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THE SURGICAL TREATMENT OF PARKINSONISM

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[WITH SPECIAL PLATE]

Until recent years the surgical treatment of Parkinsonism has been largely confined to interruption of the cortico-spinal pathways at various levels: at the cerebral cortex, internal capsule, cerebral peduncle, and spinal cord. The results of these different procedures and their associated morbidity were not encouraging, and the physiological basis of their application was not sufficiently secure to inspire confidence in the pursuit of the problem in this way.

Russell Myers, of New York (1942), changed the direction of our thinking by the observation that operative interruption of the pallidofugal fibres might modify rigidity and tremor in patients with Parkinsonism. His open operative approach, through the corpus callosum and third ventricle, was formidable and necessarily hazardous. Nevertheless, the early results indicated that his basic concept was correct.

Fénélon, of Paris (1950), described an improved approach using a subfrontal route to the anterior perforated substance, interrupting the ansa lenticularis immediately above the termination of the optic tract by a thermal lesion, using electrocoagulation. The results were promising, and his method was adopted by Guiot and Brion (1953) and others, including ourselves, with conspicuous success.

In the meantime Spiegel *et al.* (1947) had described the first stereotaxic apparatus for operations on the human brain. In so doing they laid the foundations for the development of this type of surgery, with corresponding reduction in mortality and morbidity. Others, notably Talairach *et al.* (1952) in Paris, Leksell (1949) in Lund, Riechert (1954) in Freiburg, Cooper (1955) in New York, Guiot (1958) in Paris, and Bertrand (1958) in Montreal, each developed their own stereotaxic technique. The accumulating information from these various operative procedures has supported Myers's original concept and observations. It would now seem that the strategic interruption of the pallidofugal fibres is an effective surgical means for the alleviation of rigidity and tremor in Parkinsonism, and the involuntary movements of some of the dyskinesias.

Present Study

The evolution of the surgical treatment of the disease in Edinburgh began in March, 1955. This paper is therefore concerned with the study, over a period of five years, of the effect of thermal electrocoagulation

lesions in the globus pallidus, internal capsule, and thalamus, separately or in combination, in 60 patients with Parkinsonism. Each was systematically assessed, and the findings were recorded before treatment in respect of neurological and intellectual functions and emotional state by the neurosurgeon, neurologist, and medical psychologist of the team. Similar detailed studies were made during and after operation. The surgeon and radiologist were jointly responsible for the combined surgical and radiological procedures, and for the plotting of the site and extent of the lesion on stereotaxic anatomical charts, in each case. The charts were first based on the atlas of Spiegel and Wycis (1952), and latterly on that of Schaltenbrand and Bailey (1959). Finally, an extended follow-up along these lines of up to five years, and not less than nine months, has been carried out, embodying the reports of the patient, a close relative, and the attending general practitioner.

The 60 patients were all under 65, except one, a man of 72, with strictly unilateral disease. The largest group were between the ages of 50 and 60. There was no selection of cases apart from imposing an upper age limit of 65. Before considering treatment, investigations were carried out to exclude the possibility of further medical or other surgical means of treatment—for example, hepato-lenticular degeneration and brain tumour.

Our first two patients, both with unilateral left-sided Parkinsonism, were treated by interruption of the ansa lenticularis and globus pallidus by electrocoagulation, using the open subfrontal route described by Fénélon. Both patients were greatly benefited and showed no morbidity. Two months after operation they returned to work, and have subsequently maintained their improvement over the years. One of them with post-encephalitic Parkinsonism was so disabled that he was unable to work for ten years before operation five years ago, and was confined to bed for some period of each week because of increased rigidity, tremor, inertia, malaise, and sweating. These features of his illness disappeared after operation.

The open operative procedure, however satisfactory in these two patients, is exacting under local anaesthesia and has obvious hazards (Gillingham, 1958). Because of this we soon followed a simple stereotaxic method based on that described by Guiot (1958). The remaining 58 patients have therefore been treated in this way since

April, 1957, with considerable development of the apparatus and its method of application over the past three years. We feel that the merits of this method lie in the relatively short operative procedure and in its accuracy and simplicity. Its principles are based on the fact that the globus pallidus and thalamus bear a reasonably constant anatomical relationship to the anterior and posterior commissures, the intercommissural line, and the mid-sagittal plane of the head (Spiegel and Wycis, 1952; Housepian and Carpenter, 1957).

Radiological and Operative Techniques

The operative procedure is carried out in two stages. These are normally separated by an interval of at least 48 hours, but sometimes in very disabled patients we have waited two weeks. The first stage, under general or local anaesthesia, determines the mid-sagittal plane of the brain, the position of the anterior and posterior commissures, and the length of the intercommissural line.

With the patient supine and later prone, three short scalp incisions are made and a series of radio-opaque markers (lead shot) are inserted into the outer table of the skull in holes made with a small dental burr 1 mm. apart. These markers are placed astride the mid-line of the skull at three points: at the upper margin of the frontal sinus, at the coronal suture, and 5 cm. above the external occipital protuberance. Exposure of the coronal and lambdoid sutures and their junction with the interparietal suture gives an approximate guide to the mid-sagittal plane. In addition, a right frontal burr-hole is made 2-3 cm. from the mid-line at the level of the coronal suture. Through it a rubber catheter is passed into the frontal horn of the lateral ventricle for the insertion of radio-opaque "myodil" (ethyl iodophenylundecylate) at the second stage. If the second stage of the operation is purposely delayed the catheter is not inserted. The wounds are sutured and the patient is seated erect.

Lumbar pneumoencephalography is immediately carried out, using about 25 c.cm. of air. It is important to obtain a good lateral erect film in order to demonstrate the posterior commissure. The anterior commissure may also be visible on the lateral erect film. Further films are obtained in the supine position. The lateral supine film, the neck being extended if necessary, shows the anterior commissure. The posterior view is of great importance and must be obtained in the true sagittal plane. This is best achieved by exposing one film in what is judged to be the correct position, together with another two, the x-ray tube being shifted a few degrees to either side. One of these three films is usually satisfactory.

The lead markers corresponding to the mid-sagittal plane of the brain, as judged by the position of the septum pellucidum and the third ventricle, are chosen and recorded. Then the wounds are reopened, and the selected markers are removed and replaced by special stainless-steel screws, the heads of which are recessed to accommodate the pins of the stereotaxic frame. These screws are left in permanently. The wounds are closed and the patient is returned to the ward (Special Plate, Fig. 1).

The second stage is usually carried out 48 hours later, under local anaesthesia in order that the patient's co-operation can be obtained and his reactions observed.

Minimal sedation is given, yet patients tolerate the procedure very well and co-operate to the full.

The patient is first placed on his side and the pins of the stereotaxic frame are inserted through the sutured wounds into the heads of the three special screws (Special Plate, Fig. 2). He is then turned into the prone position, the cheeks being supported in a special face-rest and the image amplifier moved into position on either side of the head. About 6 ml. of myodil is injected through the ventricular catheter inserted at the first stage, or through a brain cannula. The frontal horn is filled until the contrast medium just spills over into the anterior part of the third ventricle and outlines the anterior commissure. The minimum quantity of contrast medium compatible with the clear demonstration of this landmark is advised, though much can be removed at the end of operation. In our experience reactions have been very few and temporary in any case. The injection of the myodil is controlled fluoroscopically by the use of the image amplifier.

Next the transverse bar or cursor is applied to the stereotaxic frame posteriorly, its optimum position on the frame having been determined already from the x-ray film obtained at the first stage (Special Plate, Fig. 3). The sights attached to the cursor can then be aligned opposite the target point in the globus pallidus. For practical purposes this is a constant point 3 mm. posterior to the posterior margin of the anterior commissure and 1 mm. below the intercommissural line. The adjustment of the sights into the correct position is controlled fluoroscopically by the radiologist using the image amplifier. Provided that the target is kept strictly in the centre of the field of the image amplifier, x-ray distortion can be neglected. An x-ray film of the correctly aligned sights is usually taken, and while this is being processed the surgeon makes a burr-hole in the occipital region immediately beneath the electrode guide tube (Special Plate, Fig. 4). The guide tube is usually fixed at 16 mm. from the mid-line, but enlargement of the third ventricle increases this measurement proportionally, especially at the level of the globus pallidus.

The length of the electrode to be inserted is measured against the sights, and it is passed gently through the occipital lobe and across the lateral ventricle. Its contact with the pulvinar of the thalamus can be felt clearly, and the distance between it and the target point in the globus pallidus measured. The electrode is gently pushed on through the ependyma into the thalamus to a point calculated to be at the junction of the internal capsule and thalamus. Confirmation that the tip of the electrode lies in the ventro-lateral nucleus of the thalamus adjacent to the internal capsule is usually evident on stimulation or with low-output coagulation, the patient experiencing a tingling sensation in the contralateral side, usually at the angle of the mouth and over the thumb and index finger. At the higher voltages of stimulation between 5 and 8 volts, or if the electrode lies more anterior in the capsule, there may be involuntary movement of fingers, wrist, and arm, or, if more anterior still, of the face. Movement or disturbance of sensation in the contralateral lower limb is unusual at this distance from the mid-line, occurring in more lateral positions (Guiot, 1959).

When the surgeon and radiologist are satisfied with the correct siting of the electrode, electrocoagulation is carried out over periods of five seconds, and its intensity

increased from a low to a predetermined level according to the size of the lesion required (usually 7 by 5 by 5 mm.). Tremor is often damped down during the period of stimulation, and indeed sometimes disappears with the insertion of the electrode into the thalamus. Coagulation usually abolishes tremor and lessens rigidity. There is, in addition, colour change, the hand becoming pink and less puffy as compared with a somewhat cyanosed, puffy limb with marked venous distension. Motor contractions or paraesthesiae with low coagulation suggest malplacement of the electrode, and it should be readjusted until these cease. Finally the electrode is gently passed across the internal capsule to its final target point in the globus pallidus. As it crosses the capsule and enters the globus pallidus there is a further, and often complete, loss of rigidity and restoration of facility of movement in the contralateral limbs. Stimulation at this point usually causes no subjective sensation to the patient (occasionally he may see a poorly localized flash of light with higher voltages). Electrocoagulation is then carried out as before, creating a lesion of similar volume to that in the thalamus (see Diagram). Intractable pain, which is sometimes associated with rigidity, decreases with the creation of the thalamic lesion, and disappears altogether with the further pallidal lesion. Depth recording with the standard electrode in a few patients has been relatively unfruitful.

Showing situation of lesions in thalamus and globus pallidus.

The electrode is withdrawn and gently replaced by a similar instrument with a detachable tip along the same track. The tip is a stainless-steel ball 1.5 mm. in diameter, and when detached marks the anterior margin of the lesion. The instrument is withdrawn and the stereotaxic apparatus removed. Finally, the wounds are closed in layers after withdrawing myodil and removing the ventricular catheter. The stainless-steel screws remain in the skull and are used for subsequent treatment of the other hemisphere in patients with bilateral Parkinsonism.

Immediate post-operative radiographs are taken without moving the patient, to determine the position of the marker in relation to the anterior commissure, the intercommissural line, and the sagittal plane. No movement of the marker has been noted at this early stage, and we have felt secure in using it as a basis for charting the lesions. After some weeks or months it has been shown to move a little (less than 5 mm.), probably within an area of coagulation necrosis (Special Plate, Fig. 5), or possibly within a cystic cavity, or back along the track. We have observed no ill-effects from its retention.

In charting our lesions we have been fully aware of an individual variation of the basal ganglia to the

commissures, the internal capsule, and to one another. The co-ordinates used from the beginning of this study were the anterior and posterior commissures, the intercommissural line, and from August, 1958, the addition of a vertical line drawn from the mid-point. Subsequent charting of the lesions on the atlas of Schaltenbrand and Bailey has consequently been a simple matter (Special Plate, Fig. 6). Individual variations have been partly overcome by relating the length of the intercommissural line, and latterly the distance between the anterior commissure and pulvinar, in each patient to those measurements of the standard brain of the atlas (Brierley and Beck, 1957). The probable size of our electrocoagulation lesions was determined from studies on fresh necropsy material, and calibration of our diathermy apparatus was done in this way. These estimations have been confirmed by the careful study of three patients who died some time after operative treatment.

In every patient active physiotherapy was started one week after operation. Most patients began to get up and about on the third post-operative day. Attention was particularly paid to posture and walking and to the rehabilitation of the improved limbs. Some patients showed a tendency to neglect the improved limbs temporarily. There were no sensory deficits to account for this. No doubt the disabled limb had been neglected for some time pre-operatively because of uselessness from gross disability, but this cannot be accepted as the whole explanation.

Analysis of Results

The results are considered in Tables I to IV. In Table I each patient is presented chronologically according to the date of his or her first operation. The various columns of the table show the individual pre-operative state, the results of operations, and the particular lesions made in achieving these results. Suitable grading scales have been used in the columns, and these are explained in the table and its footnotes. It is necessary, however, to regroup the patients in order to analyse the results further, and this is done with the aid of Tables II, III, and IV.

In Table II the 60 patients have been divided into three broad pre-operative groups, for it is impossible to assess the results of any method of surgical treatment for Parkinsonism unless the pre-operative severity and extent of the condition are known exactly in the sample of cases under discussion. In the first group, 19 patients had rigidity and tremor almost entirely confined to the limbs on one side of the body, and there was little or no other evidence of Parkinsonism. In the second group, 24 patients were afflicted with bilateral limb tremor and rigidity, one side often being affected more than the other. In this group there was evidence of minor, more widespread effects of the disease, such as excessive salivation, loss of voice volume, etc. The third group was made up of 17 patients with severe bilateral tremor and rigidity, tremor predominating. There were also marked widespread effects of the disease, including degrees of mental deterioration in some patients. These widespread effects suggested to us a more diffuse underlying pathology, and that these patients would tolerate operative lesions less well, producing more complications and side-effects, particularly when large lesions were made, and this has been largely confirmed. The aetiology in each case was mostly unknown. A few patients had a definite history of

TABLE I.—Detailed Analysis of the Results of Surgical Treatment in 60 Patients with Parkinsonism

Case No.	Sex and Age	Duration of Symptoms (Years)	Month and Year of First Operation	Side and Site of Lesions*	Effect of First and Subsequent Lesions								Widespread Manifestations of Parkinsonism (Excluding Limbs)						Post-operative Neurological Deficits	Result of Operations (Neurosurgeon, Neurologist, Psychologist)	Practical Success of Operations†		Comments								
					Limbs Contralateral to First Lesion				Limbs Ipsilateral to First Lesion				Tremor‡				Rigidity‡				Mental Deterioration‡				Preop.	Now					
					Preop.	Now	Preop.	Rigidity†	Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now	Preop.	Now			Preop.	Now		Preop.			Now				
1	M 50	24	Mar. 55	RP	90	0	2	0	0	0	0	0	0	0	0	0	0	1	0	A	c	a	Persisting festination	"	Temporary deterioration during chronic urinary-tract infection. Improved again after prostatectomy. N.B. Festination	Fractured femur. Tremor returned. Suicide	Temporary deterioration from fractured spine Requires op. in contralateral hemisphere	Requires op. in contralateral hemisphere Post-op. psychosis—settled Muscle limb pain relieved by op.	Died of pneumonia 3 months post-op. Severe chest-wall rigidity	May require op. in contralateral hemisphere	c
2	M 53	12	Jan. 57	RP	75	0	2	0	0	0	0	0	0	0	0	0	1	0	A	c	a										
3	F 50	5	Mar. 57	RP/6/LP	75	5	2	0	0	0	0	0	0	0	0	0	1	0	A	c	a										
4	F 50	8	Oct. 57	LP/10/RP	100	0	2	0	0	0	0	0	0	0	0	0	1	0	C	b	a										
5	M 63	6	Nov. 57	LP/28/RP/RT	100	0	2	0	0	0	0	0	0	0	0	0	1	0	A	c	a										
6	F 60	10	Dec. 57	RP/10 RT	90	15	0	2	0	0	0	0	0	0	0	0	1	0	A	c	a										
7	F 38	24	Jan. 58	LP/17/RTP	25	0	2	0	0	0	0	0	0	0	0	0	1	0	A	c	a										
8	M 52	22	Jan. 58	LP	90	10	2	0	0	0	0	0	0	0	0	0	1	0	A	c	a										
9	M 54	5	Feb. 58	LP/9/LT	50	0	1	0	0	0	0	0	0	0	0	0	1	0	C→A	d	a										
10	M 53	6	Mar. 58	LP/4/LP	75	0	2	0	0	0	0	0	0	0	0	0	1	0	B	c	a										
11	M 54	6	"	RP	100	0	3	1	0	0	0	0	0	0	0	0	1	0	B	c	a										
12	M 47	13	"	LP/14/RT	50	20	3	1	50	20	2	2	2	2	2	2	3	1	B	c	a										
13	M 57	9	Apr. 58	LP	75	20	3	1	40	30	2	2	2	2	2	2	2	1	B	c	a										
14	M 59	6	"	LP/9/RT	80	50	2	1	40	20	2	2	2	2	2	2	1	1	B	d	a										
15	F 61	5	May 58	LP/15/RT	75	20	2	1	50	0	2	3	2	0	0	0	1	1	B	d	a										
16	M 62	10	"	LP	10	0	3	1	5	5	3	2	2	0	0	0	1	0	B	b	a										
17	F 39	7	Jun. 58	RP/11/LT/2/RT	70	10	2	0	100	20	2	1	1	1	1	1	0	0	D	c/b	a										
18	F 57	11	"	LP/6/LT	90	50	2	0	75	100	2	1	1	0	0	0	1	1	B	c	a										
19	F 51	23	"	LP/7/RT/13/LT	90	10	2	0	50	0	2	1	1	1	1	1	0	0	B	c	a										
20	M 51	5	"	RP/5/RT	5	0	2	0	0	0	0	1	1	1	1	1	0	0	A	b	a										
21	M 39	4	"	LP/27/RT/RP	5	0	2	0	10	10	2	1	1	0	0	0	0	0	A	a	a										
22	F 56	3	"	LP/12/LT	75	0	2	0	0	0	1	1	1	0	0	0	1	0	A	a	a										
23	F 56	11	"	RP/13/LT/LP	100	0	2	0	100	20	1	0	1	0	0	0	1	0	A	c	a										
24	M 61	16	Jul. 58	LP/8/RT	100	30	3	1	50	0	2	0	2	0	0	0	0	0	B	d	a										
25	M 45	7	"	RP	5	0	2	0	0	0	1	1	1	2	0	0	1	1	A	b	a										
26	M 57	20	Aug. 58	LT	75	25	1	0	0	0	0	0	0	0	0	0	0	0	B	b	a										
27	M 53	9	Oct. 58	RP/LP/LT	50	10	1	0	10	10	0	1	0	1	0	0	1	1	A	b	a										
28	F 52	4	"	RP/LP/LT	50	0	2	1	50	10	2	1	0	1	0	0	2	2	A	d	a										
29	F 42	14	"	RT/15/LP/LT	50	0	2	0	20	0	2	1	0	0	0	0	1	1	A	d	a										
30	F 52	1	"	LT	50	0	2	0	0	0	1	0	0	0	0	0	1	1	A	c	a										
31	M 51	7	Nov. 58	LT	100	20	1	0	0	0	0	0	0	0	0	0	1	1	A	c	a										
32	M 33	4	"	RT	100	0	2	0	0	0	0	0	0	0	0	0	1	1	B	d	a										
33	M 57	7	"	RT	100	20	2	0	0	0	0	0	0	0	0	0	1	1	B	d	a										
34	M 51	2	"	LT	100	10	1	0	10	10	0	0	0	0	0	0	1	1	A	b	a										
35	M 58	13	"	LP	100	0	3	1	100	100	0	3	2	0	0	0	1	2	C	d	a										
36	M 57	16	"	LP/4/RP	60	10	0	0	40	10	3	3	0	0	0	0	1	1	B	d	a										
37	M 63	1	Dec. 58	LT	80	0	2	0	20	10	0	0	0	0	0	0	1	1	A	c	a										
38	F 50	10	"	LT	75	20	2	0	40	40	0	0	0	0	0	0	1	0	A	c	a										
39	M 50	10	"	LT	10	0	3	0	0	0	0	0	0	0	0	0	1	1	B	d	a										
40	M 52	20	Jan. 59	RT	70	10	3	1	60	60	3	3	2	0	0	0	1	2	C	e	a										
41	M 72	7	"	LT	50	0	1	0	0	0	0	0	0	0	0	0	1	2	A	c	a										
42	M 59	8	Feb. 59	LP/LT	50	0	3	0	60	60	3	2	0	0	0	0	1	2	A	c	a										
43	F 63	7	"	LP	70	20	2	0	25	25	2	0	2	0	0	0	1	1	A	d	a										
44	F 53	9	"	LT	100	10	0	0	50	50	0	0	0	0	0	0	1	1	A	d	a										
45	M 52	5	"	RT/RP	75	0	2	0	0	0	0	0	0	0	0	0	0	0	A	b	a										
46	F 61	2	"	RT/RP	75	0	1	0	10	10	0	0	0	0	0	0	0	0	A	c	a										
47	F 51	2	"	RP	10	0	1	0	0	0	0	0	0	0	0	0	1	1	A	b	a										

TABLE I (continued)

Case No.	Sex and Age	Duration of Symptoms (Years)	Month and Year of First Operation	Side and Site of Lesions*	Effect of First and Subsequent Lesions												Widespread Manifestations of Parkinsonism (Excluding Limbs)						Post-operative Neurological Deficits	Result of Operations (Neurosurgeon, Neurologist, Psychiatrist)	Practical Success of Operations		Comments																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															
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* R=right; L=left; P=pallidum; T=thalamus. Intervals between operations stated in months. † Recorded as percentage depending on its duration each day. ‡ Graded on scale 0=nil; 1=minor; 2=moderate; 3=severe. § Result of operations in treated limbs in regard to rigidity and tremor. A=abolished; B=satisfactorily reduced; C=as A or B but with complications; D=unchanged or worse. || Practical estimation of pre- and post-operative level of activities (patient, relatives, general practitioner). a=full working capacity; b=reduced working capacity; c=protected circumstances—minor home responsibilities; d=ambulant but requiring some nursing care; e=bedridden invalid requiring constant nursing care.

encephalitis, and in some in the older age-groups arteriosclerosis was the probable underlying pathology. We have deliberately used the term Parkinsonism somewhat loosely on this account.

TABLE II.—Pre-operative Assessment of 60 Patients with Parkinsonism

Tremor and Rigidity			Clinical Features Indicating Widespread Effects	
Unilateral	Bilateral		Tremor	Rigidity
Confined to limbs	Essentially confined to limbs; minor widespread effects	Marked widespread effects	Jaw Tongue Head	Face Voice Swallowing Salivation Trunk Thorax
19	24	17		
			Mental deterioration	

TABLE III.—Results of Surgical Treatment in Relation to Pre-operative Assessment (60 Patients)

Results		Pre-operative Tremor and Rigidity		
Post-operative State of Tremor and Rigidity in Treated Limbs	No. of Patients	Unilateral Limbs (19 Cases)	Bilateral Limbs	
			Minor Widespread Effects (24 Cases)	Marked Widespread Effects (17 Cases)
Abolished	40	17	15 (5)	8 (3)
Significantly reduced	13	1	7 (2)	5 (4)
Abolished or reduced plus complications	6	1	2 (1)	3 (1)
Unchanged or worse	1	0	0	1
Death from operation	0	0	0	0

Figures in parentheses indicate bilateral operation.

In Table III the results of operative treatment are shown in relation to the three pre-operative groups of Table II. In 53 of the 60 patients limb tremor and rigidity were abolished or significantly reduced to give practical benefit. There were no complications in this group. Of the 60 patients, 16 had bilateral operations.

Complications

Six patients in Table III, despite successful treatment of limb rigidity and tremor, showed various types of complications. In two (Table I, Cases 7 and 10) moderately severe dysphasia followed operation in the dominant hemisphere, lasting four weeks in one and six weeks in the other. In both this was the result of misplaced lesions during the early development of the stereotaxic procedure. Subsequent charting showed the lesions to lie well within the internal capsule. Nevertheless, follow-up has shown an excellent over-all result in one and a fair result in the other, the latter due to persistence of festination and some degree of inertia. In both the dysphasia cleared up.

The third patient (Table I, Case 51), who had shown marked confusion before operation, developed a florid psychotic reaction as the electrode entered the thalamus of the dominant hemisphere. Consequently a smaller lesion than usual was made, but tremor and rigidity in the right limbs, and his general condition, showed definite improvement. The psychotic condition persisted for three weeks, but the fluctuating confusion present before operation persists. In this case the lesion was accurately sited.

The fourth patient (Table I, Case 34) was somewhat similar, for he developed a severe confusional state following operation on the thalamus of the dominant hemisphere. This also persisted for about four weeks, settling down to a somewhat fluctuating degree of confusion, which was largely part of the clinical picture

seen pre-operatively. Once more tremor and rigidity were largely relieved in the contralateral limbs. The lesion was again correctly sited.

The fifth patient (Table I, Case 3), following bilateral lesions in the globus pallidus with an interval of some eight months between each, shows a persistence of physical and mental inertia, though over-all improvement in this respect continues. This patient, early in the series, received a larger lesion than is now our practice. The second, and much smaller, lesion in the contralateral hemisphere was followed by this definite personality change.

The sixth and last patient (Table I, Case 12) to show complications was grossly disabled by his disease, and had been confined to a chair for some six years. After operation on the globus pallidus he was in a state of stupor for a few weeks, but gradually improved. The lesion was ill sited, being too anterior and too low, and in the neighbourhood of the striate vessels. The benefits ultimately obtained were sufficient to warrant consideration of the creation of a lesion on the other side. This was carried out some nine months after the first. It was unfortunately complicated by a haemorrhage into the left lateral ventricle. Thereafter he was comatose, and after many months of stupor he succumbed to a staphylococcal pneumonia.

Deaths

There were no immediate deaths from operation, but three patients have died since operation—one, the patient already described, from a ventricular haemorrhage, and the other (Table I, Case 40) from a staphylococcal pneumonia three months after operation. It was felt that, though the lesion in this second case was satisfactorily sited, it was too small, and a more radical lesion might have achieved a better result. A staphylococcal pneumonia complicated his convalescence from operation, and rigidity of his thorax, which had not been adequately relieved, made him a poor subject to withstand it. One other patient subsequently committed suicide after sustaining a fracture of the femur (Table I, Case 18). Recurrence of tremor had occurred following a fall and fracture of the femur. Thereafter she developed an acute depression and unfortunately died from coal-gas poisoning. She is included in Table III as "unchanged or worse."

Psychometry

Psychometric studies were carried out in the patients of the series both pre-operatively and at various stages post-operatively. The findings enabled us to estimate the degree of any pre-existing mental deterioration attributable to the disease in relation to such changes after operation, and are incorporated in Table I. Methods of assessment included the standard tests, Mill Hill Vocabulary Scale, Progressive Matrices (1938 version), Graham and Kendall Design Memory Test, and Rorschach Projection Test.

Evolution of Surgical Treatment

In achieving the results already described we have passed through three phases in the siting of the surgical lesions as experience accumulated. Table IV explains these phases. The first was from March, 1955, to July, 1958 (Table I, Cases 1–25), and lesions were made in the globus pallidus 17 mm. from the mid-line. In some of this group in whom tremor predominated the best

TABLE IV.—*Evolution of Surgical Treatment in 60 Cases of Parkinsonism*

Operation Dates	First Lesions		Further Lesions	
	Site	No. of Patients	Site	No. of Patients
March, 1955, to July, 1958	Pallidum	25	Ipsilateral pallidum thalamus	1
			Contralateral pallidum ..	7
			Contralateral thalamus ..	2
			Contralateral thalamus/pallidum ..	6
			Contralateral thalamus/pallidum	2
August, 1958, to January, 1959	Thalamus	14	Contralateral pallidum ..	1
	Pallidum	2	Contralateral thalamus/pallidum	2
February to June, 1959	Pallidum	2	Contralateral thalamus/pallidum ..	1
	Thalamus	2		
	Thalamus/pallidum	15		

results—that is, the elimination of tremor as well as rigidity—followed a lesion in the globus pallidus and ansa lenticularis or in the globus pallidus and adjacent internal capsule, or a lesion which included all these sites. When rigidity predominated, a lesion in the globus pallidus, between its medial and lateral parts, almost invariably gave good results. The failure to abolish tremor completely or the recurrence of rest tremor after some weeks led us to adopt the suggestion of Hassler (1957) that a lesion in the ventro-lateral nucleus of the thalamus might abolish tremor more effectively. Of 25 patients originally treated by lesions in the globus pallidus, 7 had an additional lesion made in the ipsilateral thalamus with abolition of persistent rest tremor. As a result, in Phase II, 14 patients from August, 1958, to January, 1959, were treated by thalamic lesions only, these being made in the ventro-lateral nucleus adjacent to the capsule, 16 mm. from the mid-line. Tremor was successfully abolished or greatly reduced in many more patients than previously, but rigidity did not resolve as completely as with lesions in the globus pallidus. As a result, in the last phase, from February to June, 1959, double lesions on the same side—one in the thalamus and one in the globus pallidus, both adjacent to the internal capsule—were made, with further improvement of results and without increasing morbidity. By lowering the trajectory of the track of the electrode 2 to 3 cm. below that advocated by Guiot (1958) both lesions could be made with the same track (Special Plate, Fig. 3, and text figure). In May, 1959, experience suggested the possibilities of a different type of lesion. Tremor in one patient was difficult to eliminate (Table I, Case 52), but by adjusting the position of the electrode in the sagittal plane several times, using low-coagulation current, we abolished tremor without the appearance of side-effects. On charting the lesion we found that it was narrow and elongated, starting in the thalamus, almost completely traversing the capsule, and ending in the globus pallidus 16 mm. from the mid-line and parallel to it. There were no neurological deficits. Tremor and rigidity in the contralateral limbs were abolished and facility was restored. Surprisingly perhaps, yet a matter of considerable importance, transient disturbance of consciousness, which had occurred many times a day for some years before operation and which grossly interfered with the patient's contact with others, disappeared and has remained absent for 15 months to date. This experience has led to further pursuit of this type of lesion in other more recent cases with

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FIG. 1.—Postero-anterior air encephalogram showing radio-opaque markers in the frontal, coronal, and occipital regions which correspond to the mid-sagittal plane (septum pellucidum and third ventricle).

FIG. 3.—Determination of pallidal and thalamic target points and track of electrode from lateral air encephalograms superimposed to show the anterior and posterior commissures.

FIG. 2.—Stereotaxic apparatus applied to the skull.

FIG. 4.—Sights aligned against pallidal target point.

Figs. 5 and 6 appear overleaf

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FIG. 5.—Brain of a patient, not of the present series, who died from coronary thrombosis eight weeks after operation. Sagittal section 17 mm. from the midline, showing lesions in the thalamus and globus pallidus.

FIG. 6.—Lesions in the globus pallidus and thalamus plotted on a sagittal section ($\times 3$) 16 mm. from the midline. (Schaltenbrand and Bailey's (1959) atlas.)

G. B. LEITCH: AMYLOID TUMOUR OF LARYNX PRECEDING RHEUMATOID ARTHRITIS

FIG. 1.—Tomograph of larynx (April 23, 1956) showing mass arising above glottis on left side and approximately central in position with some secondary dislocation of aryepiglottic fold on left side. Appearances favour a tumour arising from neighbourhood of false cords.

FIG. 2.—Section (April 25, 1956) showing amyloid occurring in small masses separated by fibroblasts and chronic inflammatory cells. Prominent giant-cell reaction is present.

bilateral Parkinsonism. They were successfully relieved, but one has the complication of minor paraesthesiae affecting the angle of the mouth and the tips of the thumb and index finger of the opposite limb. From these studies it would seem that tremor and rigidity are controlled most effectively by the strategic interruption of the thalamo-pallidal connexions, essentially the ansa and fasciculus lenticularis. Whether this can be best achieved in the capsule by a relatively small lesion or in the adjacent thalamus and globus pallidus is not yet clear. Certainly large lesions of the capsule in this area are followed by major deficits of motor, sensory, and language function, the last if the lesion lies in the dominant hemisphere. Fortunately we have been able, in the main, to avoid such lesions.

Discussion

A study of the results indicates the need for selection of patients for surgical treatment, and helps to define the pertinent features in the clinical picture which guide selection. The only absolute contraindication to operation is the definite evidence of increasing mental confusion of a moderately severe degree, not dependent on toxic reaction to drugs. Very advanced Parkinsonism—that is, chair- or bed-ridden patients—is not easily benefited by surgery, but some patients have responded dramatically, even to the extent of correction of a gross kyphosis. When the disease is rapidly advancing the duration of benefit is limited, and the converse applies when the disease appears to have halted or is only slowly progressive. In this respect it is important to recognize that we are, in the main, dealing with a progressive disease. However, it may be that strategically placed lesions of adequate size might halt the disease process. This is not yet clear.

Patients over 65 should be considered for surgery only when the disease is essentially unilateral and when they are in good physical and mental condition. Without question the best results are achieved in those patients under 60 in whom rigidity predominates and the disease is slowly progressive and only moderately advanced. Benefit from operative treatment may be lost temporarily during a period of intercurrent infection or emotional stress, or following an injury such as fracture of the femur.

The best type of lesion for the effective and prolonged relief of tremor and rigidity in this series would seem to be the double one, made at the same time in the ventro-lateral nucleus of the thalamus and in the globus pallidus 16 mm. from the mid-line, both lesions bordering on the internal capsule. Hemiparesis or disturbance of sensation are avoided if the lesions are not large and are confined mainly to the ganglia. Still under review is the effectiveness of long, thin lesions extending through the medial part of the posterior limb of the internal capsule from thalamus to pallidum. Early results of this lesion are encouraging. This particular method of stereotaxic cerebral surgery has the great merit of lending itself to the creation of lesions in the thalamus, internal capsule, or globus pallidus, using only one electrode track.

An explanation of the effectiveness of these lesions is not easy, but it may well be that they interrupt the pallidothalamic connexions; usually the ansa lenticularis and the fasciculus lenticularis, and possibly, in addition, connexions of these ganglia with the reticular formation.

Bilateral lesions in the treatment of bilateral Parkinsonism, provided they are small and strategically placed, would seem to be eminently practicable. Morbidity is so small as to recommend such a procedure, but usually with an interval of three to six months between the two operations. Two patients had lesions made bilaterally in rapid succession, one after minutes and the other after ten days (Table I, cases 28 and 36). The first showed some minor disturbance of recent memory which improved slowly, but there was a dramatic relief of Parkinsonism. The second showed no disturbance from bilateral pallidal lesions, the two operations following each other after ten days because of severe intractable pain from rigidity. Pain and rigidity were completely relieved and a severe kyphosis was largely corrected. A number of patients with Parkinsonism complain of pain in rigid limbs, often diagnosed as sacro-iliac pain, sciatica, rheumatism, or fibrositis. In some it is a predominant symptom. Rigidity also manifests itself in difficulty in turning over in bed, in getting out of a chair, and in swallowing. All these symptoms are markedly relieved.

Other associated symptoms which may disappear after operation are the minor attacks of disturbed consciousness and loss of concentration. Both can be benefited. Patients often report a return of their sense of well-being, and put on weight previously lost.

Post-operatively (even after unilateral operation in bilateral disease) drugs can be reduced to approximately half the original dosage, and sometimes given up altogether. This not infrequently results in some feeling of improvement in intellectual performance and sense of well-being from reduction of toxicity from the drugs.

One patient of considerable interest had moderately severe diabetes mellitus associated with Parkinsonism, and required heavy insulin dosage and a carefully supervised diet. After operation both conditions were relieved, the dosage of insulin being reduced to less than half its pre-operative level. Whether the operation had a specific effect on the diabetic condition at a hypothalamic level or whether there is some other explanation is not yet clear. Certainly in patients with Parkinsonism in whom rigidity is marked, loss of weight is a characteristic feature.

When discussing the question of surgical treatment with patients and their relatives it is important that they should know what can or cannot be achieved, and the possible hazards. The features of the disease which are benefited and the duration of relief have already been outlined. We have found that some symptoms are poorly relieved, if at all, and our experience coincides with that of others (Cooper, 1955). The festinant gait, oculogyric crises, reduction of voice volume, and excessive salivation remain difficult problems; indeed, the first two are seldom helped to any extent. Reduction of voice volume has been relieved in a few patients by about 10%, but the results in this respect are disappointing. Excessive salivation is dependent on excessive production, difficulty in swallowing, and to some extent on gravity—that is, in those with a marked kyphosis. Operative treatment helps to some extent only, by restoring swallowing and correcting the kyphosis by reduction of rigidity. In the intractable cases we have found that repeated small doses of radiotherapy to the salivary glands are of definite value.

Summary

An unselected series of 60 patients with Parkinsonism have been treated by stereotaxic electrocoagulation cerebral lesions. Of these patients 53, or 88%, have had tremor and/or rigidity abolished or significantly reduced without complications in the treated limbs, and have been followed for up to five years. Six patients, despite successful treatment of limb tremor and/or rigidity, have persisting complications of the operations. In only one case have limb tremor and rigidity been unimproved. These results have been achieved by accurate siting of the lesion and by making it as small as would be compatible with maintained improvement. The method used has evolved progressively, and is unique, in allowing the creation of lesions in the globus pallidus, internal capsule, or thalamus with one electrode track at different depths. Such combined lesions are usually necessary to eliminate contralateral limb rigidity and tremor.

As a result of our experience we believe that the selection of patients for operation should be governed by the degree of widespread manifestations of Parkinsonism pre-operatively. Where widespread manifestations are present, surgical lesions to treat limb tremor and rigidity cannot be large or inexact placed, otherwise mental deterioration characterized particularly by akinesia will be accentuated.

We wish to thank Professor Norman M. Dott for his interest in this research project; also those of the staff of the Department of Surgical Neurology who have assisted in this work, in particular Dr. A. F. J. Maloney, neuropathologist, and those who assisted in the anatomical charting of the lesions—Dr. Y. Peng Huang, Dr. B. Sira, and Dr. A. Caracalos. Mr. George Newell, of the Department of Animal Genetics of the University of Edinburgh, was initially responsible for the manufacture of the instrument, and has greatly assisted in its elaboration.

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Of the six countries which have the lowest infant mortality in the world, four are European. Statistics for 1958 published by the World Health Organization give the following infant mortality figures per 1,000 live births: Sweden, 16; the Netherlands and Iceland, 17; New Zealand, 19; Australia, 20; Switzerland, 22.

DIGITALIS AS A CAUSE OF PAROXYSMAL ATRIAL TACHYCARDIA WITH ATRIOVENTRICULAR BLOCK

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Digitalis remains probably the most useful single drug in the treatment of all forms of heart failure, though its injudicious use may result in a wide variety of toxic effects on the myocardium. Almost every form of arrhythmia and conduction defect has been attributed to the toxic effects of the drug, most of them arising from the action of digitalis on the ventricles.

The purpose of this paper is to draw attention to an important effect of over-digitalization on the atria—namely, paroxysmal atrial tachycardia with atrioventricular block (P.A.T.B.). The frequency and gravity of this form of digitalis intoxication does not seem to be widely appreciated, yet in certain circumstances very little digitalis can prove fatal. The frequency with which this arrhythmia may result from digitalis is well recognized in the American literature, owing to the work of Lown and Levine (1958), who have summarized their experience in book form. However, it appears to have escaped emphasis in this country, and it does not receive mention in the standard textbooks, where paroxysmal atrial tachycardia is usually dismissed as being of little clinical consequence. This is all the more surprising because it was, in fact, Lewis in 1909 who first described the arrhythmia, and Mackenzie (1911) who attributed it to digitalis.

There is no doubt that digitalis poisoning is occurring with increased frequency, and this is almost certainly due to the greater part played nowadays by therapy which affects the blood electrolytes, particularly the potassium. Among such therapeutic measures may be mentioned the use of salt-reduced diets, potent diuretics both mercurial and of the chlorothiazide type, ammonium chloride, especially if used continuously, cation-exchange resins, and corticosteroids. The importance of the early recognition of this arrhythmia lies in the fact that if it is mistaken for atrial flutter or atrial fibrillation, digitalis may be given, or the dose increased, with fatal results. Similarly, if paroxysmal atrial tachycardia is present but digitalis is not recognized as the cause, the dose may be mistakenly increased, as it is usually regarded as the drug of choice in that condition. In fact, Friedberg (1956) recommends the intravenous route. Provided digitalis is recognized as the cause of the arrhythmia and appropriate treatment given, the prognosis is, in our experience, less serious than has been claimed, and 9 of our 11 patients survived.

Material and Methods

We present the findings in 11 patients, collected over the past two years, in whom P.A.T.B. was present and in all of whom digitalis was believed to have played a major part in precipitating the arrhythmia (Table I).