It is not very probable that, under the conditions of the experiment, Mg acted on the contractile protein, or the energy yielding reactions involved in contraction. Most cells, including skeletal and cardiac muscle, normally contain a large store of Mg. Furthermore Mg activates rather than depresses glycerol-extracted ATP-treated smooth muscle and, to a lesser extent, also ATP-ase from smooth muscle[1].

The most likely explanation of the effect of Mg on the pressor response is that Mg ions prevent the entry of Ca from extracellular fluid into the muscle cells of the vessel wall, or in some other way interfere with excitation-contraction coupling. That such a competition between Mg and Ca might take place was suggested earlier by BOZLER[8], who experimented with isolated frog stomach.

Since anti-excitation-contraction-coupling is a cumbersome phrase, we suggest the use of the term 'disengagement' or 'disengaging action' to describe this effect. The expression 'uncoupling' already has another technical meaning[9].

Zusammenfassung. Erhöhung des Mg-Spiegels im Blut hemmt Tonus und Kontraktilität der Widerstandsgefässe im Muskel. Durch Noradrenalin hervorgerufene Verengerung wird gleich stark gehemmt wie die durch Reizung sympathischer Nerven verursachte Kontraktion. Ein Überschuss an Ca^{++} verhindert die blockierende Wirkung des Mg^{++} auf die Kontraktilität, der Tonusverlust der Gefässe wird durch Ca^{++} jedoch nicht rückgängig gemacht. Die antagonistischen Wirkungen von Mg^{++} und Ca^{++} beruhen wahrscheinlich auf deren gegensätzlicher Wirkung auf die elektromechanische Kopplung im Gefässmuskel.

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Evolution of Ovarian Grafts in Male Guinea-Pigs Castrated the First Day of Life

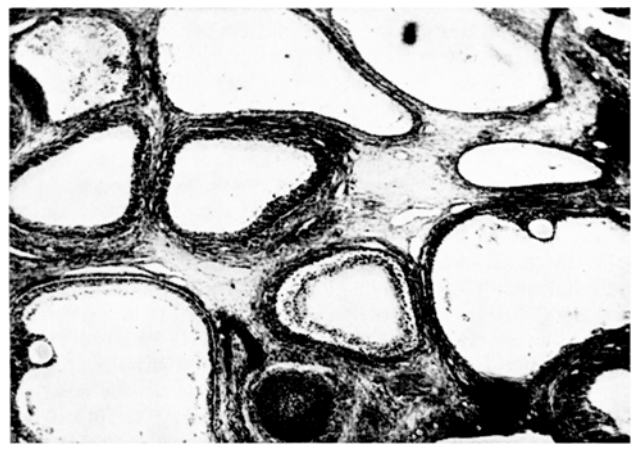
It has been shown by several authors that ovaries grafted into male rats castrated within the first 3 days of life, develop corpora lutea. In contrast to this, when the graft is made in males castrated after the fifth day of life or in adult age, only polycystic ovaries without luteinization are produced. On the other hand, it is well known that administration of testosterone in female rats before the fifth day of life induces in those animals polycystic ovaries, permanent oestrus and infertility. From these and other experiments it has been concluded that in the rat the sexual differentiation of the hypothalamic control of the gonadotrophin secretion is attained after birth and that circulating androgens secreted by the testis are responsible for that differentiation[1-3].

In the guinea-pig, conditions are diverse. We have shown in former papers[4,5] that testosterone injected in high doses in the new-born female guinea-pig, or even in the intrauterine period during the last 2 weeks of pregnancy, does not prevent normal puberty, normal oestrous cycles, both ovulation and corpora lutea, or normal pregnancy and delivery.

What we want to investigate now is whether, in the male guinea-pig, the pattern of gonadotrophic secretion is already established before birth or if, on the contrary, the presence of the testis is necessary in order to obtain that differentiation.

Material and methods. New-born male guinea-pigs were castrated, under ether anaesthesia, by a single escrotal incision within the first 24 h of life. At the age of 60 days, 9 of them were grafted with an ovary of a prepuber female guinea-pig (between 20 and 30 days of age), and 4 were grafted with adult ovaries taken on the eleventh day of the oestrous cycle. The grafts were made in the muscles of the anterior wall of the abdomen. Six control adult males were castrated, and 60 days afterwards an ovarian graft was performed in the same way as in the males castrated at birth.

The animals were kept in separate cages and fed with alfalfa and barley, and tap water was available ad libitum. After 50–60 days the animals were killed by bleeding under ether anaesthesia. The grafts were dissected, fixed in Bouin, embedded in paraffin, serially sectioned, and



Ovarian graft of immature guinea-pig into mature male castrated at birth. Well developed follicles; no corpora lutea were observed.

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stained with PAS-hematoxyline. In those animals in which the graft was not found, the area of the graft (traced by a piece of black thread purposely left there) was fixed and processed in the same way.

Results. The study of sections showed that in the animals castrated in adult life, 3 out of 6 grafts had taken satisfactorily. In the animals castrated at birth, 5 animals that received as host a prepuber ovary showed good grafts; meanwhile, only one in which an adult female was used as donor had taken. The histological pattern of all the ovaries grafted in males castrated at birth were alike; all of them showed a polycystic ovary and in none of them was a corpus luteum present (Figure). The same aspect was observed in males castrated in adult life. In one of the animals grafted with an ovary from an adult female, an old corpus luteum was present.

Discussion. The development of a polycystic ovary in the grafts made in guinea-pig males castrated at birth, seems to demonstrate that in this species the control of the gonadotrophin secretion is already patterned as the male type at birth. This fact is in accordance with our previous results, in which the administration of high doses of testosterone to the new-born female guinea-pig or to female foetuses does not change the 'phasic' type (or female type) of gonadotrophic secretion.

These various facts lead us to the conclusion that the sexual differentiation of the gonadotrophic secretion in the guinea-pig is already determined at birth, contrary to what occurs in rats. This difference might be related to the general somatic differentiation that is observed in both species at birth.

Résumé. Des cobayes mâles ont été châtrés le premier jour après leur naissance; à l'âge de 60 jours, on leur grèffa un ovaire provenant d'un cobaye prépubère et le laissa évoluer pendant 60 jours. Les ovaires greffés ont présenté, dans chaque cas, l'aspect d'un ovaire polycystique, avec des follicules bien développés et sans corps jaunes. Il en faut conclure que la différenciation de l'hypothalamus, chez le cobaye, s'accomplit avant la naissance.

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[7] With the technical assistance of D. ZIPITRIA.

Uncharted Secretory Nerves in the Parotid Gland of the Dog

Numerous observations suggest that some salivary glands may receive part of their secretory nerve supply by way of anatomically unknown channels (see BABKIN[1], EMMELIN[2]). In dogs the maximal rate of parotid salivary flow that can be induced reflexly is often greater than when the auriculotemporal nerve is stimulated electrically[3]. The most likely explanation of this finding seems to be that reflex stimulation activates additional uncharted secretory fibres as well as those in the auriculotemporal nerve. The existence of such fibres is demonstrated in the present physiological and histochemical investigation.

In 3 dogs anaesthetized with pentothal (about 30 mg/kg i.v.) the right auriculotemporal nerve was exposed according to the method of BURGEN[4] and cut. The dogs again received pentothal 7–9 days later and polythene tubes were introduced from the mouth into the parotid ducts. Saliva flowing from each gland displaced distilled water in a bottle, and the rate at which drops fell from an outlet of the bottle was recorded by an ordinate recorder on a smoked drum. Lemon juice was poured on to the tongue of the dog[3] at intervals, and as the anaesthesia became more superficial the rate of reflex salivary secretion increased from both parotid glands. Lemon juice was applied until the secretory rate had reached a maximum. The salivary flow from the right, 'denervated' parotid gland was quite marked; in 2 of the dogs it was somewhat slower than that of the normal, left gland, but in the third dog it was of the same order in both glands. When the secretory maxima to reflex stimulation had been estimated, chloralose-urethane (100 + 500 mg/kg) was given i.v. The left auriculotemporal nerve was then stimulated electrically at increasing stimulation frequencies, and the results confirmed the earlier finding[3], that the maximal reflex secretory rate was higher than when the nerve was excited electrically.

The sensitivity of the 2 glands to i.v. methacholine was estimated and some supersensitivity was found in each gland 'denervated' by section of the auriculotemporal nerve. Finally both parotid glands, from each animal, were removed, transected, fixed in formol-sucrose for 4 h at 0–4 °C, and then stored in sucrose-phosphate at 0–4 °C. Sections from 3 levels in each gland were cut on a cold microtome and stained for acetylcholinesterase (AChE) activity (as in GARRETT[5]). The normal parotid glands showed an extensive and complex arrangement of AChE positive nerves around the parenchymal structures (see Figure 1). The experimental parotid glands from the 'denervated' side each showed a patchy irregular decrease in AChE positive nerves but a fair number of nerves were still present in all parts of the glands (see Figure 2). The numbers of nerves remaining was very much greater than in the cat[6], after a similar time interval, but a more drastic avulsion of the auriculotemporal nerve had been performed closer to the gland in the cat experiments.

The auriculotemporal nerve is generally considered to contain the main secretory innervation of the parotid gland; it is thought that any sympathetic secretory fibres present do not contribute to the flow of saliva elicited reflexly in dogs. The present investigation showed that reflex secretion could still be evoked after section of the

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