

43. PARTICIPATION OF PROSTAGLANDINS (PGs) IN THE RESPONSE OF THE ADRENAL GLAND TO CORTICOTROPIC PEPTIDES. Perroteau, I., Leboulenger, F., \* Escher, E. and Vaillant, R. - Lab. Mol. Endocrinol., CNRS ERA 891, Fac. Sci. Rouen, 76130 Mt-St-Aignan, France and \* Dept. Pharmacol., Fac. Med., Univ. Sherbrooke, Quebec.

ACTH, angiotensin II (AII) and vasoactive-intestinal peptide (VIP) stimulate the production of corticosteroids by the interrenal gland of the frog. Since exogenous PGs of the E series are potent activators of frog steroidogenesis (B.B.R.C. 100, 769), we have studied the possible role of endogenous PGs in the response of the interrenal gland to ACTH, AII and VIP, using a well defined perfusion system technique. The inhibitor of PG synthesis indomethacin ( $5 \times 10^{-6}M$ ) blocked the spontaneous release of both corticosterone (-70%) and aldosterone (-76%). In addition, IDM drastically reduced the stimulatory effect of the AII analogue [Sar<sup>1</sup>-Val<sup>5</sup>]AII. Conversely, IDM did not inhibit the stimulation of corticosteroidogenesis induced by ACTH or VIP. A sub-maximal dose of [Sar<sup>1</sup>-Val<sup>5</sup>] AII could not be enhanced by PGE<sub>1</sub> whereas ACTH and PGE<sub>1</sub> gave rise to additive effects on corticosterone and aldosterone productions. These data demonstrate that, in frog, the AII-induced stimulation of corticosteroid biosynthesis is mediated by endogenous PGs, whereas PGs are not involved in the mechanism of action of ACTH and VIP.

Supported by PIRMED-CNRS n° 100482 and 100474.

44. ROLE OF VASOACTIVE INTESTINAL PEPTIDE IN CORTICOSTEROIDOGENESIS. Leboulenger, F., Leroux, P., Delarue, C., \*Coy, D.H., Tonon, M.C. and Vaudry H. Lab. Mol. Endocrinol., ERA CNRS 891, Fac. Sci. Rouen, 76130 Mt-St-Aignan, France and \* Dept. Med., Tulane University, New-Orleans, LA 70112, USA.

Using the immunofluorescence technique, we have demonstrated the co-existence of Met- and Leu-enkephalins and vasoactive intestinal peptide (VIP) in the chromaffin cells of the frog adrenal gland. Since, in the frog, the chromaffin cells are in close contact with the adrenocortical tissue, a possible action of those neuropeptides upon corticosteroidogenesis has been investigated in a perfusion system for frog interrenal fragments. Morphine and enkephalins ( $10^{-5}M$ ) had no effect on the spontaneous production of corticosteroids and did not alter the production of corticosteroids induced by ACTH. Conversely, synthetic VIP (from  $10^{-6}M$  to  $10^{-9}M$ ) elicited a dose-related increase in corticosterone and aldosterone productions. Although VIP appeared to be  $10^4$ -fold less active than ACTH on corticosteroidogenesis, these results suggest that VIP contained in the chromaffin cells of the frog adrenal gland may participate to the maintenance of a tonic production of corticosteroids.

Supported by Grant from INSERM n° 81-6031.

45. EFFECT OF 7 MINERALOCORTICOID ANTAGONISTS ON CORTICOSTEROIDOGENESIS. Netchitaïlo, P., Delarue, C., \*Capron, M.H. and Vaillant R. - Lab. Mol. Endocrinol., CNRS ERA 891, Fac. Sci. Rouen, 76130 Mt-St-Aignan, France and \*Searle Lab. 92128 Montrouge, France.

We have previously demonstrated that mineralocorticoid antagonists are powerful inhibitors of corticosteroidogenesis. Recently, several mineralocorticoid antagonists, which are more potent than spironolactone in competing for mineralocorticoid receptors, have been discovered. In this study, we have compared the steroidogenic activity of 7 of these compounds. Two of them (SC 27169 and 26304) had no effect on adrenal steroidogenesis, even at the concentration 1 mM. SC 9420, 14266, 23133 and 23992 induced a marked but reversible inhibition of aldosterone biosynthesis. SC 19886 totally inhibited aldosterone production and the activity of this compound lasted for more than 7 hours. Further experiments showed that SC 27169 was unable to block the stimulation of aldosterone biosynthesis induced by corticotropic peptides, whereas SC 14266, 19886, 23133, 23992 totally suppressed the stimulatory effect of ACTH and angiotensin II. Owing to the stimulation of the renin-angiotensin system induced by aldosterone antagonists, our results suggest that 5 of the 7 compounds tested would exert a higher natriuretic activity.

Supported by PIRMED-CNRS n° 100482 and 100474.