2 reaction types (for detailed bibliography consult ref. 1). In the first type, androgens produce complete and durable masculinization of genetically female embryos; gynogens are feminizing at low effective dosages—apparently effecting only an unstable sex inversion of genic males—but at high dosages they are masculinizing genic females. To this type belonged, so far, only the ranids; they are now joined by the hylids. In the second reaction type, represented by several families of primitive anurans (discoglossids, xenopins) and all urodeles, androgens produce either no major effects or, in some instances, they feminize genic males; gynogens however are feminizing the larvae of male genic constitution.

Experiments with the common toad indicate that in general bufonids follow the second reaction type. However, feminization by gynogens is unstable(5), so that in this regard they seem related to the first type. Their intermediary behavior is of some interest in view of the taxonomic position of the bufonids between the higher and the primitive families of the anurans.

Breeding experiments with various sex races and with sex reversed animals so far have shown that in frogs the males are heterozygous for sex determining genes, while in toads, all lower anurans, and salamanders the females are the heterozygous sex. The number of fully investigated species is still small, but all cases conform to the rule that the first reaction type (to steroids) is exhibited by the species with male heterozygosity and the second by those with female heterozygosity. The remarkable parallelism points to some characteristic difference in the mechanisms of gene action in the two types.

Summary. Testosterone masculinizes the course of gonad differentiation in genetically female larvae of treefrogs. Gynogenic steroids are only partially feminizing the gonadal development of genetic males. These results establish for hylids and ranids a common reaction type to steroid treatments, which differs characteristically from that of all other amphibian families which, so far, were submitted to tests.

1. Witschi, E., *J. Fac. Sci.*, Hokkaido Univ., 1957, v14, in press.
2. Yosida, T. H., *Nat. Inst. Genet.*, Ann. Report, 1955, p16, Misima.
3. Deal, R. E., *Anat. Rec.*, 1931, v48, 27.
4. Witschi, E., *Recent Progr. Hormone Res.*, 1951, v6, 1.
5. Chang, C. Y., *Anat. Rec.*, 1955, v123, 467.

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Copulatory Reflex by Progesterone and Desoxycorticosterone Acetate.* (23688)

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Using the persistent estrous rat as a test animal, it has been shown that progesterone (1) and desoxycorticosterone acetate (DOCA)(2) are equally effective in restoring estrous cycles. Other earlier reports(3,4,5) had established that DOCA is 1/10 to 1/15 as potent as progesterone in a variety of tests. Most recently using the elicitation of the copulatory reflex in guinea pigs, DOCA was found to be ¼ as potent as progesterone(6). Studies in progress in our laboratory for several years have indicated that the relative activity of these 2 substances in dependent upon the absolute amount used in the test, and have lead to this report.

Methods. Young, adult, female guinea pigs were ovariectomized and allowed to recover for 30 days. The completeness of the surgery was attested to by examination of the extirpated ovaries, lack of estrous behavior in untreated animals, and examination of the

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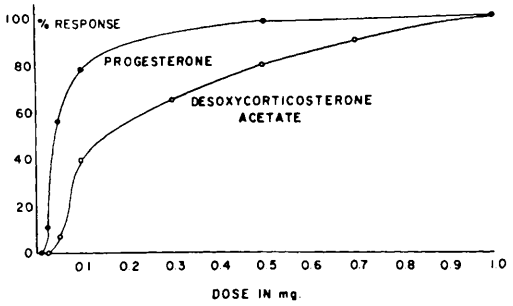

FIG. 1. Curvilinear relationship of dose-response curves of progesterone and desoxycorticosterone acetate.

operative site at time of sacrifice. The testing procedure used was essentially the same as the standard reported method(7), except: a single priming dose of 5 μg of estrone in 0.05 ml corn oil was given 24 hours before the test material, and the test material was dissolved in 0.10 ml of oil. All injections were subcutaneous. Each animal was "rested" 30 days between tests, and none was used for more than 12 tests. Hourly tests were carried out for a minimum of 10 hours, or until responding animals failed to respond for 2 hours in succession.

Results. The points with which the curves in Fig. 1 were drawn represent 20-30 animals each. In every case, doses of the 2 steroids larger than 1 mg resulted in all animals giving strong, positive copulatory responses. A latent period between the injection of the test material and the first copulatory response characterized all reacting animals. With progesterone this latent period decreased from an average of 4 hours to 2.7 hours over a dosage range of 0.025 mg to 1.0 mg. Similarly with DOCA, the length of this period decreased from 5 hours to 2.9 hours over a dose range of 0.05 mg to 5.0 mg. In contrast to this similarity, the amount of progesterone injected had little effect on the duration of responsiveness (6.2 hours at 0.025 mg to 7.0 hours at 1.0 mg), while the amount of DOCA significantly affected the duration of responsiveness (2.0 hours at 0.05 mg to 8.1 hours at 1.0 mg).

Our results with progesterone agree well with those of others(6), 56% of 25 animals responding in our series on 0.05 mg as compared with 60% of 30 animals in the reported series. Our results emphasize the necessity of comparing dose-response curves over a range of doses, since DOCA is here shown to have 13-100% the effectiveness of progesterone depending upon the absolute level of comparison.

Examination of the curves suggests another point for consideration. The progesterone curve is typically a sigmoid, biologic dose-response curve, but the DOCA curve is approximately linear above the 0.1 mg dose level. This difference may mean that an additional reaction is interposed between the absorption of the injected DOCA, and the action on the end organ. It is possible, perhaps, that the DOCA must be converted to progesterone metabolically before the reflex can be elicited. This hypothesis is supported by the greater latent period of DOCA, and by the fact that the duration of response increases directly as the dose.

Pregnenolone acetate was tested at only the 50 mg level, with negative results in 8 guinea pigs.

Summary. Using the elicitation of the copulatory reflex as a criterion, progesterone and desoxycorticosterone acetate were compared. The latter was found to be 13-100% as effective as progesterone over a range of 0.025-1.0 mg. With both substances, the latent period varied inversely as the dose, but duration of responsiveness varied directly with dosage only in the case of desoxycorticosterone acetate.

1. Everett, J. W., *Endocrinology,* 1943, v32, 285.
2. Marvin, H. N., *Anat. Rec.,* 1947, v98, 383.
3. van Heuverswyn, J., Collins, V. J., Williams, W. L., Gardner, W. U., PROC. SOC. EXP. BIOL. AND MED., 1939, v41, 552.
4. Selye, H., Masson, G., *J. Pharmacol. and Exp. Therap.,* 1943, v77, 301.
5. Leatham, J. H., Crafts, R. C., *Endocrinology,* 1940, v27, 283.
6. Byrnes, W. W., Shipley, E. G., *ibid.,* 1955, v57, 5.
7. Hertz, Roy, Meyer, R. K., Spielman, M. A., *ibid.,* 1937, v21, 533.

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