PECAZINE ("PACATAL") COMPARED WITH AMYLOBARBITONE SODIUM IN ANXIETY STATES

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A REVIEW of the literature which is accumulating on the so-called tranquillizing drugs shows:

1. A relatively small number of adequately controlled trials with, in general, more conservative conclusions than those of the much greater number of uncontrolled trials (Foulds, 1958).

2. Diffuseness in patient selection, with subjects often being chosen for behavioural qualities (e.g. overactivity) or general characteristics (e.g. chronicity) rather than for diagnosis.

The second weakness may, in part, be explained by the desire to organize trials as quickly as possible. Part of the explanation for the first may be a not unnatural unwillingness to treat patients with a placebo if this involves withholding an effective treatment.

While in many categories there is uncertainty about the effectiveness of different drugs, it appears clear that amylobarbitone (or amylobarbitone sodium) has definite therapeutic properties in neurotic anxiety states and this has been shown in two recent controlled trials (Raymond *et al.*, 1957; Scott, 1955).

Pecazine (Mepazine, "Pacatal") has been previously assessed in controlled studies by Mitchell *et al.* (1957) in chronic psychotic female patients who found it effective as far as certain symptoms are concerned but too toxic for general use. Lomas (1957) and Thorpe and Baker (1956) compared pecazine with chlorpromazine, the former in new admissions with schizophrenia, paraphrenia and schizo-affective reactions, the latter in deteriorated schizophrenics. On the whole in both studies the results favoured chlorpromazine.

The manufacturer's literature, however, claims that Pacatal produces "tranquillity without dulling of alertness which often occurs with large doses of sedatives or other ataractic drugs" and also that it is "effective and the remedy of choice in a wide variety of psychiatric disorders; anxiety and tension states, phobic reactions . . ." etc. These claims are in effect assessed in the following study.

METHOD

A "double blind" trial was conducted with out-patients diagnosed as suffering from anxiety states. The method described by Davies and Shepherd (1955) was adopted and prescriptions for the drugs—amylobarbitone and

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pecazine—were sealed in envelopes and thoroughly shuffled. The tablets—containing 1 gr. amylobarbitone sodium or 25 mg. pecazine—were identical in appearance and only the pharmacist was aware of the actual drug used on any patient until the end of the trial period.

Each patient was examined at an initial interview and the actuarial date, diagnosis, prognostic rating, a clinical assessment of intelligence, previous treatment, previous history of mental illness, symptom score and personality rating were recorded. The initial prescription for 1 tablet twice daily was then issued. The patient was seen again after a fortnight and the symptom score again recorded. The dose of tablets was raised from 1 to 2 t.i.d. if improvement was not evident. The patient was seen a third time after four weeks and the symptoms again recorded. The symptoms about which definite enquiry was made are listed below (Tables IIIa and b). Symptoms volunteered were added to this list.

Group Matching

Twenty-five consecutive cases were treated in all, in three out-patient departments. Eleven patients completed one month on pecazine but one was not examined by the author at the end of the month trial owing to his absence from the clinic. Ten patients completed one month on amylobarbitone sodium but one was not seen at the second visit again owing to the author's absence. Twenty-one patients, therefore, completed the trial period.

One patient discontinued pecazine because of unpleasant effects which were attributed to the drug and one patient discontinued amylobarbitone for the same reason. Two further patients failed to return for assessment after the course of treatment was prescribed and both of these were given pecazine (see Table I).

Table I

	Number of observations		
	Pecazine Subjects	Amylobarbitone Subjects	Total
Commencement of Trial ..	14	11	25
At two weeks	11	9	20
At four weeks	10	10	20

The prognosis rating was after Davies and Shepherd (1955) simply based on a three-point scale from "1" indicating the best prognosis to "3" indicating the worst.

The symptom chart was constructed from standard textbooks (Henderson and Gillespie, 1950; Curran and Guttman, 1947; Mayer-Gross *et al.*, 1954) and from the reported toxic effects of the drugs used (Martindale, 1958; Meyler, 1957; A.M.A. Council on Drugs, 1958). The symptoms were recorded as mild or severe (Tables IIIa and b). Some have been reported both as toxic effects of the drugs as well as symptoms of anxiety states (Table IIIb). For scoring purposes a mild symptom was valued at 1 point and a severe symptom 2 points. The patient was required to define the severity of the symptoms.

The two groups (totalling 21 patients) who completed the trial corresponded closely (Table II) in their sex distribution, age, civil state, personality types,

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TABLE II

Comparison of Pecazine and Amylobarbitone Sodium Groups

	Pecazine	Amylobarbitone Sodium
Sex: Female	7	8
Male	4	2
Age: −20	1	1
−30	6	3
−40	2	5
−50	1	1
−60	1	–
+60	–	–
Civil state: Single	1	1
Married	10	9
Separated, etc.	–	–
Clinics attended: A (urban)	7	3
B (semi-urban)	1	2
C (metropolitan)	3	5
Length of illness: 1 year	7	6
−2 years	2	1
+2 years	2	3
Intelligence assessed clinically: Above average	3	6
Average	7	3
Below average	1	1
Prognosis rating: 1	5	5
2	4	4
3	2	1
Previous treatment recorded in current attack	6	6
No. of previous attacks: 1	4	5
2	1	–
3+	–	–
Night sedation used	7	5
Previous attack treated by:		
Conservative measures	5	4
Physical treatments	–	1
Leucotomy	–	–
Precipitant: Illness	2	–
Work	3	2
Finance	1	1
Housing	–	1
Domestic	5	6
Personality type: Obsessive	1	5
"Neutral"	1	1
Hysteroid	9	4
Total symptom score: Mean	37·8 ± 15·2	38·7 ± 10·4

precipitating factor, duration of illness, type of treatment given previously and concurrently, clinical assessment of intelligence, prognosis as estimated by the psychiatrist, symptom total scores and symptom frequency.

The personality type was defined as obsessive or hysteroid (according to which characteristic predominated) or neutral if the scores for the different characteristics cancelled each other out, using the rating scale devised by Foulds and Caine (1958). In a small number of cases records were kept of weight, pulse rate, blood pressure, red cell count, white cell count, plasma alkaline phosphatase, thymol turbidity and serum bilirubin level. No significant variation was noted between patients or groups in these measures and as they were time-consuming and often offensive to the patients they were abandoned.

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TABLE IIIA

Comparison of Symptoms of Anxiety States in Pecazine and Amylobarbitone Groups

	Pecazine				Amylobarbitone Sodium			
	A	B	C	D	A	B	C	D
1. Tremor	4	5	14	4	3	1	5	10+
2. Fidgety	7	4	15	3	5	4	13	5
3. Muscle twitching	4	1	6	10+	1	2	5	9
4. Paraesthesiae of limbs	6	1	8	10	5	2	9	10+
5. Headache	4	2	8	10	2	6	14	4
6. Muzziness or pressure	3	3	9	9	4	5	14	4
7. Tension, strung up, anxious, unrelaxed	0	11	22	1	2	8	18	1
8. Could scream or smash	5	4	13	5	3	4	11	7
9. Could cry	7	4	15	3	3	6	15	3
10. Can't get off to sleep	3	3	9	9	3	4	11	7
11. Sleep broken or restless	4	4	12	6	4	3	10	8
12. Wakes early	3	2	7	10+	4	2	8	10
13. Dreaming more	3	4	11	7	3	1	5	10+
14. Frightening dreams, nightmares	2	3	8	10	2	0	2	10+
15. Poor concentration	2	4	10	8	5	5	15	3
16. Loss of interest	4	4	12	6	1	5	11	7
17. Loss of pleasure	3	6	15	3	1	6	13	5
19. Tinnitus	1	0	1	10+	4	1	6	10+
20. Blurred vision	3	2	7	10+	4	0	4	10+
21. Spots before eyes	3	0	3	10+	1	1	3	10+
24. Worrying about trivialities	2	7	16	2	2	7	16	2
25. Asocial	2	6	14	4	1	3	7	10+
26. Ideas of reference	4	4	12	6	3	3	9	9
27. Phobias: *a.* Insanity	4	2	8	10	0	5	10	8
b. Disease	0	2	4	10+	1	2	5	10+
c. Crowds	0	3	6	10+	0	0	0	10+
d. Enclosures	1	2	5	10+	1	3	7	10+
e. Spaces	0	0	0	10+	1	0	1	10+
f. Others	1	1	3	10+	1	2	5	10+
28. Palpitations, throbbings	4	2	8	10	2	3	8	10
29. Pains or pressure in chest	2	1	4	10+	3	1	5	10+
31. Flushing or blushing	4	1	6	10+	3	1	5	10+
33. Sweating	3	3	9	9	5	2	9	9
34. Loss of weight	3	1	5	10+	3	1	5	10+
36. Anorexia	6	1	8	10	4	2	8	10
37. Globus	2	1	4	10+	3	0	3	10+
42. Frequency of micturition	3	2	7	10+	1	2	5	10+
43. Amenorrhoea	0	0	0	10+	2	0	2	10+
44. Loss of libido	3	3	9	9	1	5	11	7
45. Impotence	0	1	2	10+	0	1	2	10+

TABLE IIIB

Comparison of Symptoms of Anxiety States Equally Reported as Side-Effects of Drugs

	A	B	C	D	A	B	C	D
18. Fatigue, Lassitude	3	5	13	5	4	4	12	6
22. Dizziness, vertigo	3	2	7	10+	4	0	4	10+
23. Irritable or excitable	5	3	11	7	5	4	13	5
30. Fainting feelings	3	1	5	10+	3	0	3	10+
32. Pallor	1	0	1	10+	0	0	0	10+
35. Dry mouth	3	4	11	7	4	3	10	8
38. Dyspepsia	1	5	11	7	2	3	8	10
39. Flatulence, fullness	2	2	6	10+	1	3	7	10+
40. Constipation	0	4	8	10	0	4	8	10
41. Diarrhoea	2	1	4	10+	2	0	2	10+
46. Drowsiness	0	1	2	10+	0	1	1	10+

A = Number of subjects reporting mild symptoms.
B = Number of subjects reporting severe symptoms.
C = Total score on symptom for group.
D = Rank order of symptom.

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Results of Treatment

The results in individual patients' total symptom score is shown in Table IV.

Table IV

Results of Treatment. Total Symptom Scores

Patient	Pecazine Interview			Personality Type	Patient	Amylobarbitone Sodium Interview			Personality Type
	1	2	3			1	2	3	
A ..	43	36	36	H	O ..	41	20	27	H
B ..	24	10	6	H	P ..	50	13	18	H
C ..	29	20	37	N	Q ..	25	5	5	O
D ..	41	44	34	H	R ..	48	36	19	H
E ..	41	39	30	H	S ..	21	18	5	O
F ..	41	36	43	O	T ..	35	13	11	H
G ..	51	52	50	H	U ..	52	25	22	O
H ..	74	69	67	H	V ..	32	28	17	N
I ..	25	17	18	H	W ..	49	19	24	O
J ..	15	13	11	H	X ..	34	—	29	O
K ..	32	25	—						
L ..	35*			H					
M ..	33*			H					
N ..	13†			H	Y ..	40†			H

* = failed to return.
† = discontinued through side effects.

O = Obsessional.
N = Neutral.
H = Hysteroid.

The mean reduction (and S.D.) in the symptom score after two weeks is $5 \cdot 5 \pm 4 \cdot 6$ for pecazine treated patients and $19 \cdot 56 \pm 11 \cdot 6$ for amylobarbitone treated cases ($n=18$, $t=7$, $p=<0 \cdot 001$). After one month the pecazine cases show a reduction of $4 \cdot 6 \pm 6 \cdot 5$ and the amylobarbitone cases of $21 \cdot 0 \pm 8 \cdot 7$ ($n=18$, $t=9$, $p=<0 \cdot 001$). These differences are highly significant.

As far as individual symptoms are concerned, the group total score was reduced by half or more than half in 8 of 51 symptoms in the pecazine group and 33 of 51 in the amylobarbitone group ($\chi^2=23$, $p=<\cdot 001$). Of 276 symptoms recorded by the pecazine subjects 42 were not reported after the first interview. Of 255 symptoms recorded by the amylobarbitone subjects 78 were not again reported ($\chi^2=15$, $p=<\cdot 001$).

On the other hand 50 new symptoms were recorded in subsequent interviews in the pecazine group and only 23 were likewise recorded in the amylobarbitone group. Irritability or excitability (3 subjects), a feeling that the patient could scream or smash (3 subjects) and loss of libido (3) were reported only with pecazine as were loss of interest (2), faint feelings (2), dizziness (2), anorexia (2). Tremor (2) was reported only with amylobarbitone. Dry mouth was reported equally (3 subjects in each group) as was fatigue (2 subjects in each group).

Conclusions

It can be seen that on comparing the results in two closely matched groups of patients with anxiety states, pecazine ("Pacatal") in doses of 25–50 mg. t.d.s. is inferior to amylobarbitone sodium in doses of 1–2 mg. t.d.s. Pecazine is, moreover, associated more frequently with the development of new symptoms than amylobarbitone; and finally, at the time of writing is almost exactly ten times as expensive as amylobarbitone in the minimum doses used.

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