Summary

The administration of chloroquine to patients with symptomatic porphyria causes a transient reaction in which pyrexia and malaise are accompanied by a marked increase in urine porphyrin excretion. The excretion of porphyrin precursors, δ -aminolaevulinic acid and porphobilinogen increases only slightly.

This reaction is associated with clinical and biochemical evidence of liver damage, in particular, a rise in serum glutamic oxaloacetic transaminase activity. It is thought that the porphyrin excreted in the urine is released from the liver.

After the reaction patients are not affected by further administration of chloroquine; it is not known for how long this refractory state persists. The reaction resembles in some ways the primaquine-induced haemolysis of red cells deficient in glucose-6-phosphate dehydrogenase.

Patients with symptomatic porphyria have improved clinically after chloroquine therapy, but this is attributed to other factors; evidence of hepatic dysfunction argues against the use of chloroquine in this condition.

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Significance of the Extensor Plantar Response in Surgery of Parkinson's Disease

A. G. L. CORKILL,* M.A., M.B., B.CHIR.; A. H. CHIGNELL,* M.B., B.S.

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Parkinsonian patients showing an extensor plantar response rather than a flexor plantar response are often regarded as having more widespread disease. This is true in that the pyramidal system is being secondarily involved. That a worse prognosis is thereby indicated is, however, not so certain. Nevertheless, the presence of extensor plantar responses is often cited as a relative contraindication to surgery.

The supposed grounds for contraindication appear to be two-fold: firstly, patients with extensor plantar responses are thought to have a relatively worse prognosis in any case owing to the more widespread disease, and, secondly, there is a special danger—that of pseudobulbar palsy.

Damage to the internal capsule or other parts of the pyramidal system is an unavoidable occurrence in a small proportion of operative procedures for Parkinsonism. It is supposed that cases already showing involvement of the pyramidal system, as evidenced by extensor plantar responses, will be especially prone to developing pseudobulbar palsy.

It has been observed that a certain number of Parkinsonian patients with extensor plantar responses have concomitant cervical spondylosis or encephalitis (Brain, 1962).

To examine the post-operative prognosis of patients with and without extensor plantar responses who also had widespread

manifestations of the disease was the purpose of the present review.

Present Investigation

Clinical Material.—A group of 112 Parkinsonian patients were reviewed, representing all the cases considered as in-patients for operation by Mr. Harvey Jackson at the National Hospital, Queen Square, in the years 1959 to 1961. Of these 112, 38 were abstracted on the basis of showing widespread manifestations of Parkinson's disease. The remaining 74 patients, who as a group were generally less affected with Parkinsonism, are not further considered here. Widespread manifestations of Parkinson's disease were taken arbitrarily to be, in addition to tremor and rigidity of all four limbs, at least two of the following features: poor voice and speech change, facial akinesia, poor convergence, chairborne existence, tremor of midline structures—that is, jaw, tongue, head, or trunk—and oculogyric crises. Of the 38 patients showing widespread manifestations of the disease, eight had extensor plantar responses on one side and seven had bilateral extensor plantar responses. All 38 were operated on.

Operative Treatment.—This involved the making of a lesion under radiological and electro-stimulatory control in the ventro-lateral nucleus of the thalamus. A stiff paste of Etopalin and

* The National Hospital for Nervous Diseases, Queen Square, London.

kaolin was injected in increments of 0.2 ml. up to a total of 2 ml. The actual volume of the lesion was adjusted at operation according to its effect on tremor and rigidity shown in the patient.

Classification at Three-year Follow-up.—All patients were seen three years post-operatively and evaluated from three particular aspects: social state, widespread manifestations of the disease, and evidence of pseudobulbar palsy. The social state was considered in three classes—"A" at work (doing full housework if a woman), "B" at home but requiring some help, and "C" institutionalized. Widespread manifestations were considered as a group, but significant deterioration in any one of them was recorded as deterioration of the whole group. Pseudobulbar evidence, dysarthria, monotony of voice, and dysphagia were treated similarly in that deterioration in one feature was recorded as deterioration for the whole group. Changes (usually deterioration) in these three aspects were compared between two groups of patients, these two groups being those who had an extensor plantar response, whether unilaterally or bilaterally, and those who had not. Furthermore, an endeavour was made to establish the relation between extensor plantar responses and obvious post-encephalitic cases. The criteria for the presence of encephalitis at some stage were histories of prolonged pyrexial episodes, preferably with some degree of depression of conscious level, long histories, and other recognized signs of encephalitis—for example, loss of accommodation, sialorrhoea, oculogyric crises, and hyperhidrosis. The

incidence of worsening of pseudobulbar features was investigated in those patients showing bilateral extensor plantar responses.

Results.—These are summarized in Tables I to III. No patients developed cervical spondylosis complications sufficiently severe to merit cervical surgery.

Discussion

In a predominantly extrapyramidal disease the presence of pyramidal signs could reasonably be taken as indicating significant spread and a worse prognosis. Examination after a three-year post-operative period did not substantiate this. Cooper (1961a) states that there is a twofold relationship of pseudobulbar palsy to Parkinsonism. Firstly, it should constitute a contraindication to surgery, and, secondly, it may occur after bilaterally symmetrical operations for Parkinsonism.

In the cases of this series the features of pseudobulbar palsy were made worse in 20% of those showing extensor plantar responses as opposed to 35% of those with flexor responses. Even cases with bilateral extensor plantar responses showed only one out of seven which suffered deterioration of pseudobulbar features as a result of operation and three-year passage of time. It is evident in this series, therefore, that the dangers of developing pseudobulbar palsy are somewhat exaggerated. Furthermore, an extensor plantar response is not a bad prognostic sign, nor can it be cited as a contraindication to surgery.

In agreement with the findings of Cooper (1961b) and of Gillingham (1960) this group of patients, all of whom were extensively affected by Parkinsonism, showed a poor response to surgery.

Summary

Of 112 patients with Parkinsonism, 38 were found to have widespread manifestations in addition to tremor and rigidity of all four limbs. Of these 38, 15 had extensor plantar responses, 8 unilaterally and 7 bilaterally. At three-year follow-up post-operatively there was no significant difference between the group with extensor plantar responses and those with flexor responses. The relation between extensor plantar responses, encephalitis, and the cervical spondylosis was briefly examined.

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TABLE I.—Summary of Results

Change	Extensor Plantar Response		Flexor Plantar Response	
	No.	%	No.	%
<i>Changes in Social Status</i>				
Improved ..	2	13	3	13
No change ..	9	60	12	54
Worse ..	4	27	8	35
<i>Changes in Widespread Manifestations</i>				
Improved ..	0	0	1	4½
No change ..	9	60	12	52
Worse ..	6	40	10	43
<i>Changes in Pseudobulbar Palsy</i>				
Improved ..	0	0	0	0
No change ..	12	80	15	65
Worse ..	3	20	8	35

TABLE II.—Alteration in Pseudobulbar Palsy Features in Seven Patients with Bilateral Extensor Responses Pre-operatively

State at 3-year Follow-up				No.
Improved ..	..	..	..	0
Unchanged ..	..	..	..	3
Worse ..	..	..	..	1
No pseudo-bulbar palsy features at any time ..				3

TABLE III.—Relation of Plantar Response to Type of Disease

Type	Extensor Plantar Response		Flexor Plantar Response	
	No.	%	No.	%
Post-encephalitic ..	9	60	11	48
Other	6	40	12	52