

In the third group the 10 mothers received treatment both ante and postpartum. The antepartum treatment varied. All except one animal received 0.1 mg. 2 times daily for the first 5 postpartum days. This one animal received twice this postpartum dosage. Of the 34 female offspring in these litters, the abnormality was present in 25.

Hypospadias has been produced so far in 37 female rats. Twenty-eight untreated litters have been observed specifically for this lesion. It has not been observed in any of the 128 female offspring of this group.

Inasmuch as the urethra of the newborn female rat opens immediately in front of the rectum and the clitorine prominence displays a grossly visible cleft, it is suggested that this abnormality represents an hypotrophic rather than a hypertrophic developmental defect.

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Action of Morphine Sulphate on Intestinal Motility and its Modification by Atropine Sulphate.

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The experiments were conducted on unanesthetized female dogs with weights ranging between 12-18 kg. Two Thiery Vella loops of adjacent parts of the ileum were prepared, which enabled us to record, in the same dog simultaneously, changes in tone, rhythmic and peristaltic movements in one loop by the balloon method,¹ and the actual propulsive activity in the second loop. For the latter purpose the method of Quigley, Highstone and Ivy was followed; the bolus used was made of rubber crepe of fine quality soaked in liquid paraffin.²

Morphine sulphate in doses of 1 mg. per kilo injected subcutaneously causes an increase in tone, diminishes segmentary movements and abolishes peristaltic waves. This confirms the results of the experiments of Plant and Miller.³

The propulsive activity after this dose of morphine is at first in-

¹ Plant, O. H., *J. Pharm. and Exp. Therap.*, 1921, **16**, 312.

² Quigley, J. P., Highstone, W. H., and Ivy, A. C., *Am. J. Physiol.*, 1934, **108**, 151.

³ Plant, O. H., and Miller, G. H., *J. Pharm. and Exp. Therap.*, 1926, **27**, 361.

creased and this initial increase in the speed of propulsion is later followed by a marked decrease. While the normal time for a bolus to pass through an intestinal loop of 9-10 cm. in length varied between 6-12 minutes, the same distance was covered within 20-40 seconds after morphine. The period of increased speed of propulsion started within 1-2 minutes after the morphine-injection and lasted for an average of 20-40 minutes. After that the speed of propulsion changed abruptly, becoming much slower than normal; the latter condition lasting for about an hour.

While these results agree in general with those of Quigley, Highstone and Ivy⁴ they differ in details. In our experiments the duration of the period of increased propulsive activity was longer and the maximal speed of propulsion was greater.

According to Plant and Miller³ atropine sulphate in doses sufficient to paralyze the vagus (0.2 mg. per kilo subcutaneously) has no apparent influence on the effect of morphine sulphate on tone, segmentary and peristaltic movements of an intestinal loop of the ileum in a Thiery Vella dog (recorded with the balloon method).

Gruber, Greene, Drayer, and Crawford, however, found that the increased tone caused by morphine could be antagonized completely by a following injection of atropine. They gave in one of their 2 experiments one mg. and in the other 1.4 mg. of morphine sulphate per kilo intravenously, followed by 0.5 mg. and 0.35 mg. respectively of atropine sulphate intravenously.⁵

In dogs with 2 Thiery Vella loops atropine in a dose of 0.2 mg. per kilo subcutaneously, which was found to abolish the inhibitory influence of the vagus on the heart, invariably abolished the increased rate of propulsive activity produced by morphine. The intestinal effect always coincided with the increasing effect of atropine on the heart. Atropine given before morphine prevented the increase in propulsive activity which invariably followed morphine alone.

Our results,* using the same dose and method of administration as Plant and Miller, confirm their findings in that atropine does not have any apparent influence upon tone, segmentary and peristaltic movements altered by morphine. Larger doses of atropine, however, given subcutaneously and the same or larger doses given in-

⁴ Quigley, J. P., Highstone, W. H., and Ivy, A. C., *J. Pharm. and Exp. Therap.*, 1934, **51**, 308.

⁵ Gruber, C. M., Greene, W. W., Drayer, C. S., and Crawford, W. M., *J. Pharm. and Exp. Therap.*, 1930, **38**, 389.

* These experiments were made in collaboration with Professor Harald G. O. Holek on dogs with one Thiery Vella loop.

travenously antagonized the effect of morphine in a way similar to the results of Gruber, *et al.*

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Progesterin and Estrin of Nineteen Placentas from Normal and Toxemic Cases.*

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The purpose of this study was to determine whether placentas from toxemic pregnancy differed significantly from those of non-toxemic pregnancy in content of progesterin. Estrin was assayed coincidentally.

Within 48 hours of delivery the placentas, having been kept in the refrigerator, were cleaned of all membranes, drained and blotted, ground finely in a meat grinder, measured and vigorously shaken in 2 volumes of 95% ethyl alcohol, in which they remained until extraction. The methods of Allen^{1, 2} were employed for extraction and of Allen and Meyer³ for the separation of the estrogenic from the progestational fraction. For performing assays on the progestational fraction, which was taken up in olive oil, the Corner-Allen technique⁴ was followed. In 6 instances (Nos. 1, 2, 3, 4, 8 and 9) 1/25th of the progestational fraction was removed and tested for estrogenic activity on 2 rats (Allen-Doisy method). Negative results were obtained, showing that these fractions contained definitely less than 50 r.u. of estrogenic substance. The 33% alcoholic estrogenic fractions were assayed directly, dilution, when necessary, being made with 33% ethyl alcohol. Clinical and biological data are tabulated in Table I. Table II summarizes the averages of the biological findings.

Only cases 4, 5, 12 and 18 may be regarded as truly normal pregnancies, the premature deliveries in the other "normals" being evidence of some upset in otherwise clinically normal pregnancies. Presumably the 3 patients whose membranes ruptured spontaneously were in other respects normally pregnant.

* The Mrs. William Lowell Putnam Investigation of the Toxemias of Pregnancy.

¹ Allen, W. M., *Am. J. Physiol.*, 1930, **92**, 174.

² Allen, W. M., *J. Biol. Chem.*, 1932, **98**, 591.

³ Allen, W. M., and Meyer, R. K., *Am. J. Physiol.*, 1933, **106**, 55.

⁴ Corner, G. W., and Allen, W. M., *Am. J. Physiol.*, 1929, **88**, 326.