

## LUTEOLYTIC AND OVULATION-INDUCING PROPERTIES OF PROSTAGLANDIN $F_{2\alpha}$ IN PREGNANT MICE

A. P. LABHSETWAR\*

*Pharmaceuticals Division, Imperial Chemical Industries Ltd,  
Alderley Park, Macclesfield, Cheshire*

*(Received 2nd August 1971, accepted 6th September 1971)*

The luteolytic effects of prostaglandin (PG)  $F_{2\alpha}$  have been described in several laboratory species such as the rat (Gutknecht, Cornette & Pharriss, 1969; Labhsetwar, 1970), hamster (Labhsetwar, 1971; Gutknecht, Wyngarden & Pharriss, 1971), rabbit (Gutknecht *et al.*, 1969) and guinea-pig (Blatchley & Donovan, 1969). This PG also induces ovulation in rats (unpublished observations) and hamsters (Labhsetwar, 1971). If the PG also exerts luteolytic and ovulation-inducing effects in the mouse, this animal might prove to be more economical for experimental purposes because of its smaller size and the limited availability of PG.

Inbred mice of ICI strain were used in this study. Adult females were exposed to males and the day when a vaginal plug was found was regarded as Day 1 of pregnancy. Crystalline  $PGF_{2\alpha}$  (racemic) was made up in phosphate buffer (pH 7.4) and injected subcutaneously once a day in 1 vol. of 0.25 ml from Days 4 to 6, inclusive, of pregnancy. Control animals were injected with a similar volume of buffer only. All animals were killed on Day 8 and the condition and number of implant sites noted. Both Fallopian tubes were removed and examined for the presence of tubal ova. Ovaries were examined for the number of corpora lutea and fixed in 10% formol saline. They were serially sectioned and examined histologically.

Under the experimental conditions used, daily injections of 100  $\mu$ g (about 3 mg/kg)  $PGF_{2\alpha}$  for 3 days terminated pregnancy and caused vaginal cornification in all the treated animals (Group D, Table 1). At this dose level, a high proportion of animals showed tubal ova which were surrounded by cumulus, indicating fresh ovulations. This was further confirmed by histological examinations of the ovaries. The gonads of treated animals contained two sets of corpora lutea—one set degenerating and the other freshly formed; in the control animals, only one set was present. All this evidence taken together suggests that  $PGF_{2\alpha}$  exerted luteolytic effects and the resulting progesterone deficiency probably terminated pregnancy. The antifertility effects cannot be due to a disturbance in the zygote transport since  $PGF_{2\alpha}$  was injected from Day 4 of pregnancy when the zygotes have already reached the uterus (see Blandau, 1969).

\* Present address: Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts 01545, U.S.A.

The results suggest that  $\text{PGF}_{2\alpha}$  does exert luteolytic effects and induce ovulation in mice in a similar manner to that described in other species, notably the hamster (Labhsetwar, 1971). The effective dose of racemic  $\text{PGF}_{2\alpha}$  by the subcutaneous route in mice, approximately 3 mg/kg, may be compared with the

TABLE 1  
EFFECTS OF PROSTAGLANDIN  $\text{F}_{2\alpha}$  ON PREGNANCY AND OVULATION IN MICE

Group and treatment	No. of corpora lutea	No. pregnant/no. treated (no. of implants/pregnant mouse)	No. ovulating/no. treated (Ova/ovulating mouse)	Vaginal smear at autopsy
A. Control	11.0 ± 1.5*	4/5 (12 ± 1.5)*	0/5 —	Leucocytic
B. 50 µg $\text{F}_{2\alpha}$	11.6 ± 1.2*	2/5 (12.5)	2/5 (10)	Leucocytic
C. 75 µg $\text{F}_{2\alpha}$	9.3 ± 0.9*	2/3 (10.0)	0/3 —	Leucocytic
D. 100 µg $\text{F}_{2\alpha}$	—†	0/5 (0)	4/5 (10.0 ± 1.6)*	Cornified

\* Mean ± S.E.

† Could not be accurately counted.

effective dose in hamsters –0.5 to 1 mg/kg (Labhsetwar, 1971), and in rats >5 to 10 mg/kg (Labhsetwar, 1970). Thus, with the exception of the hamster, the mouse appears to be the most sensitive species to luteolytic effects of  $\text{PGF}_{2\alpha}$  among the laboratory animals so far studied.

The author thanks Miss Patricia Maxwell for technical assistance and Dr N. S. Crossley for the supplies of  $\text{PGF}_{2\alpha}$ .

#### REFERENCES

- BLANDAU, R. J. (1969) *Gamete transport—comparative aspects*. The Mammalian Oviduct, p. 129. Eds. E. S. E. Hafez and R. J. Blandau. University of Chicago Press, Chicago.
- BLATCHLEY, F. R. & DONOVAN, B. T. (1969) Luteolytic effect of prostaglandin in the guinea pig. *Nature, Lond.* **221**, 1065.
- GUTKNECHT, G. D., CORNETTE, J. & PHARRISS, B. (1969) Antifertility properties of prostaglandin  $\text{F}_{2\alpha}$ . *Biol. Reprod.* **1**, 367.
- GUTKNECHT, G. D., WYNGARDEN, L. J. & PHARRISS, B. (1971) The effect of prostaglandin  $\text{F}_{2\alpha}$  on ovarian and plasma progesterone levels in the pregnant hamster. *Proc. Soc. exp. Biol. Med.* **136**, 1151.
- LABHSETWAR, A. P. (1970) Effects of prostaglandin  $\text{F}_{2\alpha}$  on pituitary luteinizing hormone content of pregnant rats: a possible explanation for the luteolytic effect. *J. Reprod. Fert.* **23**, 155.
- LABHSETWAR, A. P. (1971) Luteolytic and ovulation inducing properties of prostaglandin  $\text{F}_{2\alpha}$  in hamsters. *Nature, Lond.* **230**, 528.