

veloped. Absence and underdevelopment were seen in the same animal. Mammary glands were nearly normal in appearance.

(3) The internal reproductive system with the above exceptions was intact and some degree of ovarian function was evidenced by uterine, vaginal, and mammary histology, by the presence of follicles and corpora lutea, and by fluid in the uterus and vagina.

(4) The uterus and existent portion of the vagina were greatly bloated with retained fluid in 6 of the animals (Fig. 1). The dimensions of the expanded uterine cervix and vagina were as great as 35x30x32 mm. Apparently this large distension by fluid, which followed the assumption of functional activity of the reproductive system, proved fatal in the majority of these animals, seemingly partly by compression of the colon. The urinary system was also affected, the bladder and urethra being held taut by the subjacent expansion of the reproductive system.

The preliminary study of permanent abnormalities in rats resulting from injections of hormones to the mother during pregnancy, suggest the following inferences:

(a) Pseudohermaphroditism may be produced by androgen injection, the females presenting a masculine appearance with a penis-like clitoris, scrotum-like perineum and an absence of proper development of the nipples and the outer portion of the vagina.

(b) The absence of nipples in the normal male rat may be correlated with the presence of male hormone.

(c) Possible harmful effects on the foetus must be guarded against in clinical use of hormonal substances in large amounts or at critical times during pregnancy.

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### Myenteric Activity Modifications Induced by Caffeine.

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Enteric motility is dependent largely upon mechanical distension and upon the *chemical* nature of the contents. To study the effect of the purine complex, caffeine, upon the intrinsic myogenic responses<sup>1</sup> of the mammalian small intestine, excised segments of the

<sup>1</sup> Gasser, H. S., *J. Pharm. and Exp. Therap.*, 1926, **27**, 395.

rabbit intestine were perfused with Tyrode solution separately and with the addition of caffeine. The animals were sacrificed by a blow on the occiput to avoid any possible anesthesia effect. A modification of Trendelenburg's method was used. Comparable segments of the duodenum, jejunum, and ileum were employed under constant conditions of temperature, pressure, perfusion volume rate, time of perfusion, and pH (bicarbonate-buffered).<sup>2, 3</sup>

Normal contractions of the mammalian small intestine occur as rhythmic, long peristaltic beats and in the form of irregular, shorter tonus periodicities. The records were obtained under the natural self-regulatory rhythm of the segment. The excised intestinal segment preparation provides a method for observing the direct response of the musculature to caffeine as absorbed from the lumen through the mucosa. Caffeine-in-Tyrode concentrations varied from 0.05% to 2.0% of the pure alkaloid, U.S.P. Powder (Merck). Magee and Southgate<sup>4</sup> demonstrated differences in the effects of salts upon the several areas of the small intestine. Similarly, in my experiments, the several segments show a different sensitivity to caffeine.

TABLE I.  
Effect of 1% Caffeine-in-Tyrode.

	Amplitude	Tonus	Rhythm Rate	Recovery
Duodenum	Decrease (decided)	Increase (decided)	0 or decreased slightly	Complete
Jejunum	Decrease (but less than duodenum)	Increase (but less than duodenum)	0	''
Ileum	Decrease (decided)	Increase (decided)	0	''

*Summary.* 1. The amplitude and tonus are the factors primarily modified by caffeine. 2. The presence of caffeine in the intestinal lumen in percentages below 0.50% is not effective in general. 3. Effective concentrations tend to increase the tonus and to decrease the amplitude of the contractions. 4. Full recovery occurs except occasionally with the use of caffeine-saturated (approximately) perfusion solutions.

<sup>2</sup> Cheney, R. H., *Proc. Soc. Exp. Biol. and Med.*, 1932, **30**, 3.

<sup>3</sup> Cheney, R. H., *J. Pharm. and Exp. Therap.*, 1933, **48**, 470.

<sup>4</sup> Magee, H. E., and Southgate, B. A., *Proc. Physiol. Soc. J. Physiol.*, 1928, **65**, VII.