Induction of Lactogenesis and Abortion by Prostaglandin $F_{2\alpha}$ in Pregnant Rats

THE withdrawal of ovarian progesterone at the end of pregnancy seems to be the essential step in the initiation of lactation in pregnant rats[1-5]. Although there is a decrease of plasma progesterone concentration before parturition[6,7], the mechanisms involved in the regression of the corpus luteum at parturition are unknown. It is known[8-10] that the uterus is concerned with the regression of the corpus luteum in the rat and the uterine luteolytic seems to involve a substance transported in the blood[10]. The discovery of prostaglandins in menstrual fluid and human endometrium[11,12] and the luteolytic action of prostaglandin F_2 ($PGF_{2\alpha}$) demonstrated in pseudopregnant rats[13] and normal guinea-pig[14] indicate a possible participation of prostaglandin at the end of pregnancy. The high concentration of $PGF_{2\alpha}$ in the amniotic fluid during labour[15] gives support to this hypothesis.

I have investigated the effect of $PGF_{2\alpha}$ in eight pregnant rats of the Instituto strain, housed in individual cages. They were injected intraperitoneally with 1.2 mg of $PGF_{2\alpha}$ in four doses of 0.3 mg each, every 4 h on day 17 (two rats) and day 18 (six rats) of pregnancy. $PGF_{2\alpha}$ was prepared as recommended by the makers (Upjohn). A control group of ten rats was injected with four doses of normal saline on day 17 of pregnancy. The following day, 12 and 17 h after the administration of the last dose of saline or prostaglandin, an oxytocin test[4] was performed to determine the onset of lactogenesis.

All animals were checked several times a day for signs of abortion. After parturition, maternal behaviour was watched in each treated rat.

None of the control rats gave a positive response to the oxytocin test. In this strain lactogenesis takes place 12 h before parturition on day 22 (ref. 4). All control rats delivered normal foetuses at term. But when the oxytocin test was applied to the eight treated rats 15 h after the last injection of $PGF_{2\alpha}$ visible milk appeared. No rats gave a positive response in the first test. It is interesting that after the last dose of $PGF_{2\alpha}$, rats adopted the typical posture of parturition for at least 1 h; contractions were also observed through the abdominal wall. Four rats were injected with 100 mU of oxytocin 30 min after the last dose of prostaglandin, to see whether abortion could be induced. None aborted, but blood was seen in the vagina of some rats. On day 20 of pregnancy all rats treated with $PGF_{2\alpha}$ delivered small foetuses, some of them alive. Maternal behaviour was studied by giving a foster litter to each rat on the day after parturition. Seven rats showed normal maternal behaviour but only two were able to feed the young.

These results show clearly that $PGF_{2\alpha}$ can induce lactogenesis and advance parturition when injected into pregnant rats. According to previous knowledge[13,14] $PGF_{2\alpha}$ may have a luteolytic effect in pregnant rats and may be responsible for the decrease in progesterone at the end of pregnancy. There is no evidence about the mode of action of $PGF_{2\alpha}$ in pregnant rats. The suggestion of a venoconstrictor action affecting the life span of the corpus luteum[13] has been shown to be incompatible with the normal development of the rest of the ovary after treatment with prostaglandin[14]. Further work is needed to clarify the function of $PGF_{2\alpha}$ as the luteolytic factor before parturition.

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Production of Lytic Plaques of Viral Origin in *Penicillium*

THE presence of virus particles in fungi is now established on the basis of observations in *Agaricus* (*Psalliota*) *bisporus* and in *Penicillium stoloniferum*[2,3] and *P. chrysogenum*[4]. Viruses in *A. bisporus* cause several malformations of the fruiting body[5] and some morphological variations of the colony in *P. stoloniferum*[3]. Small patches of white aerial mycelium have frequently been observed on the surface of fungi and we have confirmed this for *P. citrinum* and *P. variabile* grown on potato glucose agar at 24° C. When these organisms are grown on 18% lactose, 1% peptone, 2% agar, distilled water (*p*H 6·5) (medium A) at 24° C, lytic plaques are observed on the reverse of the patches of white aerial mycelium (Fig. 1*a*, *b*), which are morphologically similar to those produced by bacteriophages in bacteria and in streptomycetes. The mycelium taken from the centre of the lytic area consists of swollen hyphae, wholly lysed or with very little cytoplasm. Observation with the electron microscope, after fixation with phosphotungstate (PTA) at *p*H 7, has shown that the hyphae yield a large amount of virus particles (2 to 100 per field) as previously observed[1-4]. The particles have a hexagonal shape, with no tail and a diameter of 400–500 Å.

We tried to determine whether the presence of virus could cause some modification of the normal morphology of the two species under examination. Two culture types were isolated in medium A; type 1 was obtained from the mycelium taken from the centre of a lytic plaque; type 2 was obtained from mycelium taken from the white patches present on the colony surface. Type 1 gave moist, yeast-like colonies without aerial mycelium, and which were sterile; type 2 gave fluffy round colonies, with abundant aerial mycelium; they also were sterile. Only the type 2 colonies contained a large amount of virus particles (15–30 per field) like those observed in the lytic plaques. The virus particles were not found in the type 1 colonies, nor in the normal mycelium of the two species of *Penicillium* under examination. Type 2 colonies, grown at 30°–32° C, reverted to normal—that is conidia were formed again. At these temperatures therefore it seemed that the fungus recovered from the virus infection, as observed by others[1,3] for subcultures at 24° C.

To reproduce the lytic plaques, we broke each plaque with a cotton swab, took out the infected mycelium and the conidia of the surrounding healthy mycelium, and smeared this evenly on 20 ml. of medium A in 10 cm Petri dishes (the thickness of the agar seemed to be critical). After 5–10 days at 24° C a