lever (magnification x4, load on the tissue 1.5 g).

2-2'pyridylisatogen (Patterson & Wibberley, 1965) exerted two actions on the taenia caeci. Concentrations above 2.5 μM gradually relaxed the smooth muscle over a 30 min contact period; this effect was accompanied by an increase in the frequency of the spontaneous contractions (78 experiments). The second effect, seen after the tone of the smooth muscle had been restored with either histamine or acetylcholine, was a reduction in the submaximal responses to ATP (2-600 μM) after 15-30 min contact of the tissue with 2-2'pyridylisatogen (20-50 μM, 28 experiments). The blockade was specific for ATP (Figure 1). Under these conditions, cumulative concentration-response curves to ATP were displaced to the right in parallel (six experiments).

High concentrations of 2-2'pyridylisatogen ($>$100 μM for 30 min or longer) caused a general antagonism of ATP, isoprenaline and noradrenaline. These non-specific effects were not reversed by washing the tissue with 3 l McEwen's solution over 3 h (four experiments).

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Increased inactivation of prostaglandin E_2 by the rabbit lung during pregnancy

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It is well established that the lungs are extremely efficient at removing prostaglandins E and F from the circulation (Ferreira & Vane, 1967; Horton & Jones, 1969). However, during parturition these prostaglandins appear in the venous blood, and their levels fluctuate in parallel with the uterine contractions (Karim, 1968; Hertelendy, Woods & Jaffe, 1973). This raises the possibility that these prostaglandins survive passage through the lungs during late pregnancy and might therefore act as circulating hormones during parturition. Accordingly, we have estimated the lung inactivation of prostaglandin E_2 in pregnant and non-pregnant rabbits. Our results suggest that this is actually enhanced during pregnancy and immediately postpartum.

Mature Dutch female rabbits were anaesthetized with pentobarbitone sodium given intravenously. Blood pressure was recorded from a femoral artery. Intra-arterial injections of PGE_2 were given through a catheter which had been inserted into the right carotid artery and advanced into the ascending aorta. Intravenous injections were given through a catheter advanced via the femoral vein into the vena cava.

Two doses which gave clearly defined but submaximal depressor responses were selected for both the intravenous and the intra-arterial routes, the ratio between these doses being the same. These four doses were given repeatedly following a Latin square design and a dose cycle of 10 minutes. The dose required to give a 20 mmHg (1 mmHg = 1.333 mbar) fall in diastolic blood pressure was measured graphically for each route. The ratio between these doses (i.v. dose/i.a. dose) was calculated and this was taken as a measure of the apparent degree of inactivation of the prostaglandin by the lung.

In non-pregnant rabbits the ratio was 14.4 $\pm$ 2.9 (mean $\pm$ s.e., $n = 7$) whereas in pregant rabbits (days 22-28) it was 68.8 $\pm$ 3.4 ($n = 5$). These ratios are significantly different ($P < 0.001$) suggesting that the lung inactivation was greater in the pregnant rabbits than in the non-pregnant controls. During the immediate post-partum period (days 1-4) the ratio was also significantly higher than in the non-pregnant animals (39.7 $\pm$ 8.6, $n = 7$, $P < 0.02$). Thus it is unlikely that lung inactivation declines to the non-pregnant state at the time of parturition. These results also show that the increased dose ratio seeen during pregnancy is unlikely to be related to any haemodynamic changes occurring as a direct result of the presence of foetuses in utero.

We have been unable to obtain as large an effect as that found in pregnancy by treating non-pregnant rabbits for 12 days with progesterone (10 mg/kg)/day, oestradiol monobenzoate (10 μg/kg)/day or a mixture of progesterone (5 mg/kg)/day and oestradiol monobenzoate (5 μg/kg/day. However, the results of these experiments indicated that there is a connection between elevated progesterone levels and enhanced lung inactivation of PGE_2.

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

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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.

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