& Mongar, 1972). We have studied the characteristics of the dextran-phosphatidyl serine interaction at 37° C using peritoneal cells from female Canterbury Ash Wistar rats. In our experiments, dextran (mol. wt.=110,000) 6 mg/ml in Tyrode solution (1·8 mM $CaCl_2$) released only 2–3% of total histamine (above the spontaneous release of about 2%). Phosphatidyl serine (0·3–100 μg/ml), which has little releasing activity of its own, when added with 6 mg/ml dextran produces a dose-dependent release of histamine. Maximum release was about 30% of total. In the presence of 10 μg/ml phosphatidyl serine, dextran in the range 0·2–15 mg/ml produced a dose dependent release.

Disodium cromoglycate (DSCG) inhibits the response to dextran in rat skin (Assem & Richter, 1971) and reduces histamine release after injection of dextran into the peritoneal cavity *in vivo* (Hanahoe, Holliman, Gordon & Wieczorek, 1972). We have found that the release of histamine from rat peritoneal cells *in vitro* by a mixture containing 6 mg/ml dextran and 10 μg/ml phosphatidyl serine is inhibited by DSCG, 50% inhibition occurring at a concentration of 10^{-5}M DSCG. At lower concentrations (10^{-7}M) DSCG sometimes increased release (3 out of 4 experiments). DSCG depressed the slope and maximum of the dextran dose-response curve. However, when dextran was kept constant at 6 mg/ml the inhibition by 2×10^{-6}M and 10^{-5}M, but not by 3×10^{-4}M, DSCG was overcome by increasing the concentration of phosphatidyl serine from 10 to 30 or 300 μg/ml. The results suggest a non-competitive inhibition with spare receptors for phosphatidyl serine. The release by the mixture of 6 mg/ml dextran and 10 μg/ml phosphatidyl serine increased as the calcium concentration was raised to 3 mM but was depressed below the optimum by concentrations of 10 and 30 mM $CaCl_2$. Inhibition of release by DSCG was not overcome by increasing the calcium concentration. In fact, inhibition was greater in the presence of higher calcium concentrations.

The inhibition dose-response curve in the dextran system was almost co-linear with that for the inhibition of antigen-induced histamine release *in vitro* from peritoneal cells of rats actively sensitized to ovalbumin using *B. pertussis* as adjuvant (Mota, 1964). This suggests that histamine release by dextran plus phosphatidyl serine may share a common pathway with reaginic hypersensitivity reactions in the rat and may be useful for identifying anti-allergic drugs like DSCG. However, the result sheds no light on whether the dextran reaction is antibody mediated as was suggested by Goth (1967).

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Prostaglandin synthesis by the pregnant rat uterus at term and its possible relevance in parturition

K. I. WILLIAMS†

Department of Pharmacology, The Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2A 3PN

Indomethacin, an inhibitor of prostaglandin (PG) synthesis (Vane, 1971) abolishes spontaneous contractions and PG release by isolated pregnant uteri of the rat (Vane & Williams, 1972). The present communication extends these findings and demonstrates

† Present Address: Department of Pharmacology, The Medical School, Bristol BS8 1TD.

important changes in uterine PG production at term and that such synthesis is involved in parturition (Aiken, 1972).

The preparation of pregnant uteri, extraction and bioassay of PG's were carried out as described previously (Vane & Williams, 1972). Spontaneous contractions in uteri 17–20 days pregnant were abolished by indomethacin (2·8–5·6 μM) but higher doses of indomethacin (5·6–11·2 μM) were required to suppress spontaneous contractions of uteri from rats 21–22 days pregnant. After indomethacin, activity similar in frequency and form to that seen in untreated preparations could be restored by addition of PGE_2 or $PGE_{2\alpha}$ (4–16 ng/ml) to the bathing fluid.

Release of PG-like activity into the bathing fluid was also measured. Uteri taken at 19–21 days of pregnancy released 66–156 (ng/g)/h of F type PG, those taken on day 22 released 250–680 (ng/g)/h. Thus, there was an increase at term in the capacity of the tissue to synthesize PG's.

PG synthesis by uterine homogenates from pregnant rats was also studied. After removal of the foetuses, uteri were washed in ice-cold Krebs solution, dried and weighed. Endometrial and myometrial fractions were prepared by scraping the uterus and their separation ascertained histologically. The fractions were homogenized in ice-cold phosphate buffer (ph 7·4) and centrifuged (2,500 g min). Aliquots (0·5–1 ml) of the supernatant were added to 1–1·15 ml of incubation mixture (sodium arachidonate 15 μM; reduced glutathione 325 μM and hydroquinone 91 μM in phosphate buffer). Samples were incubated aerobically with or without indomethacin (5·6-44·8 μM) for 60 min at 37° C. The reaction was stopped by heating in boiling water for one minute. After extraction, the PG content was estimated in terms of $PGF_{2\alpha}$ by parallel bioassay. Net PG production by the endometrial fraction on days 19–21 was $1,790 \pm 349$ ng/g wet weight of tissue (mean, S.E. of mean, $n=9$); synthesis increased sharply to $24,220 \pm 5,743$ ng/g ($n=9$) on day 22. Net PG synthesis by the myometrial fraction was much lower (414 ± 129 ng/g; $n=3$; on days 19–21) indicating that the endometrium is the major source of uterine PG's.

The establishment of a relationship between PG synthesis and uterine contractions *in vitro* and the dramatic increase in endometrial PG synthesis at term suggests that local prostaglandin production has an important role in parturition.

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Further experiments to establish that the analgesic action of aspirin-like drugs depends on the inhibition of prostaglandin biosynthesis

S. H. FERREIRA, S. MONCADA* and J. R. VANE

Department of Pharmacology, Institute of Basic Medical Sciences, Royal College of Surgeons of England, London WC2A 3PN

Acidic anti-inflammatory drugs inhibit prostaglandin biosynthesis (Vane, 1971; Ferreira, Moncada & Vane, 1971; Smith & Willis, 1971). Ferreira (1972) suggested that prostaglandins only have a facilitatory role in inflammatory pain, for low concentrations cause a long-lasting sensitization to mechanical or chemical stimulation. Only in much higher concentrations than appear in inflammation do they induce overt pain.