

three dogs. γ -Aminobutyric acid was detected only in the samples of cortex. The present results are consistent with the interpretation that the γ -aminobutyric acid-glutamic decarboxylase system is only operative in the central nervous system, chiefly in the gray matter.

Summary. Brain weights, content of γ -aminobutyric acid, and the activity of glutamic acid decarboxylase were determined in brains of mice at various stages of postpartum development. All of the quantities studied increased greatly during postnatal development, attaining their maximal levels at 90 days. The increase in decarboxylase activity was slower during the first two weeks than that of the weight and the γ -aminobutyric acid. A cytological study revealed that the period of greatest increase in glutamic acid decarboxylase activity is correlated with the period of greatest increment in features which are related to maturation of the central nervous system. Examination of selected samples of nervous tissues of the cat, dog, and rabbit showed that the glutamic decarboxylase- γ -aminobutyric acid system is present chiefly in the gray matter of the central nervous system. The results of the present study were correlated with relevant data from the literature.

1. Roberts, E., and Frankel, S., *Fed. Proc.*, 1950,

v9, 219.

2. Roberts, E., Frankel, S., and Harman, P. J., *Proc. Soc. Exp. Biol. and Med.*, 1950, v74, 383.

3. Roberts, E., and Frankel, S., *J. Biol. Chem.*, 1950, v187, 55.

4. Awapara, J., Landua, A. J., Fuerst, R., and Scale, B., *J. Biol. Chem.*, 1950, v187, 35.

5. Roberts, E., and Frankel, S., *J. Biol. Chem.*, 1951, v188, 789.

6. ———, *J. Biol. Chem.*, 1951, v190, 505.

7. Roberts, E., Younger, F., and Frankel, S., *J. Biol. Chem.*, 1951, v191, 277.

8. Potter, V. R., Schneider, W. C., and Liebl, G. J., *Cancer Research*, 1945, v5, 21.

9. Smith, C. G., *J. Comp. Neur.*, 1934, v60, 319.

10. Peters, V. B., and Flexner, L. B., *Am. J. Anat.*, 1950, v86, 133.

11. Flexner, L. B., and Flexner, J. B., *J. Cell. and Comp. Physiol.*, 1946, v27, 35.

12. Metzler, C. J., and Humm, D. G., *Science*, 1951, v113, 382.

13. Ashby, W., and Schuster, E. M., *J. Biol. Chem.*, 1950, v184, 109.

14. Flexner, J. B., Flexner, L. B., and Strauss, W. L., *J. Cell. and Comp. Physiol.*, 1941, v18, 355.

15. Flexner, J. B., and Flexner, L. B., *J. Cell. and Comp. Physiol.*, 1948, v31, 311.

16. Hard, W. L., and Peterson, A. C., *Anat. Rec.*, 1950, v108, 57.

17. Harman, P. J., and Guth, L., *Anat. Rec.*, 1951, v109, 41.

Received November 14, 1951. P.S.E.B.M., 1951, v78.

Comparison of Actions of Dromoran (Nu-2206) and Morphine in Production of Vomiting.* (19225)

CHARLES M. GRUBER, JR., KWANG SOO LEE, ZINAIDA T. LASZICZENKO, AND
CHARLES M. GRUBER.

From the Department of Pharmacology, The Jefferson Medical College, Philadelphia, Pa.

Following the synthesis of 3-hydroxy-N-methyl morphinan by Schnider and Grussner (1) in the laboratories of Hoffmann-LaRoche, Inc., Randall and Lehmann (2) determined its analgesic potency in rats. They found it to be about 4 times as strong an analgesic as morphine. When doses having an equal analgesic action were given, the duration of action with Dromoran was 2 to 3 times that with

morphine. In an earlier series of experiments a comparison was made of the action of Dromoran on intestinal smooth muscle with the actions of morphine, metopon, methadone, Nisentil, and meperidine (3). The intent of the present work is to compare its tendency to produce vomiting to that of morphine.

Method. Eighty-five dogs weighing between 5 and 44 kg with an average weight of 14.5 kg were used in these experiments. The animals fasted for 18-22 hours prior to each

* This investigation was supported by a grant from Hoffmann-LaRoche, Inc. for research in the sciences.

TABLE I. Frequency of Defecation, Nausea and Vomiting in Dogs After Subcutaneous Injections of Dromoran and Morphine.

Dromoran, mg/kg	Defecation	Nausea	Vomiting	Morphine, mg/kg	Defecation	Nausea	Vomiting
.5	8/27 (29.8%)	—	1/27 (3.7%)	2.5	4/7 (57.2%)	—	3/7 (42.9%)
1	27/39 (69.3%)	22/39 (56.4%)	1/39 (2.6%)	5	27/51 (53%)	13/19 (68.3%)	23/51 (45.1%)
2	5/11 (45.4%)	2/11 (18.2%)	0/17 (0%)	10	4/7 (57.2%)	5/7 (71.5%)	3/17 (17.7%)

injection. A total of 83 injections of Dromoran and 75 injections of morphine were made subcutaneously using concentrations of 1% and 4%, respectively. The animals were watched for not less than one-half hour after injection, at which time all of the animals were depressed except one. This dog was excited by both Dromoran and morphine. At first the animals were watched only for vomiting, but later in the experiment observations were also made on defecation and nausea, as expressed by vomiting or salivation.

Results. Only 2 animals (or 2.4%) of the entire group receiving Dromoran vomited, whereas 29 (or 38.7%) of those receiving

morphine vomited. Dromoran and morphine caused defecation in 52% and 54% of the animals, respectively (Table I).

Conclusions. In doses calculated to have about the same analgesic effect Dromoran produces much less vomiting in dogs than does morphine. These doses produce defecation in equal frequency.

1. Schnider, O., and Grüssner, A., *Helv. Chim. Acta*, 1949, v32, 821.

2. Randall, L. O., and Lehmann, G., *J. Pharm. and Exp. Therap.*, 1950, v99, 163.

3. Gruber, C. M., Jr., Lee, K. S., and Gruber, C. M., *J. Pharm. and Exp. Therap.*, 1950, v99, 317.

Received November 14, 1951. P.S.E.B.M., 1951, v78.

Initial Effects of Pentobarbital Sodium on Water Diuresis in Dogs. (19226)

LOUIS A. TOTH.

From the Department of Physiology, Louisiana State University School of Medicine, New Orleans.

Although experimental data have appeared in the literature concerning the effects of pentobarbital sodium and other barbiturates on water diuresis no mention has been made of the early effects of the drugs when administered rapidly in anesthetic doses. In previous studies the urine rate was determined over prolonged periods and these long collection periods masked any early response of the kidney that may have occurred. A method of recording urine rates accurately over short periods is necessary if the immediate effects of the drugs on urine output are to be studied. Such a method was employed in the present study. It has been possible, therefore, to analyze the results in terms of immediate and delayed responses.

Methods. Trained female dogs, weighing 12-14 kg, were used in these experiments. The animals had access to water up to the time of the experiment but had been without food for 24 hours. Approximately 40 minutes before recording data on urine flow the dog was given 250 cc of water by stomach tube and a short time later was loosely restrained on a dog-board in a supine position in a cool, quiet room. One ureter was catheterized according to the method described previously(1) and the urine rate was determined by observing the drops of urine issuing from the catheter and recording on a kymograph. With high urine rates the volume output was determined by measuring the urine at 2-minute intervals in a 10 cc graduate. After the diuresis was