in estrous type smears for 16 of 18 days, 12 of 20 days, 19 of 22 days, and 21 of 22 days, respectively. The ovaries were small, the mammary glands were not stimulated, and the uteri were large.

The amazing effect of dehydroandrosterone in the adult normal female led us to administer this treatment to 4 hypophysectomized females. To our surprise, particularly in view of its failure to change the vaginal picture in the spayed rat, the hypophysectomized female reacted in a manner even more striking than the normal female. Estrous type smears were shown for 21 of 25 days, 22 of 22 days, 22 of 22 days, and 12 of 14 days, respectively. The ovaries were only slightly decreased, the mammary glands were not stimulated, and the uteri were enlarged.

All animals showed a marked enlargement of the preputial glands and in many instances a striking enlargement of the clitoris.

The marked tendency of cis-androstene-diol and dehydroandrosterone to produce periods of prolonged estrus in normal female rats may be due to their conversion by the ovary to an estrogenic substance. If this is true it seems apparent that ovarian function is not entirely suppressed by hypophysectomy since dehydroandrosterone shows the same effect in the hypophysectomized female rat.

9413 P

Maintenance of Spermatogenesis in Testis of the Hypophysectomized Rat with Sterol Derivatives.*

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Walsh, Cuyler and McCullagh[1] reported that the administration of urine concentrates containing male sex hormone would prevent for as long as 20 days the degenerative changes which occur in the testes of hypophysectomized rats. These observations were confirmed and extended by Nelson and Gallagher[2] and Nelson,[3] who were able to show that spermatogenesis could be maintained for at least 60 days after hypophysectomy, and that such males were able

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1 Walsh, E. L., Cuyler, W. K., and McCullagh, D. R., *Am. J. Physiol.*, 1934, **107**, 508.

2 Nelson, W. O., and Gallagher, T. F., *Science*, 1936, **84**, 230.

3 Nelson, W. O., *Anat. Rec.*, 1936, **67**, 110 (suppl.).

TABLE I.

Hypophysectomized Males Treated with Androgenic Hormones. Weights are given as averages.

No. of rats	Body Wt. First	Body Wt. Last	Treatment Hormone (daily dose) mg.	Organ weights (gm.) Testes	Seminal vesicles (full)	Seminal vesicles (empty)	Prostate	Sperm motility
			Testosterone					
3	229	195	2	1.287	2.982	.877	.733	++++
4	275	232	1	1.243	1.815	.651	.472	++++
4	234	208	0.5	1.127	1.708	.448	.398	+++
			Androsterone					
3	272	230	2.5	2.214	1.609	.529	.483	++++
3	281	237	1.5	1.882	1.159	.436	.365	++++
3	238	197	1.0	1.785	.958	.363	.277	+++
2	226	185	0.5	1.963	.498	.355	.220	+++
			Dehydroandrosterone					
3	245	210	3.0	2.120	1.145	.443	.454	++++
2	242	212	2.0	2.019	.859	.335	.359	++++
3	239	210	1.0	1.789	.627	.295	.276	++++
2	242	213	0.5	1.317	—	.163	.075	++
			Androstanedione					
5	276	219	1.5	2.379	1.529	.442	.517	++++
2	244	197	1.0	2.117	1.297	.375	.415	++++
3	248	207	0.5	2.141	.350	.206	.170	++++
2	237	208	0.25	1.221	.209	.175	.137	++
1	290	247	0.125	.899	—	.139	.073	No motility
			Androstenedione					
2	228	177	1.0	2.016	1.241	.460	.515	++++
			Androstenediol (cis)					
2	239	196	1.0	1.790	.497	.312	.215	++++
			Androstenediol (trans)					
2	225	185	1.0	.750	.142	.113	.084	No motility
			Oestrone					
5	258	174	1000 I.U.					
			Oestrone, 1000 I.U., and Androstanedione	.329	—	.074	.063	No sperm
5	247	183	1.0	1.909	1.183	.349	.373	++++
12	278	217	Controls	.527	—	.083	.054	No sperm
21	267	—	Normals	2.432	.963	.281	.295	++++

to sire normal litters. It was shown, however, that the interstitial cells are not stimulated and that male hormone preparations failed to reinitiate spermatogenesis in rats which had been hypophysectomized for several weeks. Nelson[3-4] reported that 4 synthetic androgenic substances, viz., testosterone, androsterone, dehydroisoandrosterone, and androstanedione would maintain spermatogenesis. This report presents further evidence on these and 3 other substances, viz., androstenedione, cis-androstenediol and trans-androstenediol.

In the experiments to be reported here the administration of the synthetic androgens† was begun on the second day after hypophysectomy and continued for 20 days. Table I presents the pertinent data concerning these experiments.

It will be noted that testosterone, the most potent known androgenic substance, is the least effective, with the exception of trans-androstenediol which is very weak, of all the androgenic substances in maintaining spermatogenesis. Dehydroisoandrosterone and cis-androstenediol, relatively weak androgens, are as active as the more potent, from an androgenic standpoint, androsterone. Androstanedione and androstenedione have about the same androgenic activity as androsterone, but are superior in their capacity to maintain the testes.

It seems apparent that the capacity of these substances to maintain spermatogenesis is unrelated to their androgenic activity as based on either the capon comb or rat sex-accessory tests. This is of considerable importance in view of the fact that Hamilton[5] and Cutuly, McCullagh and Cutuly[6] have recently expressed the opinion that the effect of androgenic substance on the testis of the hypophysectomized rat is due to its action in maintaining a normal scrotum. While there can be little doubt that androgenic hormone does have a stimulating effect on the scrotum we are convinced that this action plays a relatively minor rôle in the phenomenon. In animals receiving testosterone the scrotum is very large and pendant, yet the testes are markedly regressed and spermatogenesis, while in progress, is only moderately well maintained. In animals receiving

[4] Nelson, W. O., *Anat. Rec.*, 1937, **67**, 36 (suppl.).

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[5] Hamilton, J. B., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 386.

[6] Cutuly, E., McCullagh, D. R., and Cutuly, E. C., *Am. J. Physiol.*, 1937, **119**, 121.

androstane-dione at the 0.5 mg. level the scrota are definitely less well maintained, yet the testes are almost normal in size and spermatogenesis is well maintained.

Summary. Various crystalline androgens have been shown to maintain spermatogenesis in the hypophysectomized rat if treatment is begun soon after ablation of the hypophysis. They are not effective in re-initiating spermatogenesis. The capacity of these substances to maintain the testis appears to be unrelated to their male hormone activity.

9414 P

Effect of Oestrone on Hypophyses and Reproductive Organs of Thyroidectomized Rats.

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Kojima,[1] Severinghaus, Smelser and Clark,[2] and Zeckwer[3, 4] have studied the hypophyses of thyroidectomized rats. Their reports agree that the basophiles increase in number and size and that the reaction is similar to that which occurs following gonadectomy. Zeckwer[4] considers that the reaction is sufficiently different to suggest the possibility that the basophiles are of 2 distinct types, *viz.*, those which react to gonadectomy and those which react to thyroidectomy. She further suggests that these 2 basophilic types are concerned in the production, respectively, of the gonadotropic and the thyrotropic hormones. Zeckwer also reports that the acidophiles are markedly decreased. The findings of Severinghaus, *et al.*, are in essential agreement as they find extensive acidophilic degranulation. Cells which their technique would show to be recently degranulated would be classified as chromophobes with the technique used by Zeckwer.

Zeckwer's suggestion that the cells which react to thyroidectomy are a separate type from those which react to gonadectomy suggested the treatment of a series of thyroidectomized rats with

1 Kojima, M., *Quart. J. Exp. Physiol.*, 1917, **11**, 319.

2 Severinghaus, A. E., Smelser, G. K., and Clark, H. M., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 1127.

3 Zeckwer, I. T., Davison, L. W., Keller, T. B., and Livingood, C. S., *Am. J. Med. Sci.*, 1935, **190**, 145.

4 Zeckwer, I. T., *Am. J. Physiol.*, 1936, **116**, 166 (suppl.).