chosen since preliminary work indicated that depression of choline-esterase activity is most marked at that period. Results are shown in Table I.

To obviate errors in the above series, determinations were made concurrently in which morphine sulfate was added to the blood *in vitro*. In other instances blood samples were drawn at 20-minute intervals to see whether repeated punctures with the needle would cause variations in esterase activity. In 10 experiments *in vitro* the mean change in cholin-esterase activity was (−) 0.10 units; in 6 determinations repeated at 20-minute intervals (using blood withdrawn without the giving of any drug) the mean change in esterase activity was zero. While the differences between the normal values for serum choline-esterase and those following the injection of morphine sulfate are not great (20%), we feel that they are significant because of their consistency.

Summary and Conclusions. 1. Morphine sulfate added to blood *in vitro* produces no consistent change in choline-esterase activity. 2. Serum choline-esterase activity in the dog is consistently lowered following the injection of morphine sulfate. 3. The *in vivo* effect of morphine on serum choline-esterase furnishes another indication that morphine acts through a cholinergic mechanism.

11566

Response of Sex Characters of the Adult Female Starling to Synthetic Hormones.*†

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The female sex of birds is often remarkable for extensive ambisexual features. In the starling *(Sturnus v. vulgaris)* the females have paired vasa deferentia which enlarge during the breeding season and, as in males, the bills are yellow during the first 6 months of the year. In a previous paper[1] it was shown that bill color as well

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† The authors are obliged to the following, who have supplied the hormone preparations: Parke, Davis and Co.: estrone (Theelin), estriol (Theelol) and estradiol (Dihydrotheelin); Ciba Pharmaceutical Products, Inc.: Stilbestrol, progesterone (Lutocylin), androsterone, testosterone propionate (Perandren).

1 Witschi, Emil, and Miller, R. A., *J. Exp. Zool.*, 1938, **79**, 475.

as size of the wolffian ducts respond to androgens and that during the breeding season the females of this species release considerable amounts of androgenic hormone. The present series of experiments was planned to decide whether in this interesting case of hormonal ambisexuality and morphological pseudohermaphrodism male and female sex hormones are pitted against each other, forming a system of dynamic balance, or whether the female organism has become adapted in some other way to the presence of hormones of contrary sex type. In the interest of clearness of results this work was started with synthetic sex hormones. It was therefore only natural to broaden its scope by testing also some substances which do not occur or function in the normal organism as androgens or estrogens.

The results of the injection series are summarized in the 2 tables. About half of the females were castrated, though in 3 the ovarial tissues were found incompletely removed. Except for one series (Table II) the experiments were carried out during the quiescent season and always with birds that had been in captivity for a sufficiently long time to insure a relative state of inactivity of the sex organs. The ovary of untreated controls weighs under these conditions from 10 to 35 mg, the left oviduct from 25 to 50 mg and the right vas deferens (from the lower edge of the kidney to its entrance into the cloaca) from 1 to 2.5 mg. In castrates the oviducts shrink even more, weighing often less than half the minimal weight of quiescent normals (all weights given in this paper are of Bouin fixed and alcohol preserved material). In most cases the daily dose was given 10 times on consecutive days. It seems that after the first week no further increase is obtained with a constant hormone level.[2]

From our Table I it can be seen that estradiol, estrone, estriol and stilbestrol stimulate exclusively the oviducts (the rudiment on the right side also becomes enlarged). The doses given are in some instances excessive and produce oviducts nearly as large as those of wild birds killed at the height of the breeding season. In the latter the oviducts average about 3000 mg, the heaviest observed weighing 3306 mg. Since extraction of the whole bodies of birds in early breeding condition yields only small amounts of sex hormones, it appears that the injected preparations are not being economically used.

Progesterone has no influence on either the female or the male sex characters. More extensive series with sparrows, which will be described elsewhere, prove that even in combination with estrone the progesterone fails to contribute to the response.

[2] Keek, W. N., *J. Exp. Zool.*, 1934, **67**, 315.

TABLE I.

Hormone reactions in female starlings injected during the quiescent season. c, castrate; i, incomplete castrate. In the weight of the right vas deferens only the part from the lower edge of the kidney to the cloaca is included. In the last group estrone was injected 10 times, testosterone only 7 times, during the first 7 days. Weights from material preserved in alcohol.

Bird	Hormone: Name	Hormone: Daily dose γ	Ovary: wt, mg	Ovary: type	Oviduct: wt, mg	Oviduct: type	Right vas def.: wt, mg	Right vas def.: type
68 c	estradiol	0.6	—		35	0-I	(ca. 1.3)	0
79 c	estriol	100	—		110	II	(ca. 1.3)	0
57 c	estrone	5	—		149	II	(ca. 1.3)	0
232	”	50	17	0	110	II	1.4	0
233	”	50	18	0	182	II	1.7	0
228 i	”	50	—		198	II	1.6	0
231	”	500	22	0	579	II	1.0	0
178 i	”	500	—		1681	III	1.6	0
312	stilbestrol	50	15	0	1112	III	1.9	0
310	”	50	24	0	1471	III	1.3	0
306	”	50	32	0	1533	III	1.4	0
311	progesterone	500	30	0	50	0	1.9	0
227 i	”	500	—		34	0	1.6	0
56 c	androsterone	330	—		10	0	(ca. 8)	I
226 c	”	3000	—		114	II	14.1	III
80 c	testosterone propionate	100	—		16	0	(ca. 8)	I
182 c	” ”	1250	—		241	II	11.5	III
302	” ”	1250	19	0	91	I	14.3	III
303	” ”	1250	30	0	82	I	11.3	III
301	” ”	1250	15	0	559	II	14.4	III
234	estrone + testosterone prop.	50 + 1000	37	0	652	II	(ca. 10)	II-III
140 c	” ” ”	50 + 1000	—		633	II	9.3	II
83 c	” ” ”	50 + 1000	—		1536	III	10.1	III
Controls (range)	—		15-35	0	25-50	0	1-2	0
Castrates ”	—		—		5-20	0	1-1.5	0

TABLE II.
Reactions Produced by Testosterone Injections into Captive Female Starlings in the Month of May.

Bird	T. prop. Daily dose, γ	Ovary wt, mg	Ovary Type	Oviduct wt, mg	Oviduct Type	Right vas def. wt, mg	Right vas def. Type
Control 1	0	70	I	99	I	1.7	0
" 2	0	93	I	182	II	1.9	0
313	10,000	36	0	1144	III	12.4	III
316	10,000	40	0	851	III	13.9	III
307 c	10,000	—		716	III	14.8	III
305 c	10,000	—		1024	III	12.8	III

In contrast to the selective character of the gynogenic substances the androgens (androsterone and testosterone propionate) stimulate all secondary sex characters. However, the effects appear at different quantitative levels. Unpublished experiments with castrate male starlings show that the bill color has a lower threshold value than the deferent ducts (about 1 γ and 20 γ of testosterone propionate per day). The oviduct becomes stimulated only by doses well above 330 γ of androsterone or 100 γ of testosterone. Daily doses of 1.25 and 10 mg of testosterone produce oviducts of a size characteristic for birds approaching the breeding condition (early April) and vasa deferentia about twice the weight they ever attain in breeding females. The ovaries of the starling remain quiescent though in sparrows the ovaries also become stimulated (unpublished). In all groups the histological structure of the enlarged oviducts is identical with that of breeding females, no matter whether androgens or gynogens were used to stimulate their development.

It appears that the presence or absence of the ovary has no influence on the extent of development of the ducts in the injected birds, at least not at the levels of hormone dosages used in the present set of experiments. The data of Table II indicate, however, a depressive action on ovarial development. This latter series was made during the spring breeding season with birds that had been caged in the laboratory since early spring (February 10). Birds in captivity are crowded and without accommodations for nest building. Their ovaries enlarge only to a modest degree and spontaneous ovulation never occurs. In birds in the open, the ovaries and oviducts have increased in weight up to 100 and 150 times by late April while in those in captivity the increment is always less than ten fold, even one month later. The results presented in Table II suggest that the injected testosterone has inhibited the gonadotropic activity of the hypophysis. The slightly greater average weight of the oviducts in the non-castrated females is either due to the advantage which they

had from the beginning of the experiment or purely accidental. In a forthcoming paper it will be shown that the sparrow differs distinctly in the reactions to androgens, in that its ovaries are stimulated to grow and produce hormones.

Discussion. The literature of recent years contains numerous reports on gynogenic properties manifested by "androgens". In most instances the reactions were obtained by administration of large amounts of the male hormone in animal species where the normal female does not usually exhibit any evidences of the presence of considerable amounts of this hormone. In the starling, however, it seems quite possible that androgens normally contribute to the development of the oviduct. Our series of combined estrone and testosterone injections prove not only that there is no antagonism between these hormones but that they coöperate in the stimulation of the oviduct (Table I). In view of the established presence of male hormones in breeding female starlings there remains little doubt but that the 2 sex hormones also coöperate under normal conditions in the spring development of the oviducts. Since female birds exhibit many ambisexual features, the responsiveness of the oviduct to androgens may have developed as a special adaptation to this condition. The remarkable and strictly specific gynogenic potency of stilbestrol remains without explanation. While this synthetic substance seems to be capable of inducing all the gynogenic reactions of natural female sex hormones in all classes of vertebrates, its faculty of imitating testosterone and the other ambigenic "male" hormones in the starling remains limited to the female component.

Summary. Adult female starlings in the quiescent season are a favorable material for the study of the biological properties of natural and synthetic sex hormones. Their ovaries and oviducts are capable of increasing in weight 100 to 150 times and the wolffian ducts 10 to 20 times. The bill color and the wolffian ducts react only on stimulation by androgens while the oviducts react in an identical way on either male or female hormones. Stilbestrol produces purely gynogenic effects and is considerably more potent than equal doses of estrone. Progesterone even in high doses or in combination with estrone gives no effects; it does not seem to be one of the hormones that take a part, normally, in the endocrine physiology of passerine birds.