

contained 50% starch, weight loss did not occur. The Argo starch conceivably provided protein deficient, carbohydrate calories to support this slight augmentation of weight.

The difference in conception rate, however, between the starch-eating mice and the controls was striking. The same may be said for the litter size. Perhaps of greater importance was the total lack of interest or concern for the offspring exhibited by the starch-eating mice. This certainly could have contributed to the 100% 24 h mortality among the starch litters.

**Zusammenfassung.** Es wird gezeigt, dass die Amylophagie bei der Maus keine Anämie, dagegen eine Verminderung der Graviditäten und Abnahme der pro Geburt geborenen Jungtiere herbeiführt.

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## An Increase in Thyroid Radioiodine Uptake Following the Administration of Cyproterone Acetate

Cyproterone (6-chloro- $\Delta^6$ -1,2- $\alpha$ -methylene-17 $\alpha$ -hydroxyprogesterone, Schering SH 80881) and cyproterone acetate (Schering SH 80714) are two of the most potent antiandrogens. Both block the effect of endogenous and exogenous testosterone and other androgens at both peripheral<sup>1-5</sup> and central (hypothalamic)<sup>6-8</sup> receptor sites. Cyproterone acetate possesses stronger antiandrogenic activity but is also gestagenic; cyproterone is a weaker antiandrogen but has no gestagenic effects<sup>9</sup>. Apart from the principal effects (seminal vesicle and prostate atrophy), several reactions in the endocrine system in general were observed following antiandrogen administration: changes in the blood gonadotrophin level and the adenohipophysial gonadotrophin content<sup>10-12</sup>, development of the castration cells in the adenohipophysis<sup>13</sup> and a decrease in adrenal weight<sup>14</sup>. The last effect is probably due to gestagenic activity, since it is also produced by other gestagenic substances<sup>15</sup>. Although the effects of various steroid hormones on thyroid activity have been widely studied, no study on the effects of antiandrogens has so far, to our knowledge, been published. In the course of study of the effects of steroid hormones on <sup>125</sup>I-thyroxine binding by adenohipophysial proteins *in vitro*<sup>16,17</sup>, we observed that oestrogens had a stimulant effect and testosterone (as well as the thyroid hormones) an inhibitory effect. In a study of the action of cyproterone acetate, described in detail elsewhere<sup>18</sup>,

we observed an increase in thyroid radioiodine uptake following its administration. This effect, as well as its interaction with an oestrogen, oestradiol dipropionate, forms the subject of the present communication.

Cyproterone acetate was administered to adult male rats (descendants of the Wistar strain, Velaz, Prague) in a standard laboratory diet (Larsen diet, Velaz, Prague) in 1.6‰ concentration (representing about 5 mg/day/rat). Oestradiol dipropionate (Agofollin SPOFA) was administered i.m. in daily doses of 50 µg in olive oil. In the first experiment, there were 9 control rats and 9 rats treated with cyproterone acetate. In the second experiment, there were 10 controls, 10 cyproterone acetate treated rats, 10 treated with oestradiol dipropionate and 10 treated with both substances. After 20 days, the animals were given 0.5 µC <sup>132</sup>I (obtained by elution from <sup>132</sup>Te columns, Isocommerz) i.p. in 0.5 cm<sup>3</sup> physiological saline and were killed by exsanguination 4 h later. The thyroids were dissected out, weighed and hydrolyzed in 2 cm<sup>3</sup> 10% NaOH. The radioactivity of the samples was measured in an Tesla NZQ laboratory set and, after correction for decay, the percentage of the administered dose per thyroid and per mg thyroid was calculated. An analysis of variance and DUNCAN's<sup>19</sup> test was used for statistical evaluation.

The results are given in the Table. A slight but significant increase in thyroid weight was observed in all the

Group	Body weight initial (g)	Body weight final (g)	Thyroid (mg)	Thyroid (mg/100 g)	<sup>132</sup> I uptake (%/thyroid)	<sup>132</sup> I uptake (%/mg thyroid)
Experiment No. 1						
1. Controls	218.33 ± 15.16	251.33 ± 15.97 (2)	13.31 ± 1.72	5.56 ± 1.04	7.22 ± 1.63 (2)	0.54 ± 0.10 (2)
2. Cyproterone acetate	205.56 ± 15.81	198.67 ± 22.01 (1)	12.78 ± 3.32	6.33 ± 1.19	13.86 ± 3.84 (1)	1.10 ± 0.16 (1)
Experiment No. 2						
1. Controls	188.0 ± 6.57	214.2 ± 12.20 (2, 3, 4)	12.93 ± 2.25 (3, 4)	5.92 ± 0.75 (2, 3, 4)	4.25 ± 0.75 (3, 4)	0.33 ± 0.04 (3, 4)
2. Oestradiol diprop.	183.0 ± 5.64	182.5 ± 6.75 (1, 3)	12.79 ± 1.67 (3, 4)	6.99 ± 0.78 (1, 3, 4)	4.66 ± 0.96 (3, 4)	0.38 ± 0.09 (3)
3. Cyproterone acetate	190.5 ± 7.62	197.8 ± 12.38 (1, 2, 4)	18.47 ± 1.16 (1, 2, 4)	9.39 ± 0.80 (1, 2)	13.21 ± 2.32 (1, 2, 4)	0.73 ± 0.12 (1, 2, 4)
4. Oestradiol diprop. + Cyproterone acetate	187.5 ± 4.54	179.4 ± 6.75 (1, 3)	15.56 ± 2.32 (1, 2, 3)	8.68 ± 1.33 (1, 2)	7.26 ± 1.24 (1, 2, 3)	0.48 ± 0.10 (1, 3)

Means ± 95% confidence limits. In brackets are given the numbers of groups with statistically different means (DUNCAN's test). 9 (Exp. No. 1) or 10 (Exp. No. 2) animals in each group.

- <sup>1</sup> H. HAMEDA, F. NEUMANN and K. JUNKMANN, *Acta endocr., Copenh.* 44, 380 (1963).
- <sup>2</sup> K. JUNKMANN and F. NEUMANN, *Acta endocr., Copenh.* 90, 139 (1964).
- <sup>3</sup> F. NEUMANN and W. ELGER, *J. Invest. Dermat.* 46, 561 (1966).
- <sup>4</sup> F. NEUMANN and R. VON BERSWORDT-WALLRABE, *J. Endocr.* 35, 363 (1966).
- <sup>5</sup> F. NEUMANN and W. ELGER, *Acta endocr., Copenh.* 52, 54 (1966).
- <sup>6</sup> F. NEUMANN, W. ELGER and R. VON BERSWORDT-WALLRABE, *Acta endocr., Copenh.* 52, 63 (1966).
- <sup>7</sup> A. L. WOLLMAN and J. B. HAMILTON, *Endocrinology* 81, 350 (1967).
- <sup>8</sup> Y. ARAI and R. A. GORSKI, *Proc. Soc. exp. Biol. Med.* 127, 590 (1968).
- <sup>9</sup> W. ELGER, R. VON BERSWORDT-WALLRABE and F. NEUMANN, *Naturwissenschaften* 54, 549 (1967).
- <sup>10</sup> R. VON BERSWORDT-WALLRABE and F. NEUMANN, *Neuroendocrinology* 3, 332 (1968).
- <sup>11</sup> R. VON BERSWORDT-WALLRABE and F. NEUMANN, *Neuroendocrinology* 2, 107 (1967).
- <sup>12</sup> D. C. JOHNSON and R. H. NAQVI, *Endocrinology* 84, 421 (1969).
- <sup>13</sup> F. NEUMANN, *Acta endocr., Copenh.* 53, 53 (1966).
- <sup>14</sup> C. DENEFF, M. VANDEPUTTE and P. DE MOOR, *Endocrinology* 83, 945 (1968).
- <sup>15</sup> G. K. WINKLER and R. A. HARKNESS, *J. Endocrin.* 30, 3 (1964).
- <sup>16</sup> V. SCHREIBER, T. PŘIBYL and J. ROHÁČOVÁ, *Physiol. bohemoslov.* 19, 501 (1970).
- <sup>17</sup> V. SCHREIBER, T. PŘIBYL and J. ROHÁČOVÁ, *Physiol. bohemoslov.* 19, 511 (1970).
- <sup>18</sup> V. SCHREIBER, T. PŘIBYL, J. ROHÁČOVÁ, *Physiol. bohemoslov.* 20, in press (1971).
- <sup>19</sup> D. B. DUNCAN, *Biometrics* 11, 1 (1955).
- <sup>20</sup> Cyproterone acetate was kindly supplied by Dr. L. STÁRKA, Research Institute of Endocrinology, Prague.

experimental groups in experiment No. 2. Cyproterone acetate stimulated thyroid radioiodine uptake in both experiments. Oestradiol alone produced no significant effect but significantly inhibited the effect of cyproterone acetate.

The mechanism by which cyproterone acetate produced an increase in thyroid radioiodine uptake and the cause of the unexpected blocking effect of simultaneous oestrogen administration are unknown. Theoretically, changes in the availability of binding sites for thyroid hormones might be one possibility; none of the other steroid hormones produce such an increase in thyroid radioiodine uptake, however<sup>20</sup>.

**Zusammenfassung.** Die Wirkung des Cyproteron acetates auf die  $J^{131}$ -Aufnahme der Rattenschilddrüse wurde untersucht. Die Radiojodaufnahme der Schilddrüse wurde durch diese Substanz erhöht, wobei gleichzeitig eine mässige Zunahme des Schilddrüsengewichtes festgestellt werden konnte. Gleichzeitige Verabreichung von Oestradiol hob diesen Effekt auf.

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## Neurosecretion in Thyroidless *Xenopus laevis* Larvae

Giant non-metamorphosing larvae, showing an inborn lack of the thyroid gland can be found among laboratory-bred *Xenopus laevis*<sup>1</sup>. These larvae attain a size of about 12 cm, remaining at the premetamorphic stage for several months (Figure 1). Histological examination<sup>1</sup> showed that in such animals the thyroid gland is absent both from its normal position and possible ectopic sites.

The brains of 5 non-metamorphosing giant *Xenopus laevis* 6-month-old larvae were examined histologically, following Gomori's chrome haematoxylin phloxin method for the neurosecretory material. The brains of these animals were much larger than in larvae of corresponding developmental stage (49 according to NIEUWKOOP and FABER<sup>2</sup>). They had a typical larval shape, the brain walls being thin and compensated by distended brain ventricles.

The pars magnocellularis of the preoptic nucleus, i.e. the hypothalamic neurosecretory centre, was developed to a stage comparable to that shown by normal larvae at the prometamorphic period. The neurosecretory cells were only slightly larger than surrounding non-secretory neurons. The neurosecretory material was very scanty and present only in the perikarya. The Nissl substance in the neurosecretory cells was abundant. Normal,

<sup>1</sup> A. JURAND, *Folia biol., Kraków* 3, 315 (1955).

<sup>2</sup> P. D. NIEUWKOOP and J. FABER, *Normal Table of Xenopus laevis* (Ed. DAUDIN; North-Holland Publishing Comp., Amsterdam 1956).

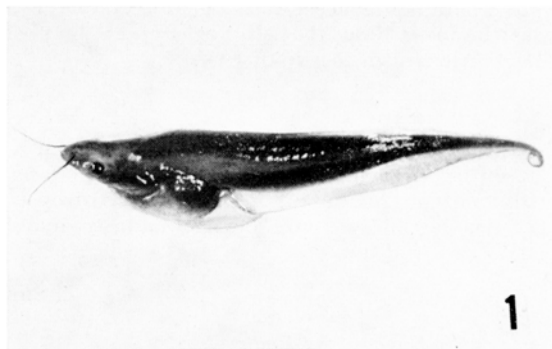


Fig. 1. Thyroidless larva, 6 months after hatching. Developmental stage 49.  $\times 0.8$ .



Fig. 2. Normal littermate.  $\times 0.8$ .