# THE TREATMENT OF EPILEPSY WITH PSYCHOSIS BY PROMINAL.

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PROMINAL was first favourably reported on by several German and other continental observers (1, 2, 3, 4) in 1932. More recently (6, 7, 8, 9, 10) there has been evidence of its value from workers in this country, mainly of its use in epileptics with mental defect. In the reported cases results have indicated that only 3 out of 66 cases failed to show diminution in the number of their fits. In the epileptic psychotics treated at Claybury during the past eighteen months the drug has been found useful in a less striking way.

All the cases shown here had already received treatment for long and varying periods with either phenobarbitone or bromides or a combination of these drugs. Owing to the practical consideration that withdrawal of treatment for control observation would not have been justifiable, the results only provide a running comparison between the efficiency of prominal, phenobarbitone and bromide. The last-named two drugs have been used separately in 15 cases and combined in 11. The features of an epileptic psychosis were exhibited in every case, with frequent fits, mainly of the grand mal type. The fits began in infancy in 5 cases, at puberty in 15, in adult life in 4, and in 2 the time of onset was unknown. Eighteen cases were capable of various occupations.

The close chemical alliance of prominal with phenobarbitone is shown by its formula, sodium methyl-ethyl-phenyl-malonylurea. The change from phenobarbitone and bromides to prominal was effected gradually over a period of 12 days. One-third and later two-thirds of the phenobarbitone or phenobarbitone-bromide dosage was replaced by prominal before the transition was completed. Polstorff's estimation that 3 gr. of prominal (1 tablet) are equivalent to 15 gr. of potassium bromide or 1½ gr. of phenobarbitone was taken as a basis in assessing the dosage in each case. Alterations in dosage were eventually found necessary to suit individual cases. In these patients relatively high doses were required in order to achieve the best results. Six grains twice daily were well tolerated in the cases with most frequent fits, while 3 gr. sufficed for the milder ones. This dosage did not cause drowsiness or loss of working ability such as would have occurred with a corresponding dose of phenobarbitone or bromide.

| Case No. | Treatment period of each drug in weeks. | Phenobarbitone. Fits. | | | Prominal. Fits. | | | Actual increase (+) or decrease (−) in number of fits. | Percentage increase (+) or decrease (−) in number of fits. | Physical health. | Behaviour. | Working ability. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | G.M. | P.M. | Total. | G.M. | P.M. | Total. | | | | | |
| 1 | 52 | 43 | 39 | 82 | 21 | 52 | 73 | −9 | −11 | + | + | + |
| 2 | 52 | 34 | 0 | 34 | 6 | 0 | 6 | −28 | −83 | + | + | 0 |
| 3 | 21 | 12 | 22 | 34 | 17 | 20 | 37 | +3 | +9 | 0 | 0 | 0 |
| 4 | 21 | 18 | 0 | 18 | 12 | 0 | 12 | −6 | −33 | 0 | 0 | 0 |
| 5 | 39 | 14 | 15 | 29 | 8 | 10 | 18 | −11 | −38 | 0 | 0 | 0 |
| 6 | 19 | 41 | 0 | 41 | 44 | 0 | 44 | +3 | +7 | 0 | 0 | 0 |
| 7 | 39 | 78 | 0 | 78 | 14 | 0 | 14 | −64 | −82 | + | + | + |
| 8 | 42 | 71 | 1 | 72 | 149 | 0 | 149 | +77 | +110 | − | − | 0 |
| 9 | 78 | 19 | 2 | 21 | 11 | 0 | 11 | −10 | −49 | 0 | 0 | 0 |
| 10 | 10 | 95 | 0 | 95 | 26 | 0 | 26 | −69 | −70 | 0 | 0 | 0 |
| 11 | 16 | 17 | 0 | 17 | 31 | 15 | 46 | +29 | +170 | 0 | 0 | 0 |
| | | Phenobarbitone and bromide. | | | | | | | | | | |
| 12 | 52 | 238 | 8 | 246 | 225 | 3 | 228 | −18 | −7 | 0 | + | 0 |
| 13 | 8 | 74 | 0 | 74 | 20 | 0 | 20 | −54 | −73 | + | + | + |
| 14 | 52 | 146 | 33 | 179 | 49 | 2 | 51 | −128 | −71 | + | 0 | 0 |
| 15 | 52 | 128 | 9 | 137 | 91 | 6 | 97 | −40 | −29 | + | + | + |
| 16 | 42 | 90 | 0 | 90 | 62 | 0 | 62 | −28 | −31 | 0 | + | + |
| 17 | 16 | 16 | 0 | 16 | 20 | 0 | 20 | +4 | +25 | 0 | 0 | 0 |
| 18 | 17 | 17 | 11 | 28 | 24 | 13 | 37 | +9 | +32 | + | 0 | 0 |
| 19 | 26 | 68 | 2 | 70 | 40 | 3 | 43 | −27 | −38 | − | − | − |
| 20 | 21 | 104 | 22 | 126 | 109 | 1 | 110 | −16 | −13 | 0 | 0 | 0 |
| 21 | 21 | 105 | 27 | 132 | 176 | 5 | 181 | +49 | +37 | − | − | 0 |
| 22 | 21 | 23 | 25 | 48 | 30 | 18 | 48 | 0 | 0 | 0 | 0 | 0 |
| | | Bromide. | | | | | | | | | | |
| 23 | 21 | 14 | 1 | 15 | 14 | 2 | 16 | +1 | +6½ | + | 0 | 0 |
| 24 | 21 | 16 | 4 | 20 | 16 | 20 | 36 | +16 | +80 | 0 | + | + |
| 25 | 18 | 36 | 0 | 36 | 26 | 0 | 26 | −10 | −28 | 0 | − | 0 |
| 26 | 21 | 31 | 0 | 31 | 48 | 0 | 48 | +17 | +55 | 0 | − | 0 |

Improved = +; no change = 0; worse = −.

### *Results on a Percentage Basis.*

No change indicates an alteration of less than 10%.

| Drug. | Fits. | | | Number of cases. |
|---|---|---|---|---|
| | Improved. | No change. | Worse. | |
| Phenobarbitone . . . | 7 | 2 | 2 | 11 |
| Phenobarbitone and bromide | 6 | 2 | 3 | 11 |
| Bromide . . . . | 1 | 1 | 2 | 4 |
| Total . . . . | 14 | 5 | 7 | 26 |

In comparing results the following points were observed:

1. Fits—number and type, etc.
2. Behaviour.
3. Physical health.
4. Capacity for work.
5. Toxic effects.
6. Duration of effect.
7. Leucocyte variations.

Commenting on these features, it is noted that in no case did the fits cease entirely during the use of prominal, though Jekelius (5) has reported this to occur in 40% of cases. In two cases, Nos. 3 and 16, the fits have swung from the major to the minor type. One of these, No. 16, has lost much of the stupor and mental confusion which were formerly an unusually marked after-feature of her fits. Petit mal attacks are less influenced than grand mal by prominal.

Physical health tended to improve where the fits decreased. Similar observations were found with regard to ability in following occupations.

Attempts to compare the efficacy of bromide, phenobarbitone and prominal by the use of intelligence tests proved impracticable.

Toxic effects were very infrequent. Drowsiness occurred in a very few cases shortly after the beginning of treatment, but rapidly passed off. One case complained of a dry mouth in the mornings. Another case has shown weakness of the lower limbs and impairment in walking since the use of prominal. Her mental state has deteriorated and the fits have increased, making her true walking capacity difficult to assess.

The duration of effect was at least as long as with phenobarbitone or bromides.

In one case (No. 22) the onset of regular menstruation coincided with the exhibition of prominal. Menstruation was formerly irregular and infrequent in this case.

Blood examination, consisting of white cell counts, both total and differential, were performed at the start and finish of prominal treatment in 80% of cases. The examinations were performed between 8 and 9 a.m., the patients being in a fasting condition, and as far as possible removed from disturbing influences before being tested. Ten cases showed a rise in total white cell counts of over 25%. Nine of these had previously been receiving phenobarbitone. Three cases formerly on bromide alone showed no appreciable change in white cell count. No significant alterations were noted in the differential counts.

In estimating the value of prominal, the natural variability of epilepsy should be taken into account. It is said that this disorder improves in the summer. In the majority of these cases this factor favours the control period. Some epileptics tend to improve for a time on any new medicine,

nevertheless it was found that those cases in which the fits diminished during the first four weeks of treatment were likely to maintain their improvement over longer periods.

In cost, prominal is equivalent to the proprietary luminal, but is considerably more expensive than phenobarbitone B.P.

Prominal does not prevent the progress of mental deterioration where this is already in evidence. A decrease in number of fits is not necessarily followed by an improved mental state. Suppression of fits in two cases appeared to make their mental condition worse. In patients whose mental disorder was of a less severe nature prominal gave better results, both as regards fits and behaviour, while in those already subject to severe mental disturbance the drug was less effective than phenobarbitone or bromide in diminishing fits and retarding the decline of their mental health.

Neither the number of years during which a patient had suffered from epilepsy nor the actual frequency of fits gave any indication as to the possible benefit to be expected from prominal. A trial of at least two months appears to be the only way of finding out its effect with certainty in a given case.

*Conclusions*.—These examples of idiopathic epilepsy in psychotic patients showed—

1. That prominal was active in a majority in reducing the number of fits.

2. That improvement may be obtained mentally, physically and in occupational capacity in patients showing less severe degrees of mental disorder.

3. That the more advanced insane epileptics are unlikely to be benefited, and may be made worse by its use. Phenobarbitone or bromides are the more useful with this type.

4. Confirmation of the idiosyncrasy of epileptics to different drugs, and the necessity for dosage on a strictly individual basis.

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