

changed metabolic rate during the treatment. The final increase in metabolism after thyroid treatment was well within the limits of the normal rat, whether or not the methyltestosterone injections had been continued.

*Summary.* The oxygen consumption of castrate male rats is lower than that of normal, but higher than that of thyroidectomized rats. In castrate-thyroidectomized rats it is not lower than that found in non-castrate thyroidectomized rats. Treatment with methyltestosterone, within the conditions of these experiments, did not affect the metabolic rate of non-castrate animals, nor that of castrates. It caused a moderate increase in thyroidectomized-castrate rats. The latter rats showed also an increased sensitivity to treatment with thyroid, which, however, was neither caused nor influenced by methyltestosterone.

### 13644

#### Effects of Gonadotropic Hormone in the Fish, *Xiphophorus helleri* Heckel.

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The administration of mammalian gonadotropins from pregnancy urine and other preparations to a teleost fish, *Lebistes reticulatus*, has been reported by Berkowitz.<sup>1</sup> These substances stimulated the precocious development of male secondary sex characters, as well as the precocious but normally-patterned development of immature testes. The response of adult male *Lebistes*, if any, was by a decreased gonad size and an interstitial hypertrophy of the stroma. The latter phenomenon persisted only in some but not all of his fish when treatment was prolonged. He reported there was no effect on the secondary sex characters nor gonads of immature female *Lebistes*. The action of the hormones on mature females of this species was not mentioned. Saphir<sup>2</sup> found that injection of *prolan* from urine of pregnant women caused inconstant response of the "wedding dress" in male *Chromosomus erythrogaster*. Owen<sup>3</sup> produced this chromatophore reaction in 75% of male *Phodeus amarus* by employing the *prolan* in aquarium water, while he failed

<sup>1</sup> Berkowitz, P., *J. Exp. Zool.*, 1941, **86**, 247.

to induce the elongation of ovipositor in females so treated. Wholly negative results were reported by Koch and Scheuring,<sup>4</sup> Johnson and Riddle<sup>5</sup> in gonads of *Phoxinus* and *Salmo* by injection methods. Also similar results were reported by Landgrebe<sup>6</sup> on *Salmo* and eel. Still no general conclusions can be drawn in adult fishes of other species. In connection with some other phases of hormone administration, it was thought of some interest to study further the effects of a human chorionic gonadotropic hormone (pranturon\*) on the adult female and adult male of a teleost fish, *Xiphophorus helleri* (swordtail).

Twenty virgin females were injected intraperitoneally for 10 to 20 weeks. Each fish received 25 I.U. (2.5 mg) gonadotropic hormone in .05 cc of distilled water weekly. A group of 10 virgin females were similarly injected with pure distilled water, and another group of 5 were left untreated. After 5 injections, a male-like gonopod was observed to develop on 4 of the treated females. Attempts at copulation simulating male behavior also occurred. One of these altered females was killed 60 days after the initial injection. Histological examination revealed a small unilateral maturing testis. A caudal sword developed in 2 of the 3 remaining females after 10 weekly injections. Gonads of these treated females show various stages of spermatogenesis with a moderate amount of interstitial cells. Secondary sex-coloration was observed in the completely sex-reversed fish.

While the masculinization of females by the administration of gonadotropic substances has been recorded in several higher vertebrates, *i. e.*, fowl,<sup>7, 8</sup> guinea pigs,<sup>9</sup> and rats,<sup>10, 11, 12</sup> the experimental induction of complete sex-reversal in fishes by the mammalian gonad-

<sup>2</sup> Saphir, W., *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 864.

<sup>3</sup> Owen, S. E., *Endocrinology*, 1936, **20**, 214.

<sup>4</sup> Koch, W., and Scheuring, L., *Zool. Anzeig.*, 1936, **116**, 62.

<sup>5</sup> Johnson, M. W., and Riddle, O., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 260.

<sup>6</sup> Landgrebe, F. W., *J. Exp. Biol.*, 1941, **18**, 162.

\* By the courtesy of Dr. M. Gilbert of the Schering Corporation, Bloomfield, New Jersey.

<sup>7</sup> Domm, L. V., *Cold Spring Harb. Sympos. Quant. Biol.*, 1937, **5**, 34.

<sup>8</sup> Uotila, U. U., *Anat. Rec.*, 1939, **74**, 165.

<sup>9</sup> Papanicolaou, G. N., and Falk, E. A., *Proc. Soc. Exp. Biol. and Med.*, 1934, **31**, 750.

<sup>10</sup> Greene, R. R., and Burrill, M. W., *Proc. Soc. Exp. Biol. and Med.*, 1939, **40**, 514.

<sup>11</sup> Bradbury, J. T., and Gaensbauer, F., *ibid.*, 1939, **41**, 128.

<sup>12</sup> Marx, L., and Bradbury, J. T., *Anat. Rec.*, 1940, **78**, 79.

otropic hormones has not been reported before. In the genetical gonochorist, *Xiphophorus helleri*,<sup>13</sup> Essenberg<sup>14</sup> has observed 2 cases of natural complete sex-reversal from female to male. The transformation of the female anal fin into a gonopod,<sup>15-18</sup> and a complete sex-reversal<sup>17, 19</sup> in *Xiphophorus* can be induced by the administration of androgenic substances. Essenberg<sup>20</sup> has pointed out that any adverse condition, be it extrinsic or intrinsic, acquired or inherited, which tends to reduce the capacity for hormone production beyond a certain limit may become the immediate cause of sex-reversal in the female *Xiphophorus helleri*.

Germ cells in various stages of the ovarian cycle were found in ovaries of both the unaffected and control females in our experiments. So far as could be observed, the gonadotropin of pregnant urine has no marked effect on the secondary sex characters in the unaffected female fish.

Twenty-eight sexually mature males were used in this experiment in which 8 served as controls. Twenty males were kept separately in 7 aquaria, each containing 1500 cc of water. The powdery gonadotropin was dissolved in the sterile diluent immediately before using. Seven hundred and fifty I.U. (75 mg) of the hormone were added weekly to each aquarium. From the surrounding water the hormone administered was absorbed by the gill tissue of the fish. All specimens were maintained at a temperature of 18° to 21°C during the experiments.

The experiments on adult males were conducted over a period of 4 months. Examination of testes from fish which were treated for 10 to 12 weeks as against controls show the gonadotropin had accelerated spermatogenesis; since the lumina of the sperm tubules were crowded with spermatophores, and distended with spermatozoa. It is indeed difficult to find spermatids and spermatocytes in these treated testes. *This accelerated effect of mature sperm formation* induced by the gonadotropin hormone was not noted by Berkowitz<sup>21</sup> in adult fish. In some instances, the testes appear to have under-

<sup>13</sup> Witschi, E., Chapter 4, *Sex and Internal Secretions*, 1939, Williams and Wilkins Company, Baltimore.

<sup>14</sup> Essenberg, J. M., *Biol. Bull.*, 1926, **51**, 98; 1923, **45**, 46.

<sup>15</sup> Regnier, M. T., *Bull. Biol. de France et Belg.*, 1938, **72**, 385.

<sup>16</sup> Witschi, E., and Crown, E. N., *Anat. Rec.*, 1937, **70**, 121 (supplement).

<sup>17,18</sup> Baldwin, F. M., and Goldin, H. S., *Proc. Soc. Exp. Biol. and Med.*, 1939, **42**, 813; 1941, **46**, 283.

<sup>19</sup> Noble, G. K., and Bornc, R., *Anat. Rec.*, 1940, **78**, 147 (supplement).

<sup>20</sup> Essenberg, J. M., *Biol. Bull.*, 1926, **51**, 98; 1923, **45**, 46.

<sup>21</sup> Berkowitz, P., *J. Exp. Zool.*, 1941, **86**, 247.

gone a state of precocity indicative of exhaustion, where some tubules even contained the desquamated epithelial cells and debris only. This gives evidence of hypotrophy and reduction in size. In all cases, a marked increase in interstitial tissue is evidently accompanied by vascular tissue growth, so that the testes are dense and compact in transection, as contrasted to those in controls. One may postulate that this interstitial hypertrophy of the stroma is a direct result of an attempt on the part of the testes to counteract the excess of the gonadotropins, and that this may terminate in sterility if the treatment is prolonged. It is well-known that many of the sex hormones have the power to suppress the hypophyseal functions.<sup>22</sup>

*Summary.* (1) This paper reports for the first time the possibility of complete sex-reversal in the adult female *Xiphophorus helleri* by administration of gonadotropic (human chorionic) hormone from pregnancy urine. (2) Gonadotropin when administered to the adult males of this species increases not only the amount of interstitial stroma (Berkowitz), but hastens spermatogenesis and brings about an exhaustion effect simulating a condition of sterility. (3) There were no significant effects on the secondary sex characters of the adult males and unaffected females under this treatment.

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#### Exploration of a Method for Standardizing Hemorrhagic Shock.

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The urgency in developing standardized laboratory procedures for production of shock which will enable us to evaluate the efficiency of remedial measures with greater certainty is generally recognized. While no claim to such achievement can be made, we desire to report results which point to certain trails that ought to be explored more thoroughly.

Since the bulk of experimental work<sup>1</sup> strongly suggests that the progressive decline in arterial pressures is associated with reduced

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<sup>22</sup> Moore, C. R., and Price, D., *Am. J. Anat.*, 1932, **50**, 13.

<sup>1</sup> Wiggers, C. J., *Physiol. Rev.*, 1942, **22**, 74.