growing 13-day-old left female ducts showed a lower average specific incorporation activity than the partially involuted 9-day-old male ducts. Although the sizes of the intracellular amino acid pools have not been determined in the various kinds of preparations due to the minute size of the organs, it seems safe to conclude that proteins were synthesized at a remarkably high rate even by regressing ducts. Thus, the negative protein balance of the regressing organs is not readily explicable on the basis of a general loss in the proportion of active polysomes, but seems mainly due to an increased rate of protein degradation. The experiments suggest that the breakdown of the cell contents primarily takes place in an organized manner, e.g. by 'focal degradation'[10-12], since vital cell functions seem to go on without much interference until fairly late in the degeneration process.

Zusammenfassung. Es wird gezeigt, dass die Müllerschen Gänge weiblicher Hühnchenembryonen die gleiche Fähigkeit zum Einbau von Aminosäuren besitzen, trotzdem der rechte Gang sich allmählich zurückbildet. Auch erwies sich die Differenz zwischen männlichen und weiblichen Embryonen im Hinblick auf den Aminosäureneinbau als nicht besonders auffällig.

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Pressor and Oxitocic-Like Effects of Angiotensin Affected by Aldosterone Pretreatment in Guinea-Pigs

It has been proved that there are many connections between the production and biological activity of angiotensin and the secretion of aldosterone. Laragh et al.[1], Carpenter et al.[2] and Kaplan et al.[3] observed that angiotensin is able to stimulate aldosterone secretion respectively in man, in intact animals and also in vitro. Later Davis et al.[4] reported that angiotensin is a true aldosterone-stimulating-hormone (ASH). Observations were also made on the reduced vascular reactivity towards angiotensin in adrenalectomized dogs[5] and cats[6] and on increased vascular reactivity towards the same peptide in dogs pretreated with aldosterone[7,8]. Moreover, reductions of the NaCl content of the suspension media of isolated guinea-pig ileum preparations caused conspicuous losses of the spasmogenic activity of angiotensin[9-11].

No report was found in the literature about the in vivo effects of angiotensin on extravascular smooth muscles in aldosterone pretreated animals.

Materials and methods. Guinea-pigs weighing 400–650 g were anaesthetized with ethyl urethane (1.0–1.5 g/kg i.p.). Uterine activity in situ was studied following Rothlin's procedure[12]. The 2 uterine horns were suspended to a strain-gauge microdynamometer (Ditta Ugo Basile, Via Campiglio 9, Milano, Italia) and their movements recorded by means of a d'Arsonval galvanometer writing on a smoked paper kymograph. Blood pressure was recorded from the common carotid artery using a mercury manometer.

The animals were set into 2 groups (7 non-pregnant guinea-pigs in each one) and treated as follows: control animals received daily saline (1 ml s.c.) for 5 days and were then prepared for the experiment; treated animals were administered daily for 5 days with aldosterone (Aldosten® CIBA) at the dose of 200 µg/kg/day in 1 ml of saline s.c. and then prepared for the experiment.

Synthetic angiotensin (α-L-Asp[1]-Val[5]Hypertensin II – Ipertensina® CIBA) was administered i.v. through a cannula in the external jugular vein. The injections of the peptide followed the same regimen both in control and in treated animals: 0.5, 1.0, 2.0, 10.0, 20.0 µg/kg i.v., according to preliminary experiments and to the data reported by Fregnan and Glasser[13].

Results. The averages of the results obtained in control and in aldosterone pretreated animals are given graphically in the diagram. Both in control and in treated animals, angiotensin showed a pressor activity at all the doses employed.

At the doses of 0.5, 1.0 and 10.0 µg/kg i.v. angiotensin has shown higher pressor activity in pretreated than in control animals. From the graph it can be seen that there is a clear difference in the 2 groups of guinea-pigs: in control animals the pressor effects are always increased by increasing the doses, while in pretreated animals the

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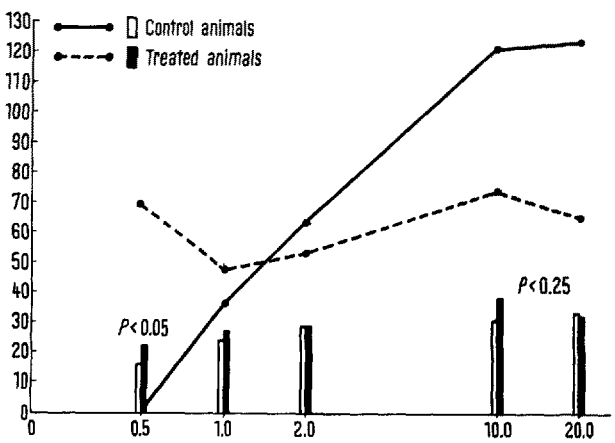
effect of 2.0 μg/kg i.v. is equal to that of the preceding dose, and that of 20.0 μg/kg i.v. is even lower than that of 10.0 μg/kg i.v.

On uterine contractility, it can be seen that in control animals there is a good dose-effect relationship by increasing the doses of angiotensin. In these animals the smallest active dose was 2.0 μg/kg i.v., the dose of 1.0 μg/kg i.v. being active only in 2 of the 7 guinea-pigs examined.

In pretreated animals, even at the dose of 0.5 μg/kg i.v., angiotensin always provokes a clear tonic contraction, by eliciting an effect higher than that elicited by 2.0 μg/kg i.v. in control animals. The second dose of the set (1.0 μg/kg i.v.) is still more active in pretreated than in control animals, but tachyphylaxis seems to be arising because the higher doses employed do not elicit potentiated effects; on the contrary the responses obtained in treated animals are always lower than those in control animals.

Discussion. The results obtained show that aldosterone pretreatment promotes a potentiation of the pressor activity of 0.5, 1.0 and 10.0 μg/kg i.v. of angiotensin, while the doses of 2.0 and 20.0 μg/kg i.v. of the same peptide are not potentiated, since tachyphylaxis takes place. Such a suggestion has been strengthened by the results obtained on uterine contractility. In fact our results show that the first 2 doses of angiotensin employed are clearly potentiated by aldosterone pretreatment (mainly the first one) in eliciting uterine contractions. With successively higher doses, the responses obtained in treated animals were always lower than those obtained in control animals. The potentiation of the lower doses of angiotensin by aldosterone is a confirmation of the results of previous experimental works both in vitro[9-11] and in vivo[7,8] and is due, in our opinion, to an alterate Na^+ distribution in the smooth muscle ensuing to aldosterone Na^+ retentive action. We suggest therefore that aldosterone is able to potentiate angiotensin activity on vascular as on extravascular smooth muscles, and can also induce tachyphylaxis to angiotensin. It was pointed out that a prolonged aldosterone administration decreases renal content of renin and renin secretion[14], and it was postulated that aldosterone is able to regulate the renin-angiotensin system by controlling renin secretion[15], thus acting as a curb to spontaneous pathological hypertensions. In our opinion the tachyphylaxis towards angiotensin induced by aldosterone administration might be another mechanism by which aldosterone itself could play an important role in regulating these functions.



Semilogarithmic graph. On the abscissa the doses of angiotensin in μg/kg i.v. The curves represent the effects (in arbitrary numerical values) of the various doses on uterine contractility. The columns represent the pressor effects (in mm Hg) elicited by the different doses employed. Statistical significance $P < 0.05$ and $P < 0.25$.

Résumé. Les auteurs examinent l'augmentation de l'action de l'angiotensine sur la pression carotidienne et sur la contraction utérine chez des animaux traités avec de l'aldostérone. Ils pensent aussi que le traitement conditionne le développement du phénomène taquiphylactique de l'angiotensine.

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Antihypertensive Effect of Co-Factors of the Synthesis and Precursors of Nucleic Acids in Experimental Hypertension

The present study is based on 2 premises: (1) The evidence obtained on the incretory antihypertensive function of the kidney[1,2] and on the role of sodium in the pathogenesis of hypertension[3-5] suggests that the excessive use of sodium chloride produces in humans a prolonged hyperfunction of incretory antihypertensive structures of the kidneys. In consequence of a gradual wearing-out of these structures, the antihypertensive renal function is reduced and hypertension develops.

(2) A prolonged continuous hyperfunction of most differentiated cells is followed first by activation of nucleic acids and protein synthesis in these cells. Then occurs normalization of the synthesis and much later there develops an inhibition of the synthesis which becomes the basis of the wear of structures and of the functional disturbance in the cells and organs[6-9].

All these facts have suggested that the disturbance of nucleic acids and protein synthesis may be of great importance in the wearing-out of the antihypertensive incretory renal structures and in the development of hypertension produced by an excessive use of sodium chloride. On the basis of this suggestion, an attempt has been made in the present work to prevent the wear of the antihypertensive structures with the aid of co-factors of the synthesis and the precursors of the nucleic acids and thus to act on the development of the salty hypertension in animals.