The results of the second group of experiments are shown in Table I. Although a definite hypertension was present, a pressor agent was not present in the perfusate. (In order to obtain the 6 hypertensive dogs, the vessels of 10 dogs were clamped.) The slight transient rises observed in dogs 4, 5, and 6 were produced when the same quantity of Locke's solution was injected at the same rate.

Summary. We were unable to obtain a pressor substance in significant amounts from the ischemic kidney of hypertensive dogs by perfusing such kidneys for from 20 to 60 minutes with Locke's solution.

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Comparison of Intravaginal and Subcutaneous Tests for Estrone and Estradiol Monobenzoate.

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It was known from previous experiments[1, 2] that by administering estradiol monobenzoate intravaginally, cornification of ovariectomized rats' vaginæ could be induced with about 1/200th of the amount needed subcutaneously. It was also known that by the subcutaneous rat test, estradiol monobenzoate in oil is 5 to 10 times as potent as estrone in oil. It seemed of interest, therefore, to determine the relative potencies of these two substances as judged by the intravaginal method. For, it might be argued, that if estradiol monobenzoate appears more potent merely because of slower absorption and excretion following subcutaneous injection, the local test might find it no more potent than estrone. If, however, it is more potent because a greater growth-stimulating property is determined by its chemical structure the ratio (estradiol monobenzoate: estrone) might be expected to remain the same, or be even greater because fewer variables are involved in the local test.

[1] Lyons, W. R., and Templeton, H. J., PROC. SOC. EXP. BIOL. AND MED., 1936, **33**, 587.

[2] Yerby, L. D., *ibid.*, 1937, **36**, 496.

Sixty adult rats of the Long-Evans strain were ovariectomized, and 2 or more weeks later were "primed" with 1γ of estradiol monobenzoate. One week later, after the vaginal reaction had subsided the higher levels of estrone and estradiol monobenzoate were tested, and then the successively lower levels, at weekly intervals. The International Standards* were dissolved in and diluted with sesame oil, and a single subcutaneous injection of 0.1 cc made. Vaginal smears were examined 48 and 72 hours later. For intravaginal tests, 0.01 cc of the various dilutions was administered on 2 successive days by means of a micropipette,[1, 2] and vaginal smears examined 24 and 48 hours after the second administration.

In both intravaginal and subcutaneous tests, a rat was considered a positive reactor if cornification was induced even though epithelial cells and some leucocytes were still present (border-line reaction). Groups of 20 rats, chosen at random, were administered a given dose and at some dose levels duplicate groups were tested by us independently. It was noticed that even on the higher doses, one or 2 rats would not show cornification, and this was usually attributable to the presence of pus.

TABLE I.

Showing the Number of Ovariectomized Rats Reacting with Vaginal Cornification to Different Levels of International Standards of Estrone and Estradiol Monobenzoate Administered Intravaginally and Subcutaneously.

Estrone			Estradiol Monobenzoate		
		Subcutaneous			
No. of rats	Dose in γ	Reactors	No. of rats	Dose in γ	Reactors
20	4.0	19	20	.2	16
20	2.0	18	20	.1	14
20	1.0	14	20	.1	12
20	.5	9	20	.05	6
20	.5	9			
20	.25	4			
		Intravaginal			
20	.02	14	20	.0025	18
20	.02	12	20	.0012	14
20	.01	10	20	.0006	12
20	.01	9	20	.0005	9
20	.005	6	20	.0003	5

Table I contains the results obtained from 400 tests. It will be observed that the subcutaneous rat unit (level at which at least 50% of the rats show cornification) of estrone is 0.5-1.0γ and of estradiol benzoate 0.05-0.1γ. The intravaginal unit of estrone is 0.01-0.02γ, and of estradiol benzoate, 0.0005-0.0006γ.

Thus it may be concluded that the intravaginal unit of estrone is

* Kindly supplied by Dr. Oliver Kamm of Parke, Davis and Company.

approximately 1/50th of the subcutaneous unit, while the intravaginal unit of estradiol monobenzoate is 1/100-1/200th of the subcutaneous unit. And whereas estradiol monobenzoate is about 10 times as potent as estrone when tested subcutaneously in rats, it is approximately 30 times as potent by the intravaginal method.

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Experimental Uterine Bleeding in Monkeys Following a Single Injection of Various Estrogens.*†

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Uterine bleeding in the rhesus monkey occurs after withdrawal of an adequate estrogenic stimulus. In routine treatments of 100 to 400 I.U. per day for 10 days, bleeding occurs in from 5 to 16 days after the last injection. In our experience, the most frequent day for bleeding of estrone withdrawal is day 7, or 17 days after the first injection.

The present series of experiments was performed with adult female macacus monkeys all of which were previously castrated. A single massive injection of an estrogen was given and the day on which uterine bleeding occurred was noted. Vaginal lavages were made daily in each animal from the time of the maximal sex skin response.

Treatment with estradiol benzoate oleosum (Progynon B Schering). A single injection of 150,000 I.U. (15 mg) of estradiol benzoate in oil was made. The site of injection in 2 monkeys was into the uterine cervix. By means of a vaginal speculum and adequate lighting 1 cc of the preparation was injected into the dense, fibromuscular tissue of the vaginal portion of the cervix with a number 25 hypodermic needle. The site was cleansed before and after injection with alcohol. Due to the great density of the tissue it was necessary to make 5 or 6 separate injections into the cervix around the

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