

THE EFFECT OF SOME BARBITURIC ACID DERIVATIVES ON THE  
INTESTINE OF THE CAT\*.

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## ABSTRACT.

All members of this series stimulate gastric and intestinal movements, when administered intravenously. The action is peripheral for it is not abolished by Section of vagi or splanchnic nerves, or after the injection of atropine.

The action of diethyl barbituric acid (Veronal), or its sodium salt, and other members of this group, on the blood pressure has been investigated frequently. There is a fall in blood pressure caused partly by a depression of the vasomotor centre and partly by a direct depressent action on the blood vessels. Sodium amytal and luminal act in a similar fashion. The depressent action on smooth muscle appears to be a direct one. Recently Gruber<sup>1</sup> and his co-workers have described the depressent effect of sodium phenobarbital on the intestine of the unanaesthetized dog. The doses employed, intravenously, varied from 33 to 42 milligrammes per kilogramme. The rate of injection and concentration of the solutions are not stated, and this may account for the difference in the results obtained in the present investigation on the cat's intestine.

The method employed has been described elsewhere<sup>2</sup>. All injections were made intravenously and dosage refers to milligramme per kilogramme. All the barbiturates were converted into the sodium salts and these were dissolved in 0.9% sodium chloride solution. Each injection took from five to ten seconds. The concentration of the solutions was usually

<sup>1</sup> Gruber, Crawford, Greene and Drayer: *Journ. Pharm. and Exp. Therap.*, Vol. XLII, 1931.

<sup>2</sup> Babkin: *Die Aussere Sekretion der Verdauungsdrusen*. 2nd Edition, 845, 1928.

\*Preliminary Report.

1%, as higher concentrations required slower rates of injection and, further, they have been known to cause serious depression of the circulation.

*Results.*—The first salt tested was sodium phenobarbital. In the first series of observations the dosage never exceeded ten milligrammes. The result was always a pure stimulation.

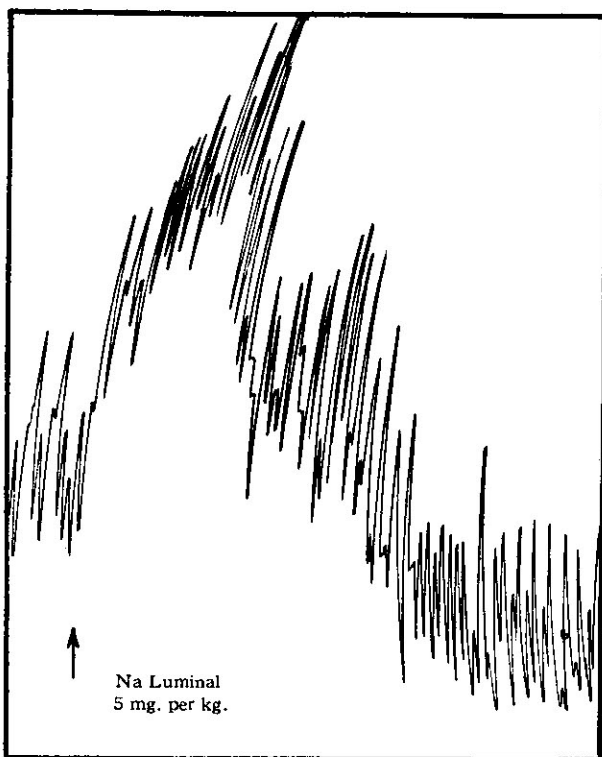


Fig. I.

Quantities varying from 2.5 milligrammes to ten milligrammes produced similar effects (Fig. I). This was in marked contrast to the results of Gruber, who obtained a pure depression. The quantities injected into their dogs varied, as stated above, from 33 to 42 milligrammes per kilogramme. Since the cats were already anaesthetized it was not possible to inject large

quantities of a hypnotic for fear of depressing respiration and circulation too much. To overcome this the following procedure was adopted. Cats were anaesthetized with ether, the abdomen opened and a loop of intestine prepared. Following this the cat was decerebrated and allowed to recover from the shock of the operation. An initial injection of 2.5 milligrammes gave a stimulation as in the anaesthetized cat. Instead of the small doses previously given, the second quantity injected was increased to twenty-five milligrammes. The result was still a stimulation, the tonus being increased very considerably and the movements were but slightly changed. The intestine returned to its initial state after a period of about twenty minutes. A second injection of 25 milligrammes of sodium phenobarbital gave an effect like the first, but in this instance the movements were larger. The cat's circulation and respiration were not depressed by this amount of drug. Morphine, 1 milligramme, was next injected, but the stimulation from this was slight. A third injection of 25 milligrammes of phenobarbital caused an increase in tone of the intestine. Finally the quantity of phenobarbital was raised to 50 milligrammes per kilogramme, an amount exceeding that recorded by Gruber. Instead of an immediate depression of movements, there was a stimulation lasting for a few minutes, before an abrupt fall in tone and decrease in amplitude set in, but this coincided with the failure of respiration and circulation. The effect of high concentration of drug has not yet been tried, but it is possible that concentration may play a part in producing a depression of movements.

The extrinsic nerve supply did not interfere with this stimulant action of sodium phenobarbital, for identical results were obtained after section of the vagi and splanchnic nerves. Increased intestinal tonus following morphine injection or section of the splanchnic nerves did not alter the effect of the phenobarbital. The result of injection of this drug in all the conditions studied so far was a stimulation of intestinal movements.

Sodium amytal (isoamylethyl barbituric acid), which is largely used as a basal narcotic, was also investigated. The

results resembled those of phenobarbital, and will not be described in detail. The doses employed were comparable to those of phenobarbital.

Other barbituric acid derivatives were tested and every one gave responses similar to amytal and phenobarbital. In some cases the action was not so prolonged, while in others the stimulation was more intense, but of short duration. In this group are included diethyl barbituric acid (veronal), diallyl barbituric acid (dial), cyclohexemyl ethyl barbituric acid (phanodorn), and pentobarbital.

The large intestine reacted like the small intestine in its responses to habiturate injections.