the neck the most common site for rigidity is at the wrist, and here the characteristic " cog-wheel " element is elicited by frequent passive flexion and extension of the joint. This is a most important physical sign, and it varies considerably, even from minute to minute in the earlier stages of the disease. Later, similar rigidity is constantly present at all joints, though it is always more obvious at the periphery. A tendency to propulsion or retropulsion is usually a late sign, only demonstrable when the diagnosis is all too obvious. It is important to remember that Parkinsonism, though often bilateral, is usually asymmetrical, and in many patients it is strictly unilateral for very long periods. In a considerable number tremor never appears, nor is it ever seen in the absence of the characteristic rigidity. Though often asymmetrical in the limbs, involvement of the eyes and facial muscles is always bilateral and symmetrical.

In the well-established case, but probably never as a presenting symptom, excessive salivation is frequent, particularly in the post-encephalitic patient, in whom the skin is often very greasy. To the Parkinsonian every movement is an effort, and it is usually easier for him to sit quite still than to move about ; some, however, have a feeling of restlessness and an anxiety to move about, which is a practical impossibility. Not infrequently there is a complaint of pain or discomfort in the joints of the affected limbs, and stiffness or ankylosis is apt to appear in the shoulder-joints.

Apart from any question of psychogenesis, there are very important psychological aspects of the established disease. The patient finds himself living in a continuously contracting environment, in which he becomes more and more dependent on other members of the family, and small worries and problems assume unduly large proportions. Immediate emotional factors adversely affect all the signs and symptoms of the disorder—an observation usually made by every sufferer.

## Prognosis

Parkinsonism is an irreversible process, and no patient has ever been cured. A small proportion of post-encephalitic cases become stationary for very long periods, and perhaps indefinitely, but all other forms of Parkinsonism are inevitably progressive sooner or later, though often with stationary phases. The rate of progress is extremely variable, but it is usually many years before the patient becomes bedridden.

## Medical Treatment

Drugs of the solanaceous group have been used for over 80 years. It was pointed out about 1929, mainly by the late Sir Arthur Hall, that these drugs are most effective when given in increasing dosage up to the point at which toxic symptoms appear. This dosage is sometimes enormous ; for example, the normal dose of tincture of stramonium (5 to 15 min.—0.3 to 0.9 ml.) can be increased to 100 min. (6 ml.) three times a day or even more. Tolerance has to be acquired slowly, but is lost very rapidly. If for any reason a patient who has been taking maximal doses suddenly omits his treatment it is essential that tolerance shall again be acquired slowly, otherwise serious toxic symptoms make their appearance. Occasionally when a patient omits to take his treatment a Parkinsonian crisis is precipitated, and he becomes totally rigid and immobile. This rare but alarming state of affairs soon responds to a renewal of drug treatment.

When large doses of the belladonna group are being taken there is always complaint of difficulty in reading, owing to paralysis of accommodation, and of dryness of the mouth ; these can respectively be relieved by eserine drops and by adding pilocarpine nitrate to the mixture. At this point, however, medicinal treatment has become complicated, and in my experience very few patients acquire tolerance for such very large doses and then maintain them. This may well be because in the course of time drugs which at first help later become ineffective. A group of chronic Parkinsonian patients have recently been discovered, in a hospital for the chronic sick, who had been taking large doses of these drugs for many years ; treatment was suddenly withdrawn, apparently with no detrimental effect. The drugs of the solanaceous group, in the approximate order of popularity, are stramonium, hyoscine, belladonna, and hyoscyamus.

About 1935 " Bulgarian belladonna " had a phase of popularity, though there was no evidence that it was, in fact, any more effective than other members of the group. The effect of these drugs is usually to give the patient a feeling of increased activity and of lessening stiffness. It is doubtful whether any of them really affect the tremor, although it has been temporarily abolished by intravenous hyoscine and other drugs. Little is really known about the mechanisms of tremor, and it has been suggested that rigidity may in some way hold tremor in check ; at the same time it is only very rarely that a patient will claim that his rigidity has lessened and his tremor increased. The prolonged use of any of these drugs over a number of years carries with it the risk of chronic glaucoma.

Curare was tried about 1927, but was soon abandoned. Mephanesin (" myanesin ") has been in use since 1947 ; it is usually given in the form of an elixir, the initial dose being 1 dr. (3.5 ml.) three times a day, which can be increased up to 4 dr. (14 ml.) taken four or five times a day. The larger doses should be well diluted with water. As with most other drugs, mephanesin may reduce the rigidity but is not likely to affect the tremor, and on the whole it has not been very popular.

Numerous synthetic drugs have been introduced for the treatment of Parkinsonism in the past few years, and the list is steadily increasing. As with the solanaceous group, all these drugs are preferably given by mouth in increasing dosage until toxic symptoms appear, and it is still important that the dosage should be increased or decreased slowly. Any of these drugs may be combined with one of the solanaceous group. The general feeling is that the new drugs are perhaps more effective than the old, and they certainly seem to produce effects more quickly.

Perhaps the most popular at the time of writing is trihexyphenidyl ("artane"), which has a pharmacological action similar to that of atropine. The initial dose is 1 mg. on the first day, increased by 1 or 2 mg. daily up to a total of about 12 mg. divided into three or four doses. Toxic symptoms may appear at or before this level, though some patients will take as much as 15 mg. and very rarely 20 mg. daily. The toxic symptoms include dryness of the mouth, nausea, dizziness, and, less commonly, blurring of vision. This drug again may produce apparent relief of rigidity and sometimes reduces salivation, though it does not appear to relieve the salivation of the post-encephalitic; its effect on tremor is very questionable.

Ethopropazine hydrochloride ("lysivane") is supplied in orange-coloured tablets containing 50 mg. of the drug, the initial dose being 50 to 200 mg., which can be steadily increased up to 500 mg. over a period of three to four weeks. Side-effects include drowsiness and dizziness, nausea, paraesthesiae, and cramp in the limbs.

"Parpanit" is supplied in tablets of two strengths, the smaller containing 6.25 mg. and the larger (parpanit forte) containing 50 mg. It is usual to start with six small tablets daily (two tablets three times a day), increasing up to a maximum of about 24 tablets a day (one large tablet is the equivalent of eight small ones). Toxic symptoms again include dizziness as well as palpitation and tinnitus.

Diethazine hydrochloride ("diparcol") has now been largely abandoned, because toxic symptoms have included mental confusion and agranulocytosis.

As with the older drugs, it is unusual to find a patient who is prepared to take the trouble to acquire tolerance for a high dosage and to maintain it. The more usual state of affairs is to find that the patient has of his own accord made a considerable reduction in the total dosage. It would often seem likely that the finally accepted dosage is not much more than a placebo. It has also been found that the antihistamine drugs sometimes benefit the rigidity and general slowness. The usual practice is to combine these drugs with one of the previously named preparations. When large doses of these new drugs are given in combination over a long period it is possible, and indeed highly likely, that toxic symptoms will appear which have not yet been described. The antihistamine drugs tend to produce drowsiness and are sometimes better limited to an evening dose only.

Oculogyric crises never respond to any of the above-mentioned drugs, though their frequency is sometimes lessened under the continuous action of amphetamine. If attacks are very frequent and prolonged, electric convulsion therapy is worthy of trial and in my experience has often proved effective. In the very rare Parkinsonian who has serological evidence of neurosyphilis antisyphilitic treatment must be instituted, but it will not be found to reverse the Parkinsonian syndrome.

Physiotherapy is probably as important as medicinal treatment. The essential part of physiotherapy is vigorous active exercises employing all four limbs, and in the very advanced Parkinsonian daily passive movements of all joints are essential. Hot baths will often relieve the disability in the joints and to some extent the general stiffness. Massage, all forms of electricity, and all emanations have no particular therapeutic value in this disease.

The psychological aspects of treatment have to be left largely in the hands of the family. There is a natural tendency to pay too much attention to the Parkinsonian, who should in fact be given every encouragement to remain at work as long as possible and to fend for himself in the house. At the other end of the scale, and particularly in the early stages before the diagnosis has been established, the patient is sometimes accused of idleness, and I have seen a case in which a nagging wife was murdered by the infuriated patient.

### Surgery in Parkinsonism

The position of surgery is at present unsettled, and publicity in the lay press has often been quite irresponsible. Surgical procedures aim at abolishing tremor and replacing it by weakness or paralysis, and operations may be performed either on the cerebral cortex or on the spinal cord. Since most cases of Parkinsonism are progressive careful selection of patients for surgery is vital. Surgery should probably be limited to patients under 50 who are suffering from gross tremor which is stationary or only slightly progressive and is restricted to one arm. Such rules will exclude about 95% of all patients. It has been claimed that in the ideal case tremor can be abolished, and that the resulting paralysis is not complete, but no such guarantee can be made. I have seen a patient with a post-encephalitic tremor limited to the left hand and stationary for many years who was still able to work and to play golf and tennis; after an operation on the cerebral cortex the tremor disappeared, only to be replaced by a total left hemiplegia and Jacksonian epilepsy, with very serious and permanent disability. Operative mortality figures seem never to be lower than 17%, rising to 35% in those above the age of 50.

In assessing the value of any form of treatment in Parkinsonism it must be remembered that it has always been known that a new remedy is likely to achieve results at first, but that such benefit rarely lasts. This is not surprising, because the patient who claims to feel much better as a result of medicinal treatment rarely shows any striking objective change. It is not suggested that large doses of powerful drugs have, in fact, no beneficial pharmacological action, but there seems little doubt that much of the alleged benefit is the result of suggestion. The optimism caused by early improvement is soon replaced by dejection following relapse, and this is reflected in an attitude of hostility and resentment to the doctor—often very obvious in the patient's face. Because of the factor of suggestion, and the natural tendency of the disease to have stationary phases, the assessment of treatment is as difficult as it is with such diseases as peptic ulcer, rheumatoid arthritis, or ulcerative colitis, although, unlike these, Parkinsonism never shows phases of remission.

Finally, the Parkinsonian must be encouraged to maintain his physical and mental activities and to take an interest in the nature and dosage of the large variety of drugs available to relieve his symptoms.