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Effect of Some Short-acting Barbituric Acid Derivatives on Intestinal Activity *in vivo*.*

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Controversial reports on the effect of barbituric acid derivatives upon intestinal activity have prompted the repetition of this study in an endeavor to obtain an explanation for the conflicting results. On the one hand, Gruber,[1, 2] using dogs with Thiry-Vella loops of the duodenum and jejunum, concludes that the barbiturates studied (sodium amytal, ortal sodium, and sodium phenobarbital) cause a fall in general tonus and in the amplitude of rhythmic intestinal contractions. On the other hand, Dreyer and Hebb,[3] showed that in decerebrate cats all the barbituric acid derivatives used by them (amytal, phenobarbital, dial, phanodorn, and pentobarbital) caused stimulation of gastric and intestinal movements.

The dogs used in this research were the same as those employed in earlier investigations.[4, 5] They consisted of 8 dogs prepared with Thiry-Vella loops of the upper jejunum. Tracings of intestinal movements were recorded after inserting a balloon, connected to a water manometer at 12 to 15 cm pressure, into the proximal end of the Thiry-Vella loop. Respiratory tracings by means of a pneumograph applied about the chest were simultaneously recorded in order to rule out the possibility that the tracings taken from the balloon were due to transmitted respiratory movements. These intercostal respiratory tracings also served to show the depth of anesthesia. No preanesthetic medication was administered. The barbituric acid derivatives used consisted of those most commonly employed for intravenous anesthesia: sodium N-methyl-cyclohexanyl barbiturate (evipal), sodium iso-amyl ethyl barbiturate (amytal), sodium iso-amyl ethyl thio-barbiturate (sodium thio-ethamyl), sodium

*Grateful acknowledgment is expressed to Dr. W. F. Ruggiero for his aid in the surgical preparation of the Thiry-Vella Fistulas.

1 Gruber, C. M., *J. Pharm. and Exp. Therap.*, 1936, **56**, 432.

2 Gruber, C. M., Crawford, W. M., Greene, W. W., and Drayer, C. S., *J. Pharm. and Exp. Therap.*, 1931, **42**, 27.

3 Dreyer, N. B., and Hebb, C. O., *Proc. Nova Scotian Inst. Sci.*, 1933-1934, **18**, 282.

4 Burstein, C. L., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 530.

5 Burstein, C. L., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 396.

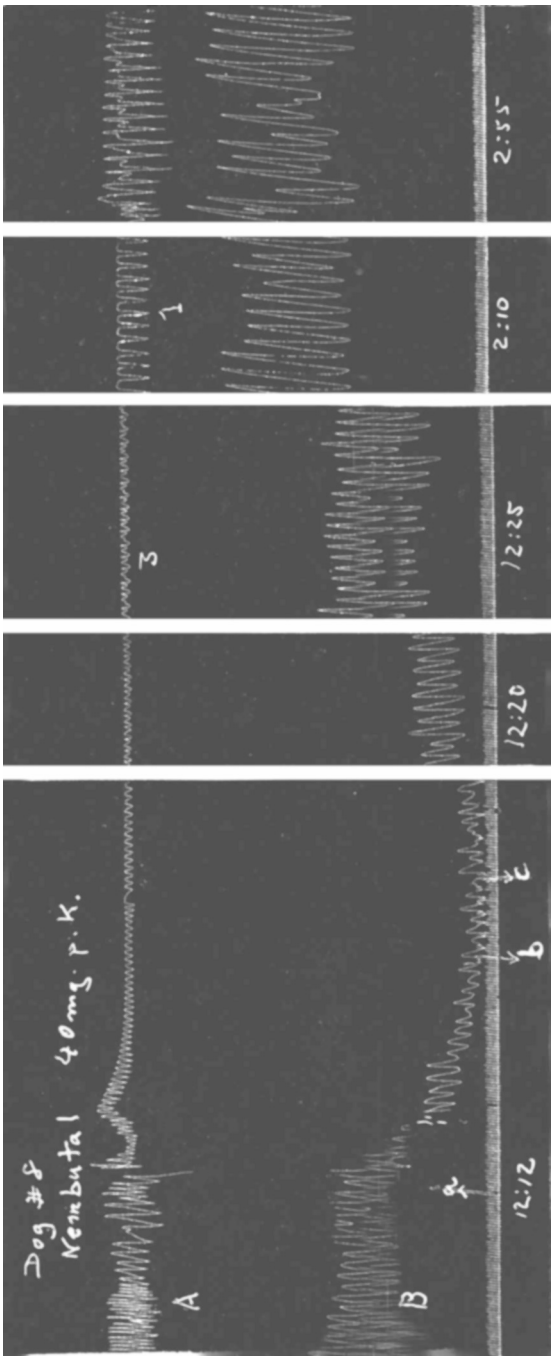

FIG. 1.

Effect of nembutal on intestinal activity of dog *in vivo*. Serial sections taken from the same experiment: Upper record (A), thoracic respirations; lower record (B), intestinal contractions. Time in second intervals. The numbers below the respiratory tracing indicate the plane of surgical anesthesia. Nembutal, 5% solution, 40 mg per kg body weight, was injected between (a) and (b). At (c) an endotracheal tube was inserted by the oral route.

N-ethyl-l-methyl butyl barbiturate (nembutal), and sodium N-ethyl-l-methyl butyl thiobarbiturate (pentothal). In each case, a 5% solution was freshly prepared and injected slowly intravenously until the lid reflex disappeared. The doses varied between 30 and 60 mg per kilo body weight. An endotracheal tube was introduced by the oral route as soon as surgical anesthesia supervened in order to assure a patent airway and obviate the effect of the ensuing anoxemia.

In every instance and with all the different barbiturates used the immediate effect, lasting from 5 to 15 minutes following the injection, consisted of a marked reduction in the amplitude of intestinal contractions and a fall in general tonus. Immediately following this primary depressing effect, however, there was a gradual rise in general tonus to above normal and increased rhythmic intestinal contractions which were maintained until the animal awakened. This secondary period during which anesthesia was still evident lasted from 10 minutes to 2 hours depending upon the rapidity of action of the particular barbituric acid derivative used. Fig. 1 shows the typical picture obtained with nembutal.

Conclusion. The short-acting barbituric acid derivatives studied when injected intravenously cause an immediate depression of rhythmic intestinal contractions and tonus. This primary effect, however, is transient and is succeeded by a more prolonged phase characterized by increase in both intestinal contractions and tonus.

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A Hematopoietic Substance in Liver.

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In two previous communications[1] the authors have shown that liver yields a peptide in some respects resembling a typical albumose capable of causing blood regeneration in pernicious anemia. Clinically active preparations were obtained which were completely free from pentose or other carbohydrate, purines, phosphoric acid, and sulphur. Other workers have stressed the presence of some or all of these groups or have postulated the accessory action of a variety of other chemical types which are absent from our material. Karrer,

[1] Dakin, H. D., and West, R., *J. Biol. Chem.*, 1935, **109**, 489; 1936, **115**, 771.