14899 P

Prolongation of Hypnosis by Epinephrine and Insulin.

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There is evidence that analgesic agents prolong sleep induced by hypnotic drugs.[1,2] That epinephrine or insulin might also potentiate hypnosis was suggested by reports which indicated that brain metabolism was retarded by a number of amine derivatives[3] and by insulin-induced hypoglycemia.[4] The purpose of this preliminary paper is to report that highly significant increases in sleeping times have been obtained in white mice pretreated either with epinephrine or insulin.

Method. Pretreatment consisted of injecting mice (20-30 g males) either with epinephrine (0.04 mg/kg, ip and im) or with insulin (0.05 U ip and im). Twenty minutes after pretreatment Evipal Soluble (100 mg/kg ip) was administered to the pretreated animals and to others which had received no pretreatment (controls). The duration of hypnosis was taken as the interval in minutes between the loss and the return of the righting reflex.

Results. The data have been summarized in Table I.

It will be noted that mice treated with epinephrine and Evipal slept approximately 1.5 times as long as those receiving Evipal alone (controls). The significance of the increases was tested by calculating the statistic t.[5] The t values given in Table I exceed by a wide margin those listed in Fisher's Tables[6] for $P = 0.001$; therefore, the observed increases in sleeping times are to be regarded as highly significant since the probability of their occurrence by chance is less than 1 in 1000. Although the dosage (0.04 mg/kg) was larger than that customarily used in human beings, it was less than 1% of the LD_{50} for the mouse as determined in these laboratories. Especially noteworthy is the fact that such potentiation occurred even though the hypnotic drug was not administered until 20 minutes after the injection of epinephrine. At this time the customary signs of epinephrine action were missing except for pilomotor activity which was definite.

That epinephrine prolonged the action of

TABLE I.
Potentiation of Evipal Hypnosis in Mice.*

Pretreatment Drug	Dosage	Route of administration	No. of animals		Avg. sleeping times (Min.)		Pretreated % of controls	t Values
			Pretreated	Controls	Pretreated	Controls		
Epinephrine	0.04 mg/k	Im.‡	10	20	59.2	31.4	188.5	15.418†
		"	29	29	56.0	33.6	166.7	13.835†
		Ip.	10	20	51.5	32.5	158.5	6.307†
		"	10	20	46.1	31.4	146.8	7.622†
Insulin	0.05 Units/ mouse	Im.	20	20	58.7	33.2	176.8	12.977†
		Ip.	20	20	47.0	32.5	144.6	6.631†
		"	16	20	61.7	34.7	177.8	12.242†

* Evipal Soluble, 100 mg per kilo ip 20 min after pretreatment.
† Highly significant.
‡ Injection made into the lateral muscles of the thigh.

1 Barlow, O. W., Climenko, D. R., and Homburger, E., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 11.

2 Loewe, S., *J. Am. Pharm. Assoc.*, 1940, **29**, 162.

3 Quastel, J. H., and Wheatley, A. H. M., *Biochem. J.*, 1933, **27**, 1609.

4 Himwich, H. E., and Fazekas, J. F., *Am. J. Physiol.*, 1937, **119**, 335.

5 Fisher, R. A., *Statistical Methods for Research Workers*, London, 7th edition, 1938.

6 Fisher, R. A., and Yates, F., *Statistical Tables for Biological, Agricultural and Medical Research*, London, 1938.

Evipal by locally retarding its absorption is untenable in view of the similarity of the results (Table I.) obtained for epinephrine by intraperitoneal and intramuscular routes of administration. The insulin-pretreated mice slept slightly longer than those treated with epinephrine. In the dosage employed (0.05 U) there were no convulsions on awakening or other untoward signs. These findings are of interest since the two agents are chemically unrelated and are both normally produced in the body. An extension of the present study is being planned to supply information regarding mechanisms of action. In this connection it is of interest to note that epinephrine has been reported to have an analgesic action in man and in animals.[7]

Summary. White mice pretreated either with epinephrine or insulin and subsequently given Evipal slept considerably longer than the control animals receiving only Evipal. The results are highly significant as determined by statistical analysis.

[7] Ivy, A. C., Goetzl, F. R., Harris, S. C., and Burrill, D. Y., *Quarterly Bull. Northwestern University Medical School*, 1944, **18**, 298.

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Penicillin as a Prophylactic in Abdominal Surgery.*

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This investigation was undertaken to study the prophylactic value of penicillin in abdominal surgery by depositing penicillin† in the peritoneal cavity and determining the absorption rate of penicillin from the peritoneum into the blood stream.

Material and Method. Seven unselected cases were chosen for this experiment.

Case 1. Clean peritoneum, multiple fibroids. Supracervical hysterectomy and bilateral salpingo-oophorectomy.

Case. 2. Many pelvic adhesions, multiple fibroids. Supracervical hysterectomy and bilateral salpingo-oophorectomy.

Case 3. Ascites, tuberculous. Biopsy.

Case 4. Fibroid, enlarged uterus, 4 months gestation. Myomectomy and hysterectomy.

Case 5. Marked adhesions, old tubal infection, multiple fibroids. Supracervical hysterectomy and left salpingo-oophorectomy.

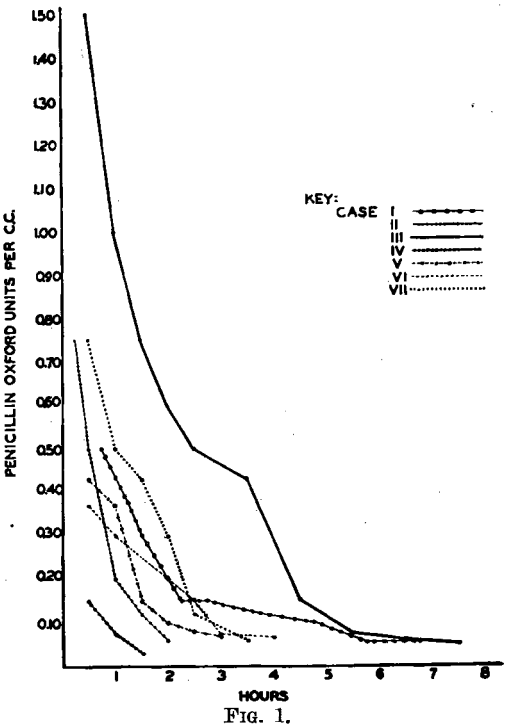

FIG. 1.

Blood level determinations after instillation of 100,000 Oxford units of penicillin into the peritoneal cavity.

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