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Phenaglycodol:* A New Antiepileptic Agent. (22954)

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Phenaglycodol (2-p-chlorophenyl-3-methyl-2, 3-butanediol) has, by rat screening methods, anticonvulsant and sedative properties.‡ These authors report the following oral doses for rats: electroshock $ED_{50} \pm SE = 63.0 \pm 6.6$ mg/kg; metrazol $ED_{50} \pm SE = 45.1 \pm 7.7$ mg/kg, ataxia $ED_{50} \pm SE = 86.5 \pm 6.1$; hypnotic $ED_{50} \pm SE = 165.7 \pm 16.6$ mg/kg; and the $LD_{50} \pm SE = 832.4 \pm 37.5$. Evaluation in humans with difficult to control grand mal, petit mal or mixed epilepsy also indicates anticonvulsant activity.§ An attempt was, therefore, made to demonstrate anticonvulsant activity in patients with focal brain damage and epilepsy.

Method. Twelve patients with focal brain damage and epilepsy received identically appearing experimental medications orally every 8 hours. Each medication was given for 3 days of one week. The medications were randomized among the patients. Focal and generalized seizures were reported by attendants who had no knowledge of the medications given. Each focal seizure was scored 1 point and each generalized seizure was scored 2 points to give a daily seizure score for each patient. The score on the fourth day when their regular medications were again given was also included. Patients with no seizures during the study periods were excluded as non-epileptics; patients with more than 6 seizure points during any 8-hour period were given sodium phenobarbital intravenously and excluded from the study. A detailed description of this method has been reported previously(1).

Results. The results with the various medications are presented in Table I. As variance analysis (Table II) indicates, significant ($p > 0.05$) effects were produced by both phenaglycodol and phenobarbital. The two together apparently have an additive effect.

Discussion. Phenaglycodol lacks the structural characteristics which have been associated with anticonvulsant activity. In comparison with phenobarbital, larger doses are required; however larger doses are also tol-

TABLE I. Sums of Daily Seizure Scores from 12 Patients. Totals are given in parentheses.

	Phenobarbital in mg												Total			
	0				25				100							
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Phenaglycodol, 400 mg	8	6	17	5	6	11	13	9	0	4	2	4	14	21	32	18
		(36)				(39)				(10)				(85)		
Blank	8	18	51	12	2	14	26	8	2	6	6	4	12	38	83	24
		(89)				(50)				(18)				(157)		
Total	16	24	68	17	8	25	39	17	2	10	8	8	26	59	115	42
		(125)				(89)				(28)				(242)		

* 'Ultran' (Phenaglycodol, Lilly).

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‡ To be published.

§ Personal communication.

TABLE II. Analysis of Data Presented in Table I.

Source	Sum of squares	Degrees of freedom	Mean square
Patients	85	11	7.7
Phenaglycodol	18	1	18.0*
Phenobarbital,	50	2	25.0*
25 mg *vs* 100		(1)	19.4*
mg blank		(1)	30.6*
Days	63	3	21.0*
Remainder	1,176	270	4.35
Total	1,392	287	

* Significant at $p > 0.05$.

erated by humans without excessive central nervous system depression. Comparable doses can therefore be given.

Usually drugs effective in grand mal are expected to increase the severity of petit mal and vice versa. Since phenaglycodol is effective in petit mal and the generalized seizures occurring in patients with focal brain damage, it may prove advantageous in epilepsy of the mixed type.

Conclusions. Phenaglycodol (Ultran, Lilly) is an effective anticonvulsant in epilepsy associated with focal brain damage.

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Protection of Mice with Polyvinylpyrrolidone Against Lethal Doses of Tetanus Toxin. (22955)

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The polymer polyvinylpyrrolidone (PVP) was introduced as a plasma expander by Hecht and Weese(1). Other German investigators(2,3) subsequently demonstrated that in experimental animals, injections of PVP caused urinary excretion of various dyes normally retained in the body. Stern(4) showed later that in mice PVP enhanced renal excretion of dyes, prevented storage of dyes in the reticuloendothelial system, and also displaced dyes already stored in the reticuloendothelial system. Prompted by these results, Schubert (5) and later Krech(6) described in both experimental animals and human cases a beneficial action of PVP against exotoxins of tetanus, diphtheria, and botulism. Further experience of the German workers(7-11) indicated that PVP with a molecular weight of 12,600 (Periston N or PVPN) was more effective, presumably because it was more rapidly and completely eliminated in urine than the original PVP having a molecular weight of 30,000.

Our previous study demonstrated that PVPN protected ABC mice against lethality of brucella endotoxin(12). In experiments summarized here, the first objective was to confirm the enhancing effect of PVPN upon urinary excretion of trypan blue in animals. Following this demonstration, the action of PVPN upon lethality of tetanus toxin was investigated and compared to its effect on trypan blue. As will be shown, the action of PVPN upon these two agents differed significantly.

Material and methods. In investigations relating to excretion of trypan blue, male albino rabbits were selected for use, since accurate quantitative collections of urine could easily be obtained by urethral catheterization. At various intervals following intravenous injection of trypan blue (13 mg/kg body weight), PVPN* in an amount approximating 20% of estimated blood volume was given intravenously. Urine was collected by urethral catheterization both prior to and following injection of PVPN. The amount of dye in the urine was determined colorimetrically, using as standards known amounts of trypan blue

* Obtained from Die Farbenwerke Bayer, Leverkusen, Germany.