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# SOCIETY FOR GYNECOLOGIC INVESTIGATION

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**PHARMACOLOGICAL EVIDENCE FOR THE PRESENCE OF INHIBITORY EP2 PROSTANOID RECEPTORS IN THE PREGNANT BABOON MYOMETRIUM.** Rafael Garcia Villar\*, Lucy Green\*, Susan Jenkins\*, Richard A. Wentworth\*, and Peter W. Nathanielsz. Laboratory for Pregnancy and Newborn Research, Dept. Physiology, College of Veterinary Medicine, Cornell University, Ithaca New York 14853. Supported by HD 21350.

Endogenous prostanoids (mainly PGE<sub>2</sub>) have been shown to be either inhibitory or stimulatory to myometrial contractions in the pregnant primate: the nature of the myometrial response to PGE<sub>2</sub> depending on the interaction with specific receptors, namely EP prostanoid receptors, divided into putatively inhibitory (EP2) and activatory (EP1 and EP3) subtypes (1). The present in vitro study was conducted to determine whether EP2 prostanoid receptors could be pharmacologically demonstrated on the myometrium of the pregnant baboon in the last third of pregnancy.

**METHODS:** Myometrium (2 x 4 cm piece) was removed from the body of the uterus of four pregnant baboons at 160-183 days gestation (term 175 - 185 days) under halothane general anesthesia. Muscle strips (0.4 x 1 cm) were suspended in an 8-chamber in vitro superfusion system (2) in the direction of the longitudinal fibers. A cumulative concentration-response curve to oxytocin (OT) was obtained over the range 10<sup>-12</sup> to 10<sup>-6</sup> M. A concentration of OT close to the EC50 was chosen, the myometrial contractility was driven at this dose, and a concentration-response curve to the putative EP2 prostanoid receptor agonist AH13205 (Glaxo, UK; range 10<sup>-10</sup> to 10<sup>-5</sup> M) was constructed.

**RESULTS:** OT dose-dependently enhanced the activity level of myometrial muscle strips with a calculated EC50 in the nanomolar range (2.5 ± 2.1 nM, n=10 experiments). In three of four baboons (Fig. 1), AH13205 dose-dependently inhibited the amplitude and the frequency of OT (4.2 10<sup>-9</sup> M) driven myometrial contractions (Fig. 1).

**CONCLUSION:** The response of the myometrium to various prostanoids produced in late gestation and at parturition will depend on the factors that regulate the expression of specific prostanoid receptor subtypes. Our study suggests that the inhibitory EP2 receptor-subtype is present in the pregnant baboon myometrium during the last third of gestation, where it probably contributes to maintaining a low level of myometrial contractility.

**REFERENCES:** 1 Senior J, Marshall K, Sangha R et al (1991). Br J Pharmacol 102, 747-753; 2 Coleman RA, Nials AT (1989). J Pharmacol Met 21, 71-86.

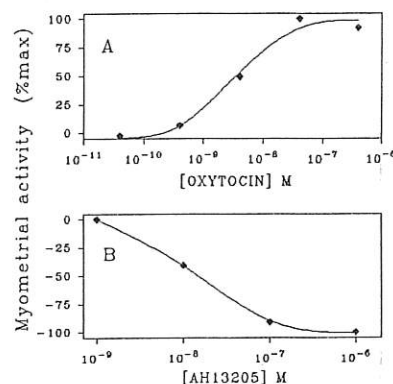


Fig. 1 OT concentration-response curve (A) and AH 13205 induced inhibition (B) of myometrial activity from two baboons near term.

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