required and blood pressure and heart rate could be monitored before, during and after ingestion of the drug for up to 4 h.

We have found this technique for insertion of arterial cannulae to be quick and reliable. Animals appear to experience little trauma from the operation, and are ready to be used the following day. The time and materials required to fashion the cannula are considerably less than that described by Popovic & Popovic (1960). The constriction formed at the end of the cannula permits easy insertion into the artery, while the main body of the cannula remains of a fairly large diameter facilitating connection procedures and the recording of heart rate. The main advantage of this method is that the cardiovascular effects of drugs can be evaluated in conscious rats in a familiar and non-restrictive environment.

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An analysis of the inhibitory effects and of possible prostaglandin antagonism of steroid sex hormones in the guinea-pig ileum

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Progesterone, pregnenolone, testosterone, ethinyloestradiol, oestrone, oestriol reversibly inhibit guinea-pig isolated ileum contractions to acetylcholine, histamine (Seaman, Famaey & others, 1977a), nicotine and 5-hydroxytryptamine (5-HT) (Seaman, Fontaine & others, 1977b) and these inhibitions could be reversed by prostaglandins (PG) E_1 or $F_{2\alpha}$. It was concluded that these steroids exert an overall spasmolytic effect on ileal smooth muscle. This was also the conclusion of Ishida, Oshima & others (1972) who noted a papaverine-like action of some sex hormones on the ileum.

Pregnenolone, testosterone, ethinyloestradiol and oestriol also caused a more specific inhibition of contractions induced by nicotine, an indirect agonist, or 5-HT a partly indirect agonist (Seaman & others, 1977b). Similar actions were observed by us with non-steroidal anti-inflammatory drugs (NSAID) (Famaey, Fontaine & Reuse, 1977a; Famaey, Fontaine & others, 1977c) and anti-inflammatory steroids (AIS) (Famaey, Fontaine & Reuse, 1975b; Famaey, Fontaine, Seaman & Reuse, unpublished) and were attributed partly to the effects of these drugs on biological membranes and partly to their effects on PG production.

PG are themselves partly direct (Bennett & Fleshler, 1970) and partly indirect agonists (Bennett, Eley & Scholes, 1968; Bennett, Eley & Stockley, 1975) on the ileum and we found high concentrations of NSAID and AIS to have a preferential antagonism towards PGE_1 and $F_{2\alpha}$-induced contractions compared with acetylcholine contractions (Famaey, Fontaine & Reuse, 1977b).

We have now investigated whether similar antagonism occurs with steroid sex hormones.

Submaximal contractions (as determined by dose-action curves) of the longitudinal muscle of the guinea-pig isolated ileum were elicited by PGE_1 (5 ng ml^{-1}) or $PGF_{2\alpha}$ (20 ng ml^{-1}) (45 s contact time, every 6 min) on ileal segments (4 cm length, removed at least 10 cm from the caecum) set up in Krebs–Henseleit solution at 37° and gassed with a mixture of 5% CO_2 in oxygen.

The hormones were added to the bath after three reproducible control contractions to PG and the ileum was again challenged with the PGs at the same intervals. After 12 min contact the hormones were washed out and two more PG doses were added.

At concentrations of the hormones similar to those used previously by Seaman & others (1977a, b) for inhibiting contractions to acetylcholine, histamine, nicotine and 5-HT we obtained after 12 min contact significant (Student's *t*-test for paired data) inhibitions of contractions to PGE_1 and $F_{2\alpha}$ which appeared to be almost totally reversible after washing out (Table 1). Except for testosterone which inhibited contractions to $PGF_{2\alpha}$ significantly (Student's *t*-test) more than to PGE_1, there was no difference between the inhibitory effects of the hormones on the two PGs.

Pregnenolone exerted a more pronounced effect on $PGF_{2\alpha}$-induced contractions than it did to acetyl-

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Table 1. *Inhibitory effects of steroid sex hormones, after 12 min contact, on the responses of the longitudinal muscle of the guinea-pig isolated ileum to PGE_1 and $F_{2\alpha}$.* The results are expressed (mean ± s.e.m.) as % of control contractions measured before adding the hormones and have been analysed statistically (Student's *t*-test for paired data; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

Hormones	Conc μg ml^{-1}	PGE_1 (n = 6)	12 min after wash out	$PGF_{2\alpha}$ (n = 6)	12 min after wash out
Progesterone	0·5	65±4**	96±3	73±3*	103±3
	1	55±11*	108±7	47±10**	83±2*
Pregnenolone	1	37±9***	93±7	30±6***	87±12
Testosterone	1	64±9*	104±5	20±7***	79±9*
Ethyinyl-oestradiol	1	20±5***	111±3	35±6***	112±5
Oestriol	5	54±5**	110±1	36±7***	122±9
	20	16±6***	112±6	11±2***	101±8
Oestrone	1	53±9**	106±11	63±5***	110±17

choline ($P < 0.05$) or histamine ($P < 0.05$) contractions. For ethinyloestradiol the effect was more pronounced on PGE_1 than with histamine ($P < 0.05$) and for oestriol on both PGs compared with acetylcholine ($P < 0.001$) and histamine ($P < 0.001$) (all Student's *t*-test) (Seaman & others, 1977a).

At the same concentrations, pregnenolone, ethinyl-oestradiol and oestriol were more active inhibitors of contractions to nicotine or 5-HT (Seaman & others, 1977b) than to acetylcholine and histamine. However testosterone, which was also more active against nicotine and 5-HT than against acetylcholine and histamine, had the same activity against contractions to $PGF_{2\alpha}$, acetylcholine and histamine and was less active against PGE_1 ($P < 0.001$ compared with acetylcholine and histamine).

These effects on PG-induced contraction confirms the spasmolytic effect of the hormones and except for testosterone, it appears that the same steroids that are more active on contractions to nicotine and 5-HT than to acetylcholine or histamine are also more effective in inhibiting contractions induced by PGE_1 or $F_{2\alpha}$.

This could be due to their inhibition of the effect of PGs (as well as of nicotine or 5-HT) on acetylcholine release, a property that could be related (i) to an effect on biological membranes similar to those observed with NSAID or AIS (Famaey, Brooks & Dick, 1975a; Famaey & others, 1977a) (ii) or even an effect similar to that described for AIS (Gryglewski, 1976) and suggested for β-oestradiol (Blackwell, Flower & others, 1978) on endogenous PG production which would be necessary for endogenous ileal acetylcholine release under the influence of exogenous agonists (including PGs themselves).

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