The disadvantages of the cat, dog and rat as assay animals for adrenal cortical extracts may be circumvented by the use of the guinea pig, because the guinea pig has no accessory adrenal cortical tissue, the surgery is comparatively simple, and the adrenalectomized guinea pig requires comparatively little extract to maintain it in an apparent normal state.

Summary. The merits of the cat, dog, rat and guinea pig as assay animals for adrenal cortical extracts is discussed. The guinea pig is found to be the most satisfactory animal because (1) it is easy to operate and handle; (2) it has no accessory adrenal cortical tissue, and (3) it requires small amounts of extract to maintain it in an apparently normal state.

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Modification of Sexual Development in the Opossum by Sex Hormones.*

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Sex hormone application modifies to some extent the embryonic development of the reproductive system in reptiles, birds and mammals.[1-7] Immature pouch young of marsupials might be expected

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2 Willier, B. H., Gallagher, T. F., and Koch, F. C., *Proc. Nat. Acad. Sci.*, 1935, **21**, 625; *Physiol. Zool.*, 1937, **10**, 101.

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to provide the most favorable objects for such study on account of direct accessibility of young for treatment. In these mammals one may apply hormones directly to the young and thus avoid the usual interferences with placental function and lactation caused by injections of hormones into pregnant mothers.

Twenty-four litters of opossum pouch young have been available, 8 of known date of birth, which have provided a normal series of 47 males and females, in age 1 to 100 days, and an experimental series of 40 males and females subjected to hormone treatments beginning on days 3 to 32 and ending on days 16 to 62. Testosterone, t-propionate, and estradiol have been applied by cutaneous ointment (for effectiveness see [8]) and the latter 2 substances also by subcutaneous injection. The opossum at birth is "sexually indifferent" with Wolffian ducts, functional urinary ducts—Müllerian ducts appear on day 3 and gonads are definitely testes and ovaries on day 5.

The experimental series reveals that male and female hormones evoke responses of both Wolffian and Müllerian ducts in pouch young of either sex by day 22; inhibitory responses of ducts have not been observed. Duct stimulation was evident in all treated young sacrificed on day 16. The most striking and unexpected modification has been the tremendous development of the Müllerian system in females treated with testosterone or t-propionate, and the less marked responses of Wolffian ducts of both sexes treated with estradiol. Table I reveals duct modifications of 8 hormone-treated animals. In each the diameter of the duct lumen was obtained from stained serial sections and does not express the great increase in the walls of the structures. Lumen diameters are given for normal ducts from similar aged untreated embryos. Thus, in the first animal, treated with an estradiol ointment by daily brush application on the skin from day 5 to 22, the greatest Wolffian duct lumen is .52 mm in comparison with .03 mm in an untreated male (increase of 17 times); the Müllerian duct lumen is .18 mm in contrast to a non-lumenate solid cord of cells in untreated males of same age. A striking result is the pronounced androgenic stimulation of Müllerian ducts in females, in contrast to males, despite similar applications in both sexes from day 3.

Prostate gland anlage do not appear in normal female opossums (present in males on day 16) but a female treated with androgen readily develops a prostate greatly in excess of similar aged un-

[8] Moore, Carl R., Lamar, J. K., and Beck, Naomi, *J. Am. Med. Assn.*, 1938, **111**, 11.

TABLE I.
Diameter of Lumen of Wolffian and Müllerian Ducts (in mm) from Stained Serial Sections of Opossum Pouch Young.

Treatment	Days		Wolffian Duct		Müllerian Duct	
			Normal control	Treated	Normal control	Treated
Estradiol Ointment	5-22	male	.03	.52	cord	.18
		female	cord	.60	.03	.22
Testosterone Propionate	10-21	male	.03	.04	cord	.01
		female	cord	.04	.01	1.05
	16-31	male	.03	.11	cord	.04
		female	cord	.05	.07	1.40
Testosterone	3-24	male	.03	.03	cord	cord
		female	cord	.06	.01	.30

treated males. A female treated with androgen from day 10 to 30 and sacrificed without additional treatment on day 62 shows enormously hypertrophied Müllerian ducts (coiled oviducts, numerous uterine glands, constricted cervix, and dilated lateral vaginal canals) and a large quantity of prostate gland tissue.

Gonad development has suffered little if any histological modification from treatment during early development and only gross size modifications are apparent; ovarian activity has continued despite tremendous stimulations of other structures by testosterone.

Contrary to typical free-martin responses noted by Lillie[9] in cattle, chemical androgens (1) although stimulating some retention of Wolffian ducts do not cause retention of their entrance into the urinogenital sinus; (2) stimulate, instead of inhibit, Müllerian ducts in females; (3) do not suppress early ovarian activity and (4) stimulate both male and female external genitalia.

Conclusions. Opossum pouch young, indifferent as to sex at birth, show stimulated responses of both sex ducts from treatment with ointments or injections of androgens or estrogens; duct inhibitions are not evident. Responses are revealed by day 16. Androgenic stimulation of Müllerian, and estrogenic stimulation of Wolffian, ducts are unexpected; female prostate induction occurs with androgenic treatment and male prostate inhibition with estrogenic treatment. Responses differ from those revealed in the free-martin.

[9] Lillie, Frank R., *J. Exp. Zool.*, 1917, **23**, 371.