

تأثير البروستاجلاندين ف٣ على الجسم  
الأصفر للأراناب

١٠١٠١ العزب ، م . ع . رض

البحث عبارة عن دراسة لتأثير هرمون البروستاجلاندين على الجسم الأصفر ، وقد  
اشتملت الدراسة على ٣٠ أنثى للأراناب الغير بالغة وذلك بقصد الوقوف على تأثير  
الهرمون المذكور على خلايا الجسم الأصفر حيث تبين ضمورا واضحا لأجزائه المختلفة  
عند حقن الهرمون في اليوم السابع للتبويض .

Dept. of Clinical Studies,  
Faculty of Vet. Science, University of Khartoum, Khartoum, Sudan,  
Head of the Dept. Prof. Dr. E.A. El-Azab.

EFFECT OF PROSTAGLANDIN  $F_2\alpha$  ON THE CORPUS LUTEUM OF RABBITS  
( With One Table and 12 Figures )

By

E.A. EL AZAB and S.E. AWAD

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SUMMARY

A study was made on 30 female immature rabbits to show the role played by Prostaglandin  $F_2\alpha$  in influencing the structure of the corpus luteum of rabbits. The drug was injected on day 2, 5 and 7 after induction of ovulation and corpus luteum formation. Luteolytic effect was not demonstrated when the drug was injected on day 2 and 5, but regression and fibrosis of the corpus luteum was clear when prostaglandin  $F_2\alpha$  was injected on day 7 after ovulation. The results were discussed in the text.

INTRODUCTION

There is a clear evidence that removal of the uterus in the presence of functional corpora lutea caused maintenance of luteal function in several species of animals, for a period equivalent to or longer than pregnancy (CALDWELL et al., 1969 ANDERSON et al., 1969). SOLIMAN et al., (1973) assumed that the maintenance of luteal cells after hystrectomy is due to decreased output of the luteolytic agent from the uterus. This uterine factor causing luteolysis was proved to be prostaglandin  $F_2\alpha$  (GODING, 1974). A decrease in luteal activity has been shown to be accompanied by distinct changes in corpus luteum morphology in the pregnant rabbit (KOERING and KIRTON, 1973).

This study was undertaken to determine the effect of prostaglandin  $F_2\alpha$  ( $PGF_2\alpha$ ) on the corpus luteum of pseudopregnant rabbits.

#### MATERIALS AND METHODS

30 female immature rabbits were used in this investigation. Their age was about 3 months and their weight varied from 800-900g. at the beginning of the experiment. Each animal was injected subcutaneously with 100 i.u. of PMS (Gestyl, Organon) followed after 48 hours by intravenous injection of 50 i.u. of HCG (Pregnyl, Organon) to induce ovulation and corpus luteum formation according to the method adopted by LABIB (1974). The animals were divided into six groups each of five animals. Three groups were injected subcutaneously with 0.5 ml (25 U<sub>g</sub>) of  $PG F_2\alpha$  (Estrucmate, ICI) and the other three groups acted as controls and injected with 0.5 ml saline solution (see Table 1). Immediately after slaughtering the ovaries and parts of the uterine horns were removed and fixed in 10% neutral formol. The organs were embedded in paraffin and histological sections were done and stained with haematoxylin and eosin.

The corpora lutea were subjected to histological examinations to evaluate the state of development or involution of the luteal cells according to the following criteria:

- A. The nature of cytoplasmic granules, when they were small and dispersed this indicated that the luteal cells are active. When such fat granules started to coalesce and the cytoplasm becomes vacuolated, it indicated the onset of degeneration.

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B. The characteristics of the nucleus were also observed according to the nature of the chromatin network, the presence of mitotic figures or pyknosis and the position of the nucleus within the cell if it is central or excentric.

A general description of the endometrium of the uterine horns, with special reference to the stromal nuclei was made. This was done according to the description of HOCKER and FORPES (1947) to evaluate the degree of activity of the corpora lutea and the secretion of progesterone. Under the effect of progesterone these stromal cells are oval or circular. Withdrawal of the progestational effect leads to stromal cell nucleus which are elongated and elliptical.

Table 1: Scheme of treatment and slaughtering the rabbits.

Group No.	Time of injection of PGF <sub>2</sub> α after HCG injection	Time of injection of saline after HCG injection	Time of slaughtering after HGG injection
1	Day 2	-	Day 7
2	-	Day 2	Day 7
3	Day 5	-	Day 9
4	-	Day 5	Day 9
5	Day 7	-	Day 12
6	-	Day 7	Day 12

RESULTS

Groups 1 and 2: Corpus luteum

The seven days old corpora lutea of the animals injected with PGF<sub>2</sub>α and those injected with saline showed more or less

the same histological picture. The cavity of the corpus luteum was completely filled with lutein cells. The cells showed mitotic figures and the majority of the nuclei were vesicular with granular dispersed chromatin (Figs. 1 and 2). The lutein cells of animals injected PGF<sub>2</sub>  $\times$  showed some vacuolation of their cytoplasm but the cells were active.

#### Uterus:

Sections of the uterine horns of rabbits having corpora lutea of the age of 7 days showed hyperplasia of the epithelial lining. The uterine glands were lined with high cuboidal cells and had an empty lumen. Stromal cells of the endometrium are somewhat young in age, having rounded or oval nuclei indicating progestational proliferation (Fig. 3 and Fig. 4).

#### Group 3: Corpus luteum:

The lutein cells completely filled the luteal cavity. The cells were active and of large size and their nuclei were prominent. Some cells showed vacuolation of their cytoplasm. Fibroblast cells originating from thecal tissue were seen extending between the lutein cells (Fig. 5).

#### Uterus:

The stromal cells were rounded in shape. The glands had wide lumen and lined by high cuboidal cells. The endometrium was slightly oedematous (Fig. 6).

#### Group 4: Corpus luteum:

Coalescence of fat granules was seen in the cytoplasm of the lutein cells. Some cells were still active and showed mitotic divisions (Fig. 7).

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### Uterus:

The uterus showed hyperplasia of its epithelial lining. The epithelium was of columnar type. The stromal cell nuclei of the submucosa were oval in shape (Fig. 8).

### Group 5: Corpus luteum:

The corpus luteum showed complete fibrosis. The luteal cavity was completely filled by fibrous connective tissue (Fig. 9). Graffian follicles were seen in their way to maturation appeared in the ovary.

### Uterus:

The uterus had a thick lamina propria. The stromal cells became mature having spindle shaped nuclei indicating withdrawal of progesterone (Fig. 10). The glands had narrow lumen. Numerous blood sinusoids were seen in the stroma of the uterus.

### Group 6: Corpus luteum:

The luteal cavity was still completely filled by lutein cells. The cells showed fat droplet coalescence as indicated from vaculation of their cytoplasm (Fig. 11). Some lutein cells were still active. Fibroblast cells were seen extending between the lutein cells.

### Uterus:

The stromal cell nuclei of the submucosa were spindle shaped, beside oval young fibroblast cells (Fig. 12).

## DISCUSSION

In the present study  $\text{PGF}_2\alpha$  has been shown to cause luteolysis. These results are in agreement with those of previous studies (PHARRISS *et al.*, 1972). It seems that  $\text{PGF}_2\alpha$  can not exert its luteolytic effect on newly formed corpora lutea. It fails to produce marked histological changes in the lutein cells when injected in rabbits having 2 and 5 days-old corpora lutea. Its destructive effect on the corpus luteum was very clear when injected on the 7th day after induction of ovulation. KOERING (1974) was able to demonstrate both morphological regression of the corpus luteum and a decrease in peripheral progesterin levels within 24 hours after administration of  $\text{PGF}_2\alpha$  to rabbits on day 8 of pseudopregnancy. However, ROWSON *et al.*, (1972) were able to induce corpus luteum regression and subsequently oestrus in cows after administration of 0.5 mg prostaglandin intrauterine in two consecutive days, provided that the treatment is carried out after day 4 of the cycle.

The corpus luteum in the rabbit is maintained by oestrogen (SPIES and QUADRI, 1967; KEYES and NALBANDOV, 1967). Moreover, LEE *et al.*, (1971) have identified a cytoplasmic estrogen receptor in the corpus luteum of pseudopregnant rabbits, which has been found to be at highest concentration at mid-pseudopregnancy.  $\text{PGF}_2\alpha$  most probably interferes with the effect of estrogen and results in corpus luteum regression. As JACOBSON *et al.*, (1972) found that the concentration of oestrogen receptors decrease when the rabbits treated with  $\text{PGF}_2\alpha$  at midpregnancy.

ABDUL-KARIM and BRUCE, (1973) found that the blood flow to the corpus luteum decrease just after mid-pregnancy in

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rabbits. LABIB et al., (1977) were able to demonstrate that the vascularity of the corpora lutea was not adversely affected during regression of the corpora lutea or at least during the first 15 days after ovulation. KOERING, (1974) assumed that the variation in the blood flow to the ovary which is possibly due to local effect of  $\text{PGF}_2\alpha$ , may be responsible for the luteolysis.

It could thus be concluded from the present investigation that successful control of oestrous could be achieved by using  $\text{PGF}_2\alpha$  on the 7th day of the cycle.

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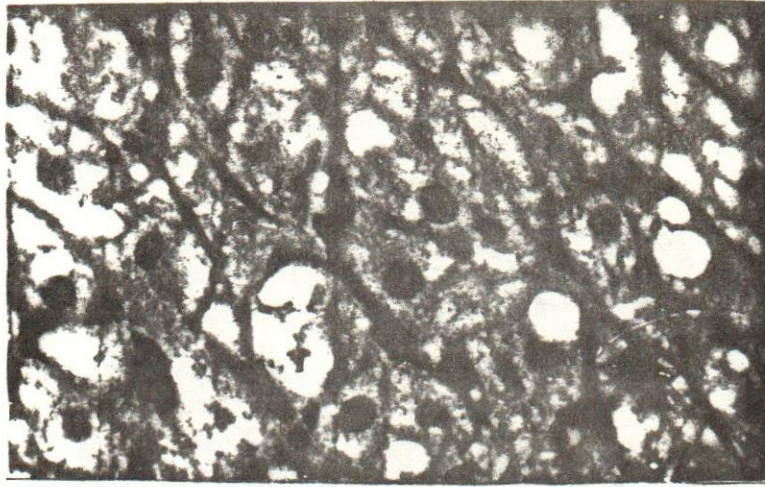


Fig.1: Seven days old corpus luteum (control).(x480)

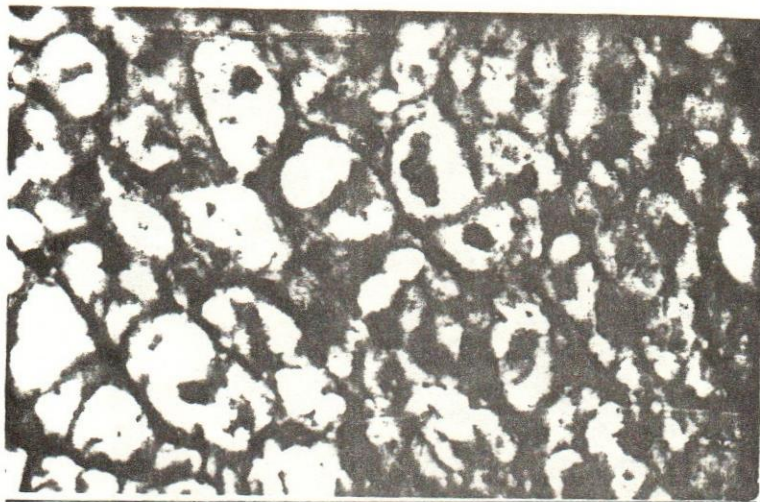


Fig.2: Seven days old corpus luteum after injection of  $PGF_2$  two days after induction of ovulation.(x480)

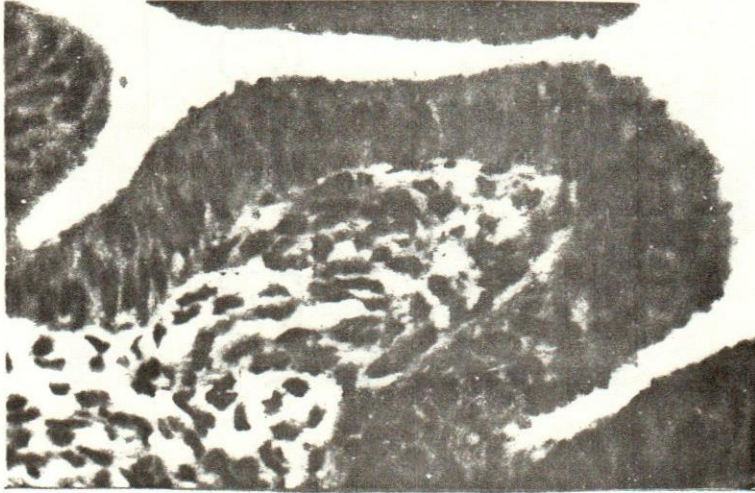


Fig. 3: A cross section in the uterus of a rabbit having 7-days old corpus luteum( control).(x480)

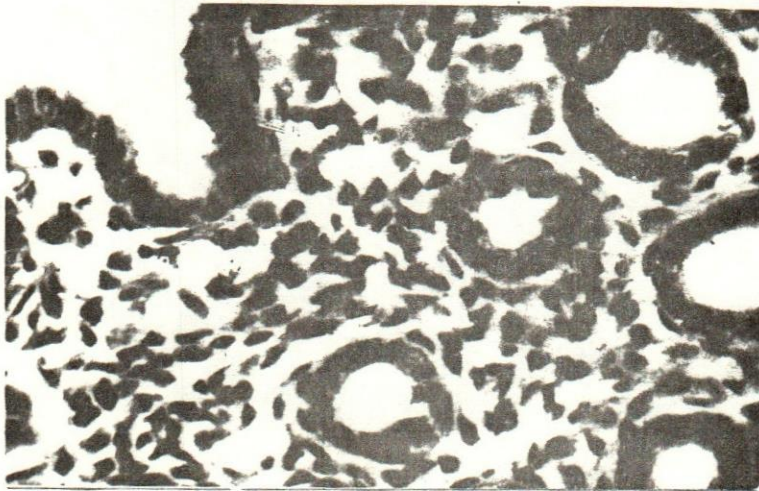


Fig. 4: A cross section in the uterus of a rabbit having 7-days old corpus luteum and treated with  $\text{PGF}_2$  two days after induction of ovulation.(x480)

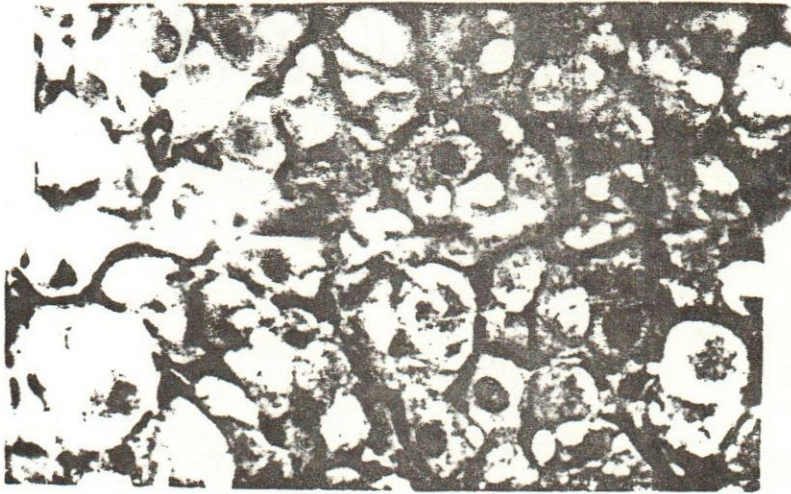


Fig. 5: Nine days old corpus luteum of rabbit treated with  $\text{PGF}_2\alpha$  on the 5th day after ovulation.(x480)

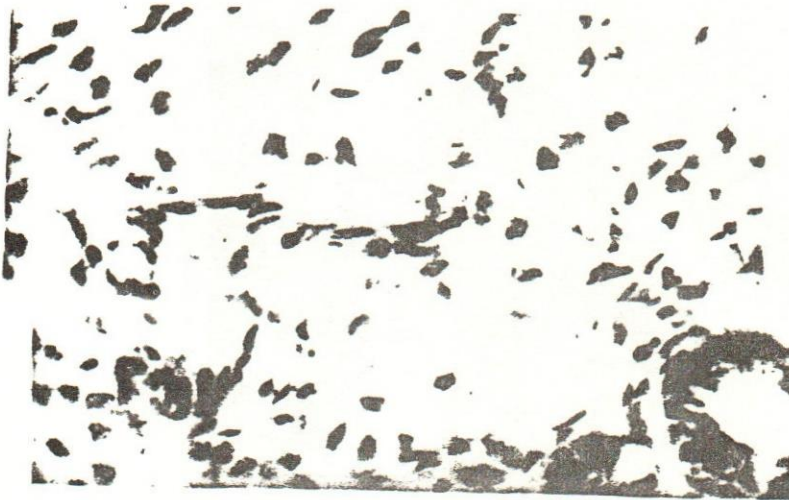


Fig. 6: Cross section in the uterus of rabbit having 9-days old corpus luteum and treated with  $\text{PGF}_2\alpha$  on the 5th day after ovulation.(x480)

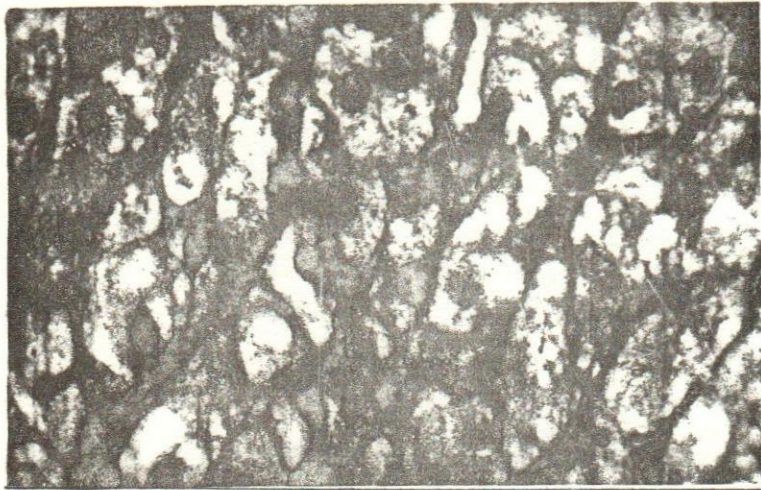


Fig. 7: Nine-days old corpus luteum(control).(x480)

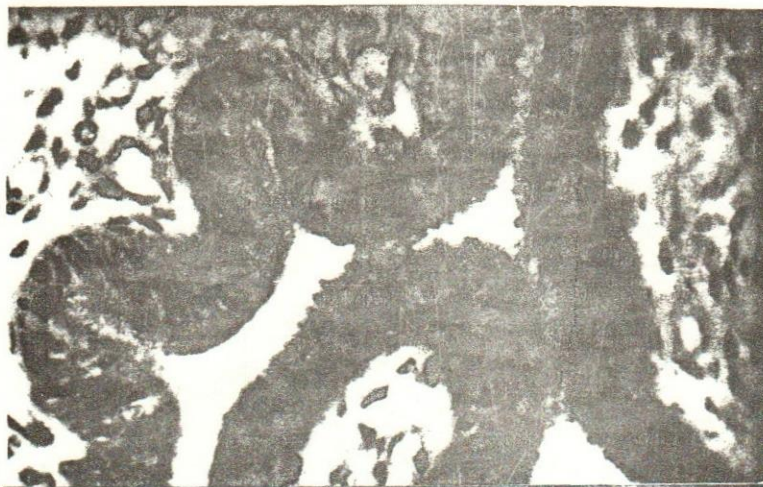


Fig. 8: Cross section in the uterus of rabbit having 9-days old corpus luteum (control).(x480)



Fig. 9: 12-days old corpus luteum of rabbit treated with  $\text{PGF}_2\alpha$  on the 7th day after ovulation.(x480)

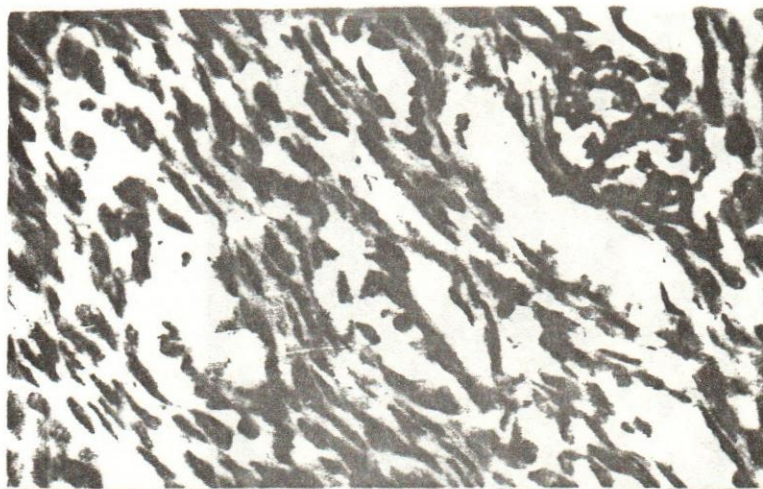


Fig. 10: A cross section in the uterus of rabbit having 12-days old corpus luteum and treated with  $\text{PGF}_2\alpha$  on the 7th day after ovulation.(x480)

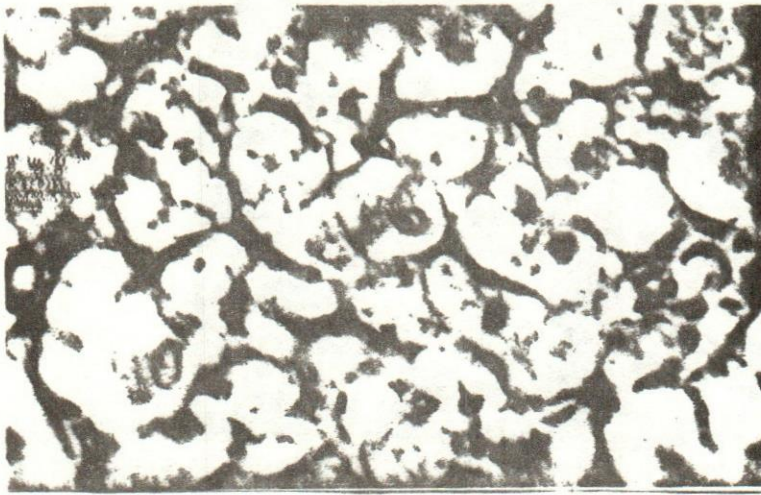


Fig. 11: 12-days old corpus luteum (control). (x480)

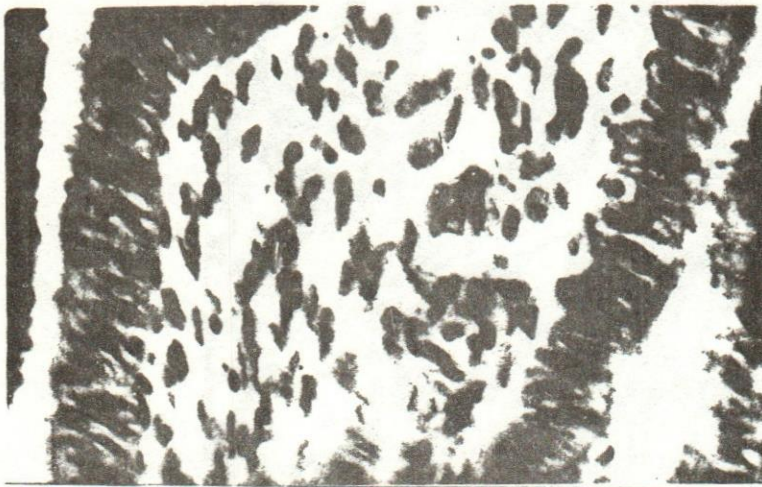


Fig. 12: A cross section in the uterus of rabbit having 12-days old corpus luteum (control). (x480)