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FAILURE OF INDOMETHACIN AND D-2-BROMOLYSERGIC ACID DIETHYLAMIDE TO MODIFY THE ACUTE OEDEMATOUS REACTION TO OESTRADIOL IN THE UTERUS OF THE IMMATURE RAT

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Treatment with oestradiol induces vasodilatation and increased vascular permeability in the uterus of the intact immature or gonadectomized adult rat. These vascular changes result in an increase in the wet weight of the uterus 4–6 h after treatment. Oestradiol itself is not vasoactive and histamine, 5-hydroxytryptamine (5-HT) and prostaglandins have been proposed as mediators of the vascular effects of oestrogens (see Spaziani, 1975). Oestradiol is known to release histamine and 5-HT from uterine mast cells (McKercher, Van Orden, Bhatnagar & Burke, 1973) and to raise the uterine prostaglandin content (Aizawa, Kogo, Yamada & Sakai, 1974) within 6 h of administration to the ovariectomized rat. Some of the vascular actions of oestrogen in the rat uterus have been reported to be inhibited by intrauterine administration of lysergic acid diethylamide, an antagonist of 5-HT (Szego & Sloan, 1961), by parenteral administration of indomethacin, an inhibitor of prostaglandin synthesis (Ryan, Clark, Van Orden, Farley, Edvinsson, Sjoberg, Van Orden & Brody, 1974) and by parenteral administration of a combination of mepyramine, a histamine H_1-, and burimamide, a histamine H_2-receptor antagonist (Brandon, 1977). Indomethacin (Kennedy, 1977) and the combination of histamine antagonists (Brandon & Wallis, 1977) have been shown to inhibit the oedematous reaction at sites of blastocyst attachment in the rat. The involvement of prostaglandins and 5-HT in the mediation of the oedematous reaction to oestradiol in the immature rat uterus was investigated in the present study.

Immature female rats (23–25 days old) from the Institute's Wistar-derived colony were randomly assigned to seven groups of six animals, each experiment comprising 42 rats. One group was not treated as previous work has established that the drug vehicles used in these experiments do not modify uterine weight. Animals in experimental groups were given saline (0·9% NaCl), indomethacin (Merck, Sharp & Dohme; 10 mg/kg) or D-2-bromolysergic acid diethylamide (Sandoz; 10 mg/kg) s.c., 1 h, 30 min or immediately before s.c. injection of oestradiol (B.D.H.; 0·75, 2·25 or 6·75 μg/kg). Indomethacin was dissolved in a dilute solution of sodium carbonate and the injection volume made up with saline, D-2-bromolysergic acid diethylamide was dissolved in saline and oestradiol was given as a solution in arachis oil. The injection volume was 4 ml/kg. The rats were killed by cervical dislocation 4 h after injection of oestradiol and the uterus was exposed and dissected free from mesentery. The oviducts were transected near the uterotubal junction and a ligature was tied across the uterus near the cervix. The uterus was removed by cutting between the ligature and the cervix and was brushed against absorbent paper to remove surface moisture and weighed. Analysis of covariance was used to correct the group mean uterine weights for variation in body weight before they were compared by the orthogonal contrasts test. The results are presented as the original data.

The increase in the wet weight of the uterus occurring 4 h after treatment with oestradiol was not significantly modified ($P > 0.05$) by indomethacin (10 mg/kg) given 1 h (one experiment, Fig. 1) or 30 min (two experiments) before or by D-2-bromolysergic acid diethylamide (10 mg/kg) given 30 min (one experiment, Fig. 1) or immediately (one experiment) before

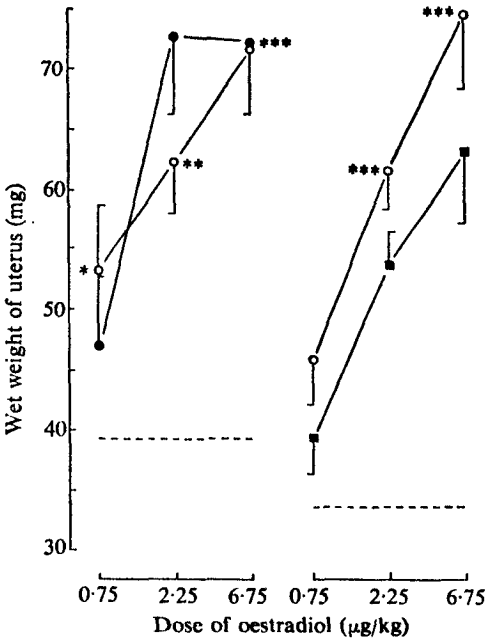

Fig. 1. Effect of indomethacin (10 mg/kg, given 1 h before oestradiol; ●) and D-2-bromolysergic acid diethylamide (10 mg/kg, given 30 min before oestradiol; ■) on the increase in uterine wet weight occurring 4 h after administration of oestradiol alone (○) to immature rats. The results are means ± S.E.M. derived from six animals; the broken lines represent the mean wet weight of the uterus in untreated rats. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$: significantly different compared with untreated control rats (orthogonal contrasts test). Note logarithmic scale of the abscissa.

the injection of oestradiol. The results indicate that neither prostaglandins (derived from de novo synthesis) nor 5-HT are involved in the mediation of the oedematous reaction to oestradiol in the immature rat uterus.

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