agreement with those presented by Fraser *et al.*,[1] Hamblen *et al.*,[2] and Callow *et al.*,[3] and contrary to the findings of Friedgood.[4]

It will be noted that in both normal and castrate animals (Tables I and II) there are two groups of animals, each showing different values. The only reason for division into 2 groups was: (a) in both Tables I and II the animals of Group 1 were older than those in Group 2 (1 to 2½ years as compared with 5 to 6 months); (b) the complete rabbit pellets fed were changed abruptly and unintentionally so that all animals in Group 1 received one brand of pellets, while those of Group 2 received a different brand (this change was instituted by the animal caretakers). It was for this reason that the animals were considered separately, and not because of their ketosteroid values.

The average urine volumes are also shown in Tables I and II. It was found that there is no statistical correlation between urine volume and 17-ketosteroids excretion in normal or castrate animals. (Correlation factor $r = -0.119 \pm 0.095$ for normals, -0.118 ± 0.136 for castrates, showing an insignificant negative correlation). This is in agreement with work done by Kimmeldorf on male rabbits,[8] as well as by Bachman *et al.*,[9] and Pincus[10] on humans.

Summary. 1. Total 17-ketosteroid urinary levels have been determined for normal and ovariectomized rabbits. There is no statistical difference between them. 2. The ratio between urine volume and 17-ketosteroid excretion has been examined statistically and no correlation found.

[8] Kimmeldorf, D., (unpublished data obtained in these laboratories).

[9] Bachman, C., Leekley, D., and Winter, B., *J. Clin. Endocrin.*, 1941, **1**, 142.

[10] Pincus, G., *J. Clin. Endocrin.*, 1943, **3**, 195.

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Effect of Orally Administered Sodium Estrone Sulfate on Total 17-Ketosteroid Excretion in Female Rabbits.*

J. DEKONING, B. KRICHESKY, AND S. J. GLASS.†

From the Department of Zoology, University of California, Los Angeles.

The effects on the total 17-ketosteroid excretion after estrogen administration have not been studied extensively. Hamblen and his co-workers[1] studied the change in 17-ketosteroid excretion titers after estrogen administration to women in the climacterium, those complaining of hypoovarianism or functional uterine bleeding.

This study was undertaken to determine the effect, if any, of the oral administration of sodium estrone sulfate (Premarin‡) on the total 17-ketosteroid excretion in normal and ovariectomized rabbits.

Materials and methods. Six female rabbits of the New Zealand strain, 4 normal and 2 castrate, were used for this experiment. The age of the animals varied from 7 months to 2-2½ years. Animals V and VI were bilaterally gonadectomized 2 months before being used in this experiment. All animals were kept in separate cages and fed complete rabbit pellets.

The urine was collected for 48-hour periods over 5 ml HCl. It was extracted and purified with Girard "T" according to Pincus,[2] and

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[1] Hamblen, E. C., Pattee, C. J., and Cuyler, W. K., *Endocrin.*, 1940, **27**, 734.

‡ Generously supplied by Ayerst, McKenna and Harrison, Ltd.

[2] Pincus, G., *J. Clin. Endocrin.*, 1945, **5**, 291.

TABLE I.
Effect of Orally Administered Sodium Estrone Sulfate on Total 17-Ketosteroid Excretion in Female Rabbits.

Animal	Normal 17-ks. mg/48 hrs	Dose of Estrogen (mg)	Mg 17-ks. after Na estrone sulfate admin. 1st 48 hr	2nd	3rd	4th	Avg
I (Normal)	2.73 (6)*	1.25	1.62	3.47	3.30	—	2.80
		0.63	1.68	1.70	1.35	—	1.58
II "	2.43 (6)	0.63	2.59	4.61	2.99	—	3.39
		0.63	1.76	1.82	1.04	—	1.54
III "	1.91 (6)	0.63	1.06	3.60	3.67	—	2.78
		0.63	2.90	1.77	2.75	—	2.47
IV "	3.92 (9)	2.50	4.24	3.18	6.10	4.18	4.42
V (Castrate)	4.94 (6)	2.50	2.30	4.09	4.47	5.34	4.05
VI "	4.44 (5)	2.50	3.51	2.58	3.63	4.04	3.44

* The figure in parenthesis represents the number of 48-hour collections.

assayed colorimetrically[3] on a Beckman spectrophotometer. A total of 38 collections were treated in this manner. The reagents were purified as described in a previous paper.[4]

The estrogen was administered, in liquid form by stomach tube and in dry form as a pill, inserted to the back of the mouth. It was administered in one dose (0.63 mg to 2.50 mg) and immediately following, the urine was collected for 3 or 4 consecutive 48-hour periods. Animals I, II, and III received a second dose one month later, and 3 determinations were made as before.

Results and discussion. All pertinent data, including 17-ketosteroid values, dosage, etc., are included in Table I. An examination of the results shows (1) statistically there is no significant change from the normal in the 17-ketosteroid excretion levels after administration of sodium estrone sulfate for at least 192 hours with a dose varying from 0.6 mg to 2.5 mg; (2) the data on excretion levels for the two castrate animals employed show no differences before and after estrogen feeding within the limits of the experiment; (3) although there is considerable variation between consecutive excretion titers on individual animals after estrone administration, there is no consistent trend for the 17-ketosteroids to increase or decrease.

Although these observations are not in accord with the reports of Hamblen's group;[1] it must be pointed out that his patients, for various reasons, all showed abnormally high 17-ketosteroid titers; and even with the decrease following estrogen therapy, in none of the cases did titers fall below what he considered the average normal excretion for healthy women.

Summary. The oral administration of sodium estrone sulfate in doses ranging from 0.6 mg to 2.5 mg to normal female rabbits or 2.5 mg to castrate female rabbits has been found to have no effect on the total urinary 17-ketosteroid excretion over a period of 192 hours.

[3] Talbot, N. B., Butler, A. M., and MacLachlan, E., *J. Biol. Chem.*, 1940, **132**, 595.

[4] DeKoning, J., *et al.*, PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 320.