(Kennedy, 1969). Also reminiscent of this sort of effect is the Parkinsonism associated with the phenothiazines used in psychiatry compared with the opposite effect of the anticholinergic phenothiazines—for example, diethazine.

In conclusion, thiopropazate seems to be an effective drug in the short term for persistent dyskinesia. This finding, if confirmed, is clinically useful in view of the increasing frequency with which the condition is being reported and its lack of response to other treatment. Whether thiopropazate can be recommended as the phenothiazine of choice in those predisposed to dyskinesia, such as the elderly and brain-damaged, cannot be decided at this stage, since its antipsychotic value relative to that of other phenothiazines has to be considered. Further research on its long-term effectiveness is needed.

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PRELIMINARY COMMUNICATIONS

Persistent Phenothiazine Dyskinesia Treated with Tetrabenazine

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Summary

Six patients with persistent phenothiazine dyskinesia were treated in a double-blind controlled trial with tetrabenazine 100 mg in divided dosage. In three patients the abnormal movements were abolished and in two others there was some improvement, but this was no greater than that achieved with the diazepam control. Tetrabenazine may be useful in the treatment of some patients with persistent phenothiazine dyskinesia.

Introduction

The persistent facial dyskinesia which sometimes occurs after treatment with phenothiazines is similar to the abnormal movements of the face and tongue seen as a complication of levodopa treatment of Parkinson's disease (Sigwald, Bouttier, Raymondeaud, and Piot, 1959; Hunter, Earl and Thorneycroft, 1964). To see whether persistent phenothiazine dyskinesia would benefit from drugs which interfere with normal dopamine metabolism we treated a small group of patients with tetrabenazine. This drug, like reserpine, produces a depletion of dopamine and serotonin in the brain (Pletscher, Brossi, and Grey, 1962) and might therefore be expected to benefit dyskinesia if abnormal movements result from excessive sensitivity to normal brain dopamine release or excessive endogenous dopamine formation.

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Patients and Methods

Six women long-stay inpatients of a psychiatric hospital aged 70 to 85 were investigated. They were moderately or severely demented. Two had had a leucotomy, three had had electric convulsion therapy, and all had been taking a phenothiazine for more than a year. The phenothiazines were chlorpromazine in doses up to 300 mg daily and trifluoperazine up to 15 mg three times a day, with or without anti-Parkinsonian agents. All had developed facial movements which had persisted for periods of from 6 to 12 years. Three of the patients were included in a series described by Hunter *et al.* (1964).

The response of the patients was recorded with a double-blind method, and three courses of treatment were given to each subject. The courses were in random sequence and consisted of one week's treatment each with placebo, diazepam, and tetrabenazine. Identical tablets were used containing either placebo, diazepam 1 mg, or tetrabenazine 25 mg. One tablet was given twice daily for three days and then four times daily for four days. Assessment was carried out on different days by two doctors who did not know the drug regimen. Cine films were taken of each patient on the last day of each trial period. The sequence of the films were later randomized and scored by Dr. D. Marsden, who had no knowledge of the patients. There were thus three independent assessments of the responses of these patients to treatment. Scoring was on a simple four-point scale.

Results

The results are shown in the Table. In three cases abnormal movements were absent during the period of treatment with tetrabenazine. In two others there was a mild reduction of abnormal movements but their response at this dosage of

Scores before and after Treatment

Case No.	Before Treatment	Treatment		
		Placebo	Diazepam	Tetrabenazine
1	9	8·5	8	7
2	8	6	4·5	4
3	4	5	3	0
4	6	6	3·5	0
5	4	4	2	0
6	7·5	6	4·5	6

tetrabenazine was no different from that achieved with diazepam. In one patient the movements remained unchanged.

In all patients the dyskinesia returned within days after cessation of the trial. One patient who showed a good response to tetrabenazine has developed a more generalized choreoathetosis since the trial. Side effects were few, though one patient with a previous history of stroke had a syncopal attack towards the end of her trial period on tetrabenazine. Most of the patients showed some drowsiness on tetrabenazine but this was no greater than the sedative effect of the diazepam control.

Discussion

The treatment of persistent facial dyskinesia is unsatisfactory. The movements can usually be improved only by inducing a Parkinsonian syndrome with large doses of the phenothiazines or butyrophenones responsible for the disorder, and such treatment is only rarely considered justifiable. Any medication that reduces the movements in a proportion of these cases would therefore seem to be useful. Our results suggest that some cases of persistent phenothiazine dyskinesia might respond well to tetrabenazine. We are continuing our investigation of its value in a larger series of patients with abnormal movement disorders.

Our results also suggest that the facial dyskinesia caused by phenothiazines may be analogous to the dyskinesia in Parkinsonian patients treated with levodopa. In Parkinsonism levodopa is probably converted to dopamine in the brain, and the abnormal movements caused by levodopa may be related to the concentration of dopamine in the brain. Pind and Faurbye (1970) showed that patients with persistent phenothiazine dyskinesia have normal amounts of the dopamine metabolite homovanillic acid in the cerebrospinal fluid. Thus there is no evidence of excessive endogenous cerebral dopamine metabolism in these patients. However, if they develop an induced hypersensitivity to normal dopamine formation the improvement shown by some of our patients on tetrabenazine might have been due to partial dopamine suppression.

We thank Dr. R. Hunter, under whose care these patients were, and Dr. D. Marsden for scoring the cine film records.

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MEDICAL MEMORANDA

Diagnosis of Extrahepatic Jaundice in Hodgkin's Disease

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Clinical jaundice in Hodgkin's disease may be due to excess haemolysis, hepatic infiltration, intrahepatic cholestasis, or involvement of the major bile ducts by Hodgkin's deposits at the porta hepatis. The latter is reported as a rare finding (Levitan *et al.*, 1961). Intrahepatic cholestasis occurs as a terminal event of unknown cause in Hodgkin's disease, histology showing only canalicular stasis (Juniper, 1963). Deep jaundice in Hodgkin's disease is, according to Sherlock (1968), due to intrahepatic deposits, and it is believed to be terminal (Bouroncle *et al.*, 1962). A survey of the literature in the English language showed no previous reports of the use of percutaneous transhepatic cholangiography in the diagnosis of jaundice in Hodgkin's disease.

Case Report

A 50-year-old man known to have Hodgkin's disease was admitted to hospital with a five-week history of anorexia, vomiting, pruritus, and increasing jaundice. Clinical examination showed deep jaundice and enlargement of the cervical, axillary, and inguinal lymph nodes. The liver edge was palpable 5 cm below the costal margin. There was no other abnormality.

Three years before the present admission the diagnosis of Hodgkin's disease was confirmed by lymph node biopsy. Lymphangiography at that time showed retroperitoneal lymph node involvement. He had received several courses of radiotherapy combined with prednisone and chlorambucil.

Present investigations were: serum bilirubin 18·0 mg/100 ml; serum alkaline phosphatase 49 King-Armstrong units; erythrocyte sedimentation rate 37 mm in 1 hour; serum proteins normal; white cell count 4,100/mm³; haemoglobin 14·2 g/100 ml. Other liver function tests were normal.

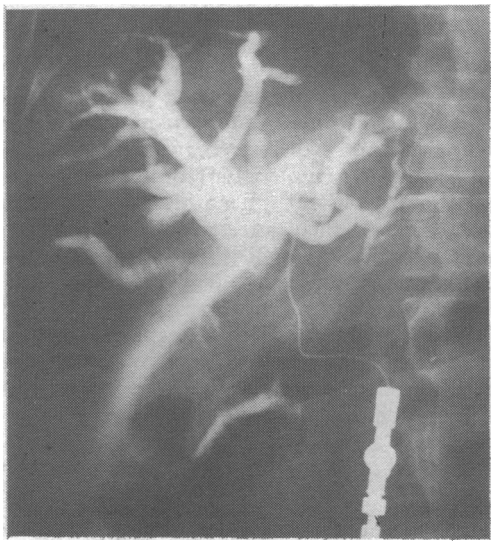

FIG. 1—Percutaneous transhepatic cholangiogram showing dilated intrahepatic ducts and complete obstruction of the common hepatic duct at the porta hepatis.

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