suggests that whatever the metabolic cause for such psychoses and cognitive defects they may be sufficient to produce their effects without the onset of coma. Initial loss of alpha rhythm in the EEG in cases of hypopituitarism and hypopituitary coma, has been described.[4 5] The EEG changes in our case and in other similar cases include disturbances of alpha rhythm and other non-specific changes compatible with severe metabolic disorder.

[1] Blau, J N, and Hinton, J M, *Lancet*, 1960, **1**, 408.
[2] Hanna, S M, *Journal of Neurology, Neurosurgery and Psychiatry*, 1970, **33**, 192.
[3] Igishu, J, *et al*, *Clinical Neurology*, 1973, **13**, 597.
[4] Hughes, R R, and Summers, V K, *Electroencephalography and Clinical Neurophysiology*, 1956, **8**, 87.
[5] Salmon, H S, *British Medical Journal*, 1956, **1**, 1397.

Maudsley Hospital, Denmark Hill, London SE5
R R PARKER, MB, MRCPSYCH, research worker, Institute of Psychiatry, and honorary senior registrar
A D ISAACS, MRCPSYCH, DPM, consultant psychiatrist

King's College Hospital, London SE5
C G McKERRON, MB, FRCP, senior lecturer and consultant physician

Long-term perhexiline maleate and liver function

Perhexilene maleate relieves angina in some patients,[1 2] but serum transaminase levels may rise after prolonged treatment, and this rise seems to be dose related.[3 4]

Patients, methods, and results

Sixteen men with stable angina resistant to other treatment had received perhexilene maleate for an average of 12·5 months. Six took 200 mg and 10 took 400 mg a day. All of them were satisfied with the drug, and therefore formed a selected group. While treatment continued baseline haematological values and electrolytes were estimated and standard liver function tests were carried out. D-glutamyltransferase (DGT) (2.3.2.1), isocitric dehydrogenase (ICD), and bromsulphthalein (BSP) excretion were also estimated. The drug was then withdrawn for one month with the patients' consent while other medication was continued. The results do not identify the six on concurrent medication from the others in the study. One took methyldopa and another clofibrate. It may be important that none was taking anticoagulants.[5] After a month without the drug all tests were repeated. The drug was restarted in the same dose and tests repeated after a further month. Seven patients, while on the drug, had abnormal serum transaminase levels at some time before the trial. In four patients this abnormality resolved spontaneously, in two it resolved with dose reduction, and in one levels were persistently abnormal at 25 IU/l.

Four patients could not complete a month off perhexilene maleate because of intolerable angina but their inclusion in the baseline findings did not produce a bias. For technical and ethical reasons it was possible to repeat the bromsulphthalein test in only 10 patients—five in each dose group. Haematological values and electrolytes were normal except in one patient with asymptomatic chronic lymphatic leukaemia. Bilirubin, alkaline phosphatase, 5′-nucleotidase, and ICD were insensitive indicators of liver function. No consistent changes were seen with alterations in therapy.

Aspartate aminotransferase was raised in three patients but did not exceed 32 IU/l. Two patients developed the abnormality while off the drug. One man had concomitant abnormalities of 5′-nucleotidase, DGT, and BSP excretion and improved biochemically when off perhexilene maleate.

DGT was the enzyme most often raised. Before altering treatment it was high in two patients on 200 mg and six on 400 mg a day (mean (± SE of mean) 49 ± 8 IU). Those completing the trial protocol improved when off treatment (see table), and a paired t test showed this to be just statistically significant ($0{\cdot}05>P>0{\cdot}02$). There was no statistically significant change on restarting the drug. Baseline BSP excretion was abnormal in three men on 200 mg and nine on 400 mg a day. Of those who managed a month off the drug BSP retention decreased significantly from a mean of 10·4 μmol/l (0·87 mg/100 ml) to 5·1 μmol/l (0·43 mg/100 ml) at 45 minutes ($0{\cdot}05>P>0{\cdot}02$). Side effects were not regarded as important by the patients although one man in this trial, and another subsequently, reported poor urinary stream and dribbling incontinence which resolved when the drug was stopped. On direct questioning 12 were impotent and nine blamed the drug. A month off treatment made no difference.

Comment

It is reassuring that with modest doses of perhexilene maleate standard tests of liver function rarely gave abnormal results even after two years of treatment. Sensitive tests such as DGT and BSP excretion, however, indicated liver specific abnormalities in 50-75% of our patients depending on the test used. These abnormalities regressed after a month off treatment.

The results of DGT and BSP excretion tests did not always run parallel, which suggested that the tests measure independent features of liver metabolism affected to different degrees in different patients.

Impotence was common but readily accepted by the patients. Dysuria seems a new side effect.

We regard the liver specific abnormalities shown in this small group of selected patients as acceptable in view of the clinical benefit but would recommend treatment with the smallest effective dose of perhexilene maleate.

We acknowledge the advice of Dr G Walters and the help of Dr G Hunt in the biochemical tests. Perhexilene maleate (Pexid) was supplied by Merrell Division, Richardson-Merrell Ltd.

[1] Burns-Cox, C J, *et al*, *British Medical Journal*, 1971, **4**, 586.
[2] Lyon, L J, *et al*, *Lancet*, 1971, **1**, 1272.
[3] Morledge, J, *Postgraduate Medical Journal*, 1973, **49**, suppl 3, p 64.
[4] Pilcher, J, *et al*, *Postgraduate Medical Journal*, 1973, **49**, suppl 3, p 115.
[5] Garson, W P, Gulin, R C, and Phear, D N, *Postgraduate Medical Journal*, 1973, **49**, suppl 3, p 90.

Bristol Royal Hospitals, Bristol BS1 6SY
D J HOWARD, MB, MRCP, senior house officer in general medicine
J RUSSELL REES, MD, FRCP, consultant physician

DGT levels and BSP retention in 12 patients according to dose of perhexilene maleate, duration of treatment, and change with variation of treatment

	Perhexiline 200 mg/day					Perhexiline 400 mg/day						
Case No (and duration of treatment in months):	1 (3)	2 (4·5)	3 (5)	4 (8)	5 (24)	6 (5)	7 (6)	8 (8)	9 (10)	10 (24)	11 (24)	12 (28)
D-glutamyltransferase (normal <25 U/l)												
Normal initially:												
On perhexiline	12	6	7			10				25		
After a month off perhexiline	18	1	9			6				27		
Month after restarting perhexiline	17	13	22			17				29		
Abnormal initially:												
On perhexiline				34	37		46	100	31		55	54
After a month off perhexiline				27	28		42	58	17		42	31
Month after restarting perhexiline				31	37		29	64	30		36	40
Bromsulphthalein at 45 minutes (normal <6 μmol/l)												
Normal initially:												
On perhexiline		6·0			6·0							6·0
After a month off perhexiline		1·2			2·4							7·2
Month after restarting perhexiline		0·6			3·6							7·2
Abnormal initially:												
On perhexiline	8·4		14·3	11·9		13·1			11·9	8·4	11·9	
After month off perhexiline	3·6		3·6	0·6		8·5			2·4	14·3	10·7	
Month after restarting perhexiline	4·8		13·1			4·8			—	9·6	—	

Conversion: SI to traditional units—Bromsulphthalein; 1 μmol/l ≈ 0·084 mg/100 ml.