experiments in hypophysectomized rats[11] have been carried out. 5 days after hypophysectomy, norepinephrine was administered s.c. in doses markedly effective in control rats. In these animals norepinephrine failed to increase oxygen consumption (Figure 1), whereas the enhancement of cardiac frequency remained unchanged. The calorigenic effects of 2,4-dinitrophenol showing no age-dependent changes after the 20th day of life and not being annulled by β-sympathicolytics[10], was hardly impaired by hypophysectomy (Figure 2).

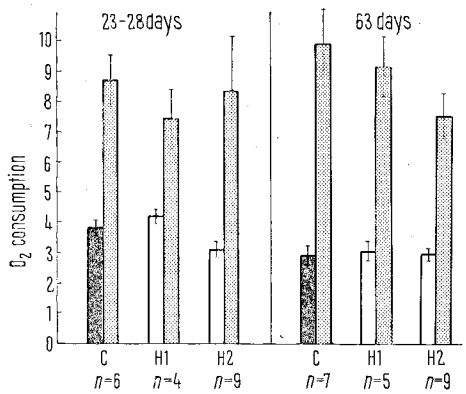

Fig. 2. Influence of 2,4-dinitrophenol (30 mg/kg body wt.) upon oxygen consumption (ml/min/100 g body wt. ± S.E.M.) in 23–28- and 63-day-old control and hypophysectomized rats. ▩ □ oxygen consumption before administration of 2,4-dinitrophenol in control resp. hypophysectomized rats; ⁞⁞ oxygen consumption after administration of 2,4-dinitrophenol. Further explanations as in Fig. 1.

Apparently the hypophysis is essential for the calorigenic action of sympathicomimetics, whereas other β-sympathicomimetic effects, as well as the calorigenic effects of substances acting otherwise, are not influenced by hypophysectomy.

Considering the age dependence of the calorigenic action of catecholamines, it may be suggested that among pituitary hormones the participation of growth hormone in metabolic responses to catecholamines is of especial importance. Further investigations will be undertaken concerning these problems.

Zusammenfassung. Durch Hypophysektomie wird die kalorigene Wirkung von Noradrenalin bei 23–28 sowie 63 Tage alten Ratten fast vollständig aufgehoben, während die Wirkung von 2,4-Dinitrophenol kaum beeinflusst wird.

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Effects of Testosterone-Stimulated Glycogen Synthesis in the Mouse Salivary Glands and 5-Fluorouracyl Inhibition

Since Laccasagne's[1] discovery of sex dimorphism in the mouse salivary gland, it appears to be well established that hormones have some effects on salivary gland morphology and metabolism[2,3]. Several investigators have found stimulatory effects of androgenic drugs on salivary glands of rats and mice[4]. On the other hand, the inhibitory effect of actinomycin, puromycin and 5-fluorouracyl on hormone stimulated growth of specific target tissues suggested the possibility of a more interesting study of testosterone-stimulated effect on organs other than the targe organs[5,6].

Material and methods. 3-week-old male A2G mice weighing 20 to 30 g were used. Mice were castrated bilaterally under ether anaesthesia. The influence of testosterone-stimulated glycogen synthesis and 5-fluorouracyl inhibition was investigated in 3 groups of castrated mice: 1. control mice; 2. testosterone-treated mice; 3. Testostenne-injected mice given 5-fluoreouracyl. Animals from each group were sacrified at 12, 24 and 48 h after administration of the last drug. Testosterone propionate (Lab. Gador, Buenos Aires) was injected in a single dosis of 10 or 5 mg each 100 g body weight. 5-Fluorouracyl (15 mg/100 g b.w.) was injected 30 min prior to the hormone. The salivary glands were excised immediately and cleaned. The tissues were weighed and immersed in 30% boiling KOH.

Glycogen was determined by the method of Roe and Daily[7]. The glycogen pellet was washed with 80% methyl alcohol with 0.1% LiCl and dissolved in water with an adequate internal standard.

Results and discussion. There are changes produced in the glycogen concentration in the submaxillary and parotid gland after a single injection of testosterone propionate. Testosterone increased salivary glycogen at 24 h to 200% as compared with the control mice. The effect of 5-FU administration on salivary glands under testosterone treatment is indicated by the data in the Table. In these experiments, both doses of testosterone caused an increase in glycogen in submaxillary and parotid gland. Similar inhibitory effect as on seminal vesicles was observed when 5-FU was given before to testosterone. After the classic investigations by Lacassagne[1] and his co-workers, other laboratories succeeded in establishing that endocrine glands are influential in the structural and biochemical configuration of the salivary glands of mice. Junqueira and Toledo[4] observed a significant increase in the protease activity in rat salivary glands by androgens. In addition,

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CHARREAU[8] found that a single injection of testosterone propionate caused growth promotion effect and stimulated RNA synthesis in salivary glands. Also, testosterone increased the growth of salivary glands and could be inhibited by antimetabolites[9]. Experiments performed by LEVI-MONTALCINI and ANGELETTI[10] show that the mouse salivary glands contain a nerve growth factor that increases in female mice upon testosterone administration. The results of the presnt work extend the above findings on the effect of androgens on the salivary glands of mice. The early effect on glycogen synthesis after testosterone on salivary glands is in agreement with the same effect on rat prostate and seminal vesicles reported by SINGHAL et al.[11]. This testosterone stimulatory effect on protein synthesis in salivary glands can be modified by antimetabolites[12].

Effect of testosterone on the glycogen metabolism and 5-FU inhibition

Treatment	Glycogen μg/100 mg gland[a] Parotid	Submaxillary
Control	15 ±1.7	24±2.8
Testosterone (5 mg/100 g b.w.)	21 ±2.2	27±2.1
Testosterone (10 mg/100 g b.w.)	48 ±1.6	37±1.4
Testosterone + 5-FU	18 ±2.1	26±1.0
Testosterone + 5-FU	14.9±1.1	23±1.7

Castrated mice were injected with testosterone, or testosterone plus 5-FU, and killed 24 h later. [a] Each result is the mean from 10 animals ± S.E.

In summary, a single dose of testosterone exerts a very specific effect on target tissues but also exerts effects in organs other than its prime target. The inhibitory action of 5-FU on testosterone-stimulated glycogen synthesis in salivary glands suggest the probability that glycogenesis depends on prior stimulation of RNA and protein synthesis.

Resumen. En el presente trabajo se estudia la accion de testosterona sobre el metabolismo del glucogeno. Se observa que despues de la inyeccion de la hormona aumenta el glucogeno y que y este es inhibido por 5-FU. Se sugiere que la sintesis de glucogeno necesite una estimulacion previa de nucleotidos de RNA y de proteinas.

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Effects of Estrogens and Progesterone upon the Biosynthesis of Melatonin by the Pineal Gland

There is considerable evidence that the pineal gland and the melatonin have an inhibitory influence upon ovarian function in mammals[1]. On the other hand the hydroxyindole-*O*-methyl transferase (HIOMT) activity in the pineal gland varies during the estrous cycle in rats, being higher in metestrus and diestrus and lower in proestrus and estrus[2]. As a single injection of 10 μg of estradiol benzoate lowered the HIOMT activity in the pineal gland measured the day after the injection, it was postulated that the lower rate of melatonin biosynthesis in estrus was due to an inhibitory estrogenic effect[2]. Surprisingly enough, the removal of the ovary did not alter the pineal gland HIOMT activity[2].

The experiments presented in this paper were performed with the object of comparing the effects of estrogens and progesterone upon the HIOMT activity in the pineal gland. Adult female rats from our animal colony were employed. Castrations were performed in all the animals the day before the respective experiment. The animals were daily injected with the drugs dissolved in 0.1 ml of the vehicle for 25 days, control rats received only the vehicle. All animals were kept in controlled lighting conditions (lights from 07.00 to 19.00 h) during the 25 days the experiment lasted. The HIOMT activity in the pineal gland was measured using the method of AXELROD, WURTMAN and SNYDER[3].

In the first experiment (Table I) the following groups of castrated rats were injected: 1. with the vehicle (ethyl oleate); 2. with estradiol benzoate (20 μg/day); 3. with progesterone (200 μg/day); 4. with estradiol benzoate (20 μg/day) and progesterone (200 μg/day).

It is shown that estrogen administration produced a significant decrease in pineal weight and a significant increase in pineal HIOMT activity. Progesterone administration did not affect the pineal weight but produced a significant decrease in pineal HIOMT activity.

In the second experiment (Table II) progesterone was injected to castrated female rats in dosis of 20 μg/day and 200 μg/day in olive oil for 25 days. It is confirmed that while progesterone administration did not change the pineal weight, it produced a significant decrease in pineal HIOMT activity.

The marked inhibitory effect upon the biosynthesis of melatonin, as obtained in these experiments with pharmacological dosis of progesterone, would not appear to be the cause of the changes in pineal gland HIOMT activity

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