HERTELENDY, F., WOODS, R. & JAFFE, B.M. (1973). Prostaglandin E levels in peripheral blood during labour. *Prostaglandins*, 3, 223-227.

HORTON, E.W. & JONES, R.L. (1969). Prostaglandins A_1, A_2 and 19-hydroxy A_1; their actions on smooth muscle and their inactivation on passage through the pulmonary and hepatic portal vascular beds. *Br. J. Pharmac.*, 37, 705-722.

KARIM, S.M.M. (1968). Appearance of prostaglandin $F_{2\alpha}$ in human blood during labour. *Br. Med. J.*, 4, 618-621.

Inhibition by prostaglandins of fluid transport in the isolated gallbladder of the guinea-pig

I.K.M. MORTON, S.M. SAVERYMUTTU & J.R. WOOD*

Department of Pharmacology, King's College, London WC2

The factors responsible for the regulation of the concentration of the bile in the gallbladder are poorly understood. In view of the modification by prostaglandins of the fluid transport at other sites (Hinman, 1972) we have studied the effect of these agents on gallbladder water transport.

Gallbladders from male guinea pigs (400-650 g) were cannulated, filled with Krebs solution and weighed at 5 min intervals. Between weighings the bladder was suspended in an organ bath of Krebs solution maintained at 37°C and bubbled with a mixture of 95% O_2 : 5% CO_2.

As has been shown by Diamond (1962) the weight loss by this preparation can be taken as a measure of fluid transport. In control experiments the weight loss per unit time was essentially linear over the 3 h period studied. The effects of three prostaglandins PGE_1, PGE_2, and $PGF_{2\alpha}$ were examined. Bath concentrations of PGE_1 in the range 10^{-8} to 10^{-5} M produced a biphasic change in the rate of fluid loss. There was an initial enhancement of fluid loss (phase 1) followed by a dose-dependent inhibition (phase 2) as compared to the initial pre-treatment rate. Qualitatively similar results were obtained with PGE_2 (10^{-8} to 10^{-5} M) and $PGF_{2\alpha}$ (10^{-6} to 10^{-5} M).

Although the phase 1 response may be due to a direct effect on the water transport mechanism, the potent spasmogenic activity of the prostaglandins suggests alternative mechanisms. To investigate this, the actions of the prostaglandins and other agents on the wall musculature were examined by measuring the changes in pressure induced within the gallbladder. The prostaglandins produced a marked increase in pressure within the concentration ranges mentioned above, as did caerulein (10^{-7} M) and angiotensin II (2×10^{-8} M) both of which also showed a phase of enhanced fluid loss in the gravimetric studies. On the other hand oxytocin (10^{-7} M) and vasopressin (10^{-7} M), which differed in that they relaxed the gallbladder, showed no such phase of enhanced loss.

The three prostaglandins studied all showed the phase 2 inhibitory effect. Concentrations producing 70-80% inhibition of fluid transport were of the following order; E_1 10^{-7} M, E_2 10^{-8} M, $F_{2\alpha}$ 10^{-5} M. At higher concentrations a total inhibition of fluid transport was observed.

The above studies raise the possibility that prostaglandins present in gallbladder mucosa or wall could influence the rate at which fluid is transported across the epithelium. However, further speculation must await determination of prostaglandin levels in this tissue in various functional states.

We are grateful to Dr J.E. Pike, of Upjohn, Kalamazoo, for the prostaglandins used, and to Dr M. Ghione of Farmitalia, Milan, for the caerulein.

References

DIAMOND, J.M. (1962). The reabsorptive function of the gallbladder. *J. Physiol., Lond.*, **161**, 442-473.

HINMAN, J.W. (1972). Prostaglandins. *A. Rev. Biochem.*, **41**, 161-178.