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PIMOZIDE: ADVERSE REACTION AND PROLONGED HALF-LIFE

DEAR SIR,

Extrapyramidal reactions to neuroleptic drugs are so frequently encountered as to be considered an inevitable concomitant of appropriate treatment in many patients. We describe an individual case where a severe and life-threatening reaction appears to have been the result of delayed drug elimination. The patient is a 28-year-old woman with minimal brain damage who was admitted on this occasion because of a hypomanic episode. The drug history is shown in Fig 1. Pimozide was chosen because of its reputedly low incidence of extrapyramidal side effects. Following an initial brief exposure to pimozide the patient was commenced on 4 mg/day and this was maintained for nearly six weeks. Towards the end of this time both thioridazine and benztropine were withdrawn because of drowsiness and of blurred vision respectively. At the time indicated by the arrow in Fig 1 the patient developed laboured breathing and intermittent sweating and the pimozide was abruptly withdrawn. However, over the next 48 hours she developed rigidity of such severity that she was unable to move, eat or speak. Benztropine and diazepam produced only limited and transient improvement and there was still marked rigidity two weeks after stopping the pimozide. Slow improvement did, however, occur and the patient was eventually discharged with no residual extrapyramidal signs.

The severity and duration of this dystonic reaction with a drug initially thought to be associated with mild and readily reversible side effects (Pinder, Brogden, Sawyer, Speight, Spencer and Avery, 1976) suggested that impaired metabolic clearance might be

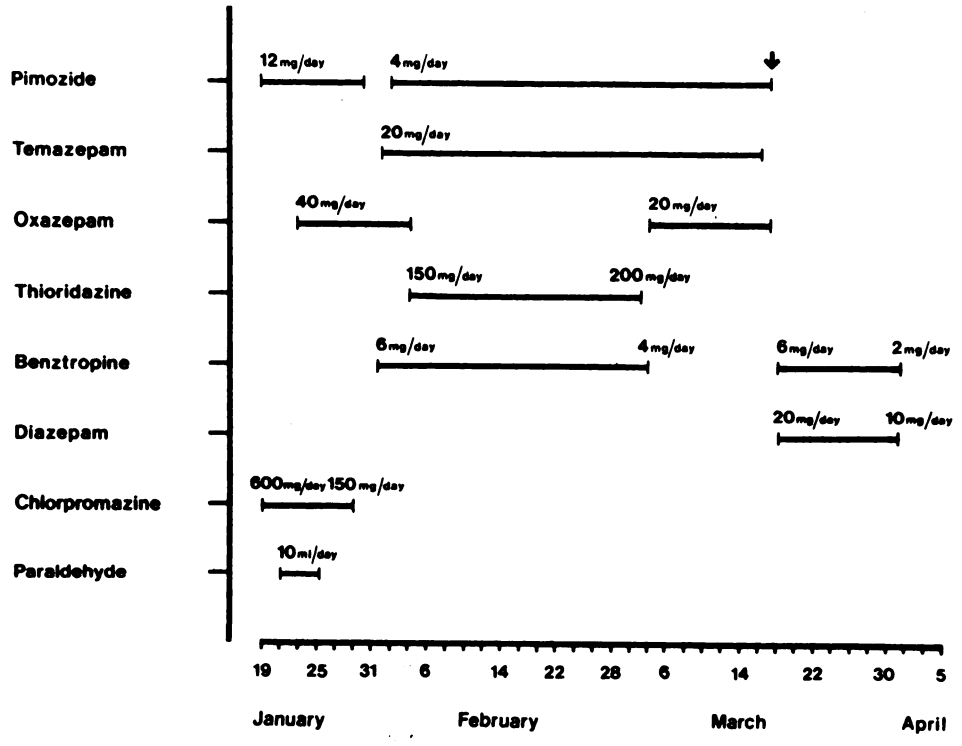

FIG.—Time course of drug exposure in this patient. The onset of severe dystonic symptoms is indicated by an arrow.

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responsible. Blood samples were collected beginning on the day following the last dose of pimozide and analysed by a sensitive and specific radioimmunoassay (Michiels, Heykants, Knaeps and Janssen, 1975). The results are shown in the Table.

TABLE

Serum pimozide concentration following withdrawal of the drug

Date	Time	Serum pimozide (ng/ml)
18.3.81	13.00	17.5
19.3.81	09.00	16.8
20.3.81	09.15	15.7
23.3.81	09.00	10.5
27.3.81	09.00	7.0

The log-linear relationship between pimozide concentration and time has a regression coefficient of 0.99 ($P < 0.001$). The slope of this line gives a pimozide half-life in this patient of 154 hours. The value previously reported following multiple dosing in hospital patients is 55 ± 7 hours (McCreadie, Heykants, Chalmers and Anderson, 1979).

Half-life is determined partly by the rate of clearance and partly by the volume of distribution. Since there was no reason to suppose that the volume of distribution was greatly altered in this patient the prolonged half-life is likely to have been the result of decreased pimozide clearance from the body.

Pimozide is metabolized in the liver by oxidative N-dealkylation (Soudijn and Van Wijngaarden, 1969). The patient had normal liver function and none of the drugs which were co-administered around the time of this adverse reaction has been reported to cause enzyme inhibition (Griffin and D'Arcy, 1979). Recently, oxidative metabolism has been shown to be under genetic control with about 10 per cent of the population being poor metabolizers (Mahgoub, Idle, Dring, Lancaster and Smith, 1977). The limited data which we present in this case report suggests that pimozide oxidation could also be under this type of control with our patient being a poor metabolizer. The patterns of pimozide metabolism in psychiatric patients would be worthy of further investigation.

F. A. LOGAN
R. N. HERRINGTON
Gartnaval Royal Hospital, Glasgow
M. M. S. MACKIE
Dumfries and Galloway Royal Infirmary
P. C. RUBIN
Glasgow University,
Stobhill General Hospital, Glasgow G21 3UW

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COMMUNITY SCREENING FOR MENTAL ILLNESS

DEAR SIR,

We were interested to read of "Community Screening for Mental Illness" using an inventory technique (Benjamin *et al*, *Journal*, February 1982, **140**, 174–80). The 60 item GHQ was used and this was further reduced (after a principal components analysis) to a 15 item single factor of the GHQ. It was suggested that this short inventory provides a satisfactory screening instrument. We were not surprised at their success, having previously reported a similar, short questionnaire technique (Donaldson *et al*, 1969; Kerry *et al*, 1970). The questionnaire we used consists of the 13 items plus 7 buffer items shown in the Table.

TABLE

Mental Health Questionnaire

1.	Do you often want to be with people who will 'cheer you up'?	Yes
2.	When you go to bed do you lie awake a long time before falling asleep?	Yes
3.	Have you ever walked in your sleep?	Buffer
4.	Do you feel adjusted to life?	No
5.	Do you cope fairly well with emergencies?	No
6.	Have you ever fainted or 'blacked out'?	Buffer
7.	Do failures make you work harder?	No
8.	Have you ever done things and, later on, found you don't know you have been doing them?	Buffer
9.	Are you inclined to worry without any reason for doing so?	Yes
10.	Do you feel you are no good and will never make a success of life?	Yes
11.	Can you usually fall asleep at any time of the day?	Buffer
12.	Are you upset if people make fun of you?	Yes

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