

## The effect of glucocorticoids on turn-over of acetylcholine and prostaglandins in the isolated guinea-pig ileum

R.M. CHICHMANIAN, I. KINSUN,  
M.A. MOULIN & E.C. SAVINI

*Département de Pharmacologie, Chemin de Vallombrose, 06034 Nice, France*

According to Ferreira, Herman & Vane (1976), pieces of rabbit jejunum kept in Krebs solution are able to release prostaglandins  $E_2$  and  $F_{2\alpha}$  during their spontaneous contractions. These secretions were changed neither by contracting substances acetylcholine and physostigmine, nor by relaxing substances (adrenaline, hyoscine or papaverine). On the other hand, Botting & Salzmänn (1974) showed that guinea-pig isolated gut also releases prostaglandins, and this secretion is inhibited by indomethacin. Finally, Bennett, Eley & Stockley (1975) brought strong evidence for the contracting effects of prostaglandins  $E_1$ ,  $E_2$ ,  $F_{1\alpha}$  and  $F_{2\alpha}$  on the longitudinal muscle of the guinea-pig ileum.

The aim of this preliminary investigation is to bring evidence for the inhibition of prostaglandins release in the organ bath fluid after administration of anti-inflammatory steroids: cortisol, prednisolone, methylprednisolone, dexamethasone, triamcinolone, betamethasone and fluorocortisol given at doses in a range of 0.1 to 1000  $\mu\text{g/ml}$ . The steroids used as soluble esters (hemisuccinate,  $\text{Na}^+$  phosphate) were introduced into the bath filled up with Krebs solution and bubbled with  $\text{CO}_2 + \text{O}_2$ . In rare cases we noticed occasional small contractions at low concentrations with cortisol, prednisolone, methylprednisolone and dexamethasone, but in most of the cases even higher subsequent doses produced no contraction. Sensitivity to acetylcholine, histamine, prostaglandins  $E_2$  and  $F_{2\alpha}$  was not changed.

During coaxial stimulation (Paton, 1955) the height of the twitches was not reduced by prednisolone and fluorocortisol while indomethacin still decreased the height of the twitch.

In another batch of guinea-pigs reserpine (5 mg/kg) was injected one day before the experiment; the corresponding ileum did not contract even after large doses of glucocorticoids but during the action of hemicholinium ( $\text{HC3}$ , 120  $\mu\text{g/ml}$  during 90 min), prednisolone and fluorocortisol were able to stimulate the ileum again probably because the synergism established between  $\text{HC3}$  and corticosteroids as far as acetylcholine release is concerned.

$\text{PGE}_2$  and  $\text{PGF}_{2\alpha}$  were measured by radioimmunoassay in a sample of liquid extracted from the organ bath. After gut contraction due to acetylcholine, an increase of  $\text{PGE}_2$  release proportional to acetylcholine concentration is observed. Acetylcholine does not influence  $\text{PGF}_{2\alpha}$  release. After coaxial stimulation of guinea-pig ileum, increase of  $\text{PGE}_2$  release after 10 volleys of DC shocks (every minute) under similar conditions, fluorocortisol (1 mg/ml in the bath) reduces  $\text{PGE}_2$  release.

### References

- BENNETT, A., ELEY, K.G., STOCKLEY, H.L. (1975). The effects of prostaglandins on guinea-pig isolated intestine and their possible contribution to muscle activity and tone. *Br. J. Pharmac.*, **54**, 197-204.
- BOTTING, J.H. & SALZMANN, R. (1974). The effect of indomethacin on the release of prostaglandin  $E_2$  and acetylcholine from guinea-pig isolated ileum at rest and during field stimulation. *Br. J. Pharmac.*, **50**, 119-124.
- FERREIRA, S.H., HERMAN, A.G. & VANE, J.R. (1976). Prostaglandin production by rabbit isolated jejunum and its relationship to the inherent tone of the preparation. *Br. J. Pharm.*, **56**, 469-477.
- PATON, W.D.M. (1955). The response of the guinea-pig ileum to electrical stimulation by coaxial electrodes. *J. Physiol. (Lond.)*, **127**, 40-41P.