soon as muscular relaxation sets in and the respiration slows, the rate of injection is reduced, the operator making brief pauses at intervals to gauge the latency and thereby avoiding the facile overdose. To measure grossly the degree of narcosis the tip of the ear or tail is pinched. Failure to resist by an outcry is determinative. The operative field can then be prepared and the incision made. Usually effective anesthesia has been obtained by this time (2 to 5 minutes). Occasionally a very small supplementary dose may be indicated just before making the incision.

The intravenous dose of pentobarbital necessary to produce good surgical anesthesia in rabbits varies in individual cases from 17.5 to 25 mg./kg. In our experience the optimal dose is 20 mg./kg. For the guidance of those who would want to use this procedure we advise injecting the first 15 mg./kg. at the rate of 1 cc. per 30 sec., then stopping for 10 sec., and following with 5 mg./kg. in 2, 3, or more squirts at intervals of 5 to 10 sec. p.r.n. The result in 98% of the cases will be satisfactory. If, on account of a too long latency as may occasionally happen an overdose has been given, an intravenous dose of picrotoxin invariably furnishes adequate protection. The optimal antidotal dose of picrotoxin is 1 mg. picrotoxin per 9 mg. nembutal, (Maloney, Fitch, and Tatum[1]). This dosage of picrotoxin is varied in accordance with the symptomatic response of the individual animal. Pentobarbital used as here described, is rapid, safe and satisfactory

9287 P

Production of Experimental Hypospadias in the Female Rat.

R. R. GREENE. (Introduced by A. C. Ivy.)

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It has been reported that the injection of large amounts of estrogenic substances into the pregnant rat during the last few days of her pregnancy caused an "hypospadias" in the female offspring.[1, 2] This same abnormality resulted when the mother rat was injected with large doses during the first 4 days of lactation.[3, 4] It was also

[1] Maloney, Fitch and Tatum, *J. Pharm. and Exp. Therap.*, 1931, **41**, 465.

[1] Hain, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 131.

[2] Hain, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 303.

[3] Hain, A. M., *Edin. Med. J.*, 1935, **42**, 101.

[4] Hain, A. M., *Quart. J. Exp. Physiol.*, 1936, **26**, 29.

produced by direct injection of the female newborn.[4]

In the normal adult female rat the urethra opens at the apex of the clitorine prominence. In these abnormal animals the clitoris is widely split and the urethral meatus is immediately cephalad to the vaginal orifice. The lesion apparently involves the integrity of the urinary sphincter, as incontinence is usually present.

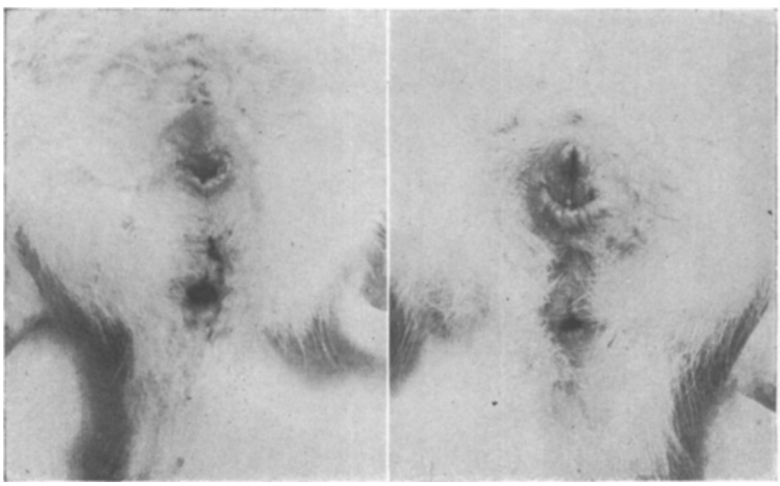

FIG. 1.

Normal Rat. Abnormal Rat.

These findings have been confirmed during the course of a study on lactation. No effect has been noted in the male offspring. An attempt to produce the lesion in the female newborn by direct injection after the seventh day of life has been unsuccessful.

The animals treated to date fall into 3 groups. The first group consisted of 9 litters in which the mothers were injected with estrone in the postpartum period only. The mothers of 7 litters were injected with a total of 0.25 mg. each during the first 5 postpartum days. None of the female offspring had the abnormality. Two mothers were injected with 2.0 mg. during the postpartum period. One of these animals was given this dosage during the course of the first 5 days. None of her female offspring had the lesion. The other animal was given this dosage during the first 2 postpartum days. Three of her 4 female offspring had this lesion.

In the second group of animals treatment was given antepartum only. The abnormality was present in the 4 female offspring of one female that had 1.0 mg. during the 24 hours preceding delivery, and in the 5 female offspring of one animal that was given 2.0 mg. in the 48 hours preceding delivery.

TABLE I (Group 3).

Litter No.	Antepartum Dosage mg.	Days of Antepartum Treatment	Postpartum Dosage mg.	Days of Postpartum Treatment	No. of Females	No. with Lesion	No. without Lesion	% of Hypospadias
63	0.2	1	1.0	5	3	3	0	100
64	0.2	1	1.0	5	3	3	0	100
71	0.2	1	1.0	5	4	4	0	100
83	0.2	1	1.0	5	1	1	0	100
65	0.3	2	1.0	5	6	6	0	100
76	0.3	2	1.0	5	4	0	4	0
68	0.4	2	1.0	5	6	6	0	100
84	0.4	1	2.0	5	4	0	4	0
72	0.5	3	1.0	5	1	1	0	100
75	0.9	5	1.0	5	2	1	1	50

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.

9288 P

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] Quigly, 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.