BIOLOGY OF REPRODUCTION 39, 839–846 (1988)

Prostaglandin Production by Corpora Lutea of Rhesus Monkeys: Characterization of Incubation Conditions and Examination of Putative Regulators[1]

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ABSTRACT

Prostaglandins (PGs) are produced by the corpus luteum (CL) of many domestic and laboratory species and may play a role in CL regulation. The production of PGs by luteal tissue of the rhesus monkey has yet to be clearly elucidated. The production of PGE_2, $PGF_{2\alpha}$, and 6-keto-$PGF_{1\alpha}$ by CL from rhesus monkeys and the incubation conditions (time and cell number) that permit assessment of their synthesis were examined. CL (n = 3 per characterization) were surgically removed from nonpregnant monkeys during the mid-luteal phase of the menstrual cycle (~8–10 days after ovulation). Luteal tissue was dissociated and the cells were incubated at varying concentrations for increasing periods of time at 37°C. Subsequent to defining incubation conditions, various exogenous factors were examined for their potential to modify PG production. Indomethacin, calcium ionophore, human chorionic gonadotropin (hCG), estradiol-17β (E_2), progesterone (P), testosterone (T), dihydrotestosterone (DHT), and 1-4-6 androstatriene-3, 17-dione (ATD) were incubated with luteal cells in increasing doses. PG and P concentrations in the medium were determined by radioimmunoassay. PGs in the medium after 6 h incubation were detectable at all cell concentrations tested (50,000, 100,000, 200,000 cells/tube). Concentrations of PGs and P increased with cell number ($p<0.05$). Luteal cells (50,000 cells/tube) were incubated for times of 0–24 h. Concentrations of P, PGE_2, and $PGF_{2\alpha}$ in the medium were relatively low prior to incubation (0 h), increased ($p<0.05$) linearly within the first 6–12 h, and plateaued through the remaining 24 h. A similar pattern was observed for concentrations of 6-keto-$PGF_{1\alpha}$. Incubation times of 6–12 h were deemed appropriate for subsequent studies as they provided PG concentrations detectable and above baseline (0 h). Indomethacin, a PG-synthesis inhibitor, decreased concentrations of PGs in the medium in a dose-dependent manner ($p<0.05$). The highest dose of indomethacin prevented any increase in concentrations of PGs above the levels prior to incubation. There was no effect on P concentrations. Conversely, hCG had no effect on PG production but stimulated P production in a dose-dependent manner ($p<0.05$). Calcium ionophore, a stimulator of PG synthesis, increased $PGF_{2\alpha}$, PGE_2 ($p<0.01$), and 6-keto-$PGF_{1\alpha}$ ($p<0.05$) in a dose-dependent manner. Other hormones (T, P, E_2, DHT, ATD) did not influence P and PG production, and thus had no acute effect on luteal function in vitro. The observations made in this study substantiate that the CL of the rhesus monkey synthesizes PGs. Further studies are necessary to identify and define the roles that luteal PGs may play in the regulation of the primate CL.

INTRODUCTION

The corpus luteum (CL) of the mammalian ovary plays a pivotal role in reproductive cyclicity and pregnancy maintenance. Currently, however, the mechanisms regulating the function of the CL are not completely understood. In domestic and laboratory species, uterine prostaglandins (PGs) influence luteal lifespan and function (Horton and Poyser, 1976; Inskeep and Murdoch, 1980). Certain PGs, such as $PGF_{2\alpha}$, inhibit luteal function, while others, such as PGE_2 (Marsh and LeMaire, 1974; Hueckstead and Weems, 1978) and PGI_2 (Milvae, 1986), seem to enhance luteal function. In the primate, uterine PGs do not play a role in luteal regulation (Neill et al., 1969; Castracane et al., 1979), but PGs from another source may influence the primate CL. This notion is supported by the observations that the human CL has receptors for PGs (Powell et al., 1974) and PGs affect

Accepted June 20, 1988.
Received March 7, 1988.
[1] Supported by NIH Grant HD-21319. Salaries and additional research support were provided by State and Federal funds appropriated to the Ohio Agricultural Research and Development Center, The Ohio State University. Journal Article No. 171-87.
[2] Reprint requests.

luteal production of progesterone in vitro (Stouffer et al., 1979; Dennefors et al., 1982; Patwardhan and Lanthier, 1984) and in vivo (Auletta et al., 1984a) in primates.

PGs that are important in luteal regulation may be produced by the CL itself. The CL of the ewe (Rexroad and Guthrie, 1978), sow (Patek and Watson, 1976), cow (Shemesh and Hansel, 1975a,b; Milvae and Hansel, 1983), and woman (Challis et al., 1976) have the capacity to synthesize PGs. Balmaceda et al. (1979, 1980, 1981), suggested that the CL of the rhesus monkey produced PGs by examining the presence of PGs in medium after 10 min of exposure to luteal tissue. However, the apparent production of PGs by luteal tissue in these studies could have been due to leaching of PGs from whole CL into the incubation medium. Slices from frozen and thawed preparations of rhesus monkey CL converted labeled arachidonic acid to substances that co-eluted with PG standards on thin-layer chromatography plates (Valenzuela et al., 1983). This suggests that the enzymes necessary for PG synthesis are present in rhesus monkey CL. In addition, Auletta et al. (1984b) found higher levels of $PGF_{2\alpha}$ metabolite in blood draining the luteal ovary versus the non-luteal ovary in the monkey. To date, however, direct evidence for PG synthesis by living luteal cells is still tenuous for nonhuman primates.

If luteal PGs are produced by the CL of the rhesus monkey and if these PGs play a role in the function of that organ, then the regulation of such PG production becomes an important issue. Many endogenous hormones could be involved in modulating PG production. The gonadotropin, luteinizing hormone (LH), stimulates PG synthesis in preovulatory follicles (Murdoch, 1985), and may stimulate the synthesis of PGs by rat CL (Chasalow and Phariss, 1972). As such, LH/chorionic gonadotropin (CG) may be involved in the regulation of PG synthesis by monkey CL. Estrogen increases endometrial PG production (Inskeep and Murdoch, 1980), and increases PGF concentrations in the ovarian vein draining the luteal ovary of rhesus monkeys (Auletta et al., 1978). Progesterone increases the ability of uterine tissue to secrete PGs in response to other stimuli (Rothchild, 1981; Ottobre et al., 1984) and modulates PG synthesis in cultured bovine luteal cells (Pate, 1987). Thus, pituitary and placental gonadotropins and locally produced ovarian steroids must be considered as candidates for regulation of luteal synthesis of PGs.

The objectives of the current study were to (1) determine if the CL of the rhesus monkey produces PGs, (2) characterize the conditions for evaluating luteal PG production, and (3) identify possible stimulators/inhibitors of luteal PG production.

MATERIALS AND METHODS

Twelve female rhesus monkeys (*Macaca mulatta*) were individually caged in a controlled environment at the Laboratory Animal Center of the Ohio State University. Monkeys were kept at room temperature with 12 h of light per day. They were maintained on a diet of Purina monkey chow (Ralston-Purina, St. Louis, MO) and water ad libitum, supplemented daily with fresh fruit. Monkeys were checked daily for menses, and menstrual records were maintained (onset of menses = Day 1 of the menstrual cycle).

Nonpregnant monkeys exhibiting normal menstrual cycles of ~28 days were bled daily (0800–1000 h) starting from Day 8 of the menstrual cycle until luteectomy. Blood samples were collected by femoral venipuncture following anesthetization with ketamine hydrochloride (Bristol Laboratories, Syracuse, NY, 10–15 mg/kg i.m.). Serum was stored at −20°C until radioimmunoassay (RIA) for progesterone. Patterns of serum progesterone were used to estimate the age of CL. Luteal progesterone is detectable in the peripheral serum beginning approximately 2 days after the luteinizing hormone (LH) surge. CL approximately 8–10 days old were collected via midventral laparotomy from monkeys anesthetized before surgery with ketamine hydrochloride supplemented with atropine sulfate (ESI Pharmaceuticals, Cherry Hill, NJ; 0.02 mg/kg i.m.) and sodium pentobarbital (Butler, Columbus, OH; 8–12 mg/kg i.v.). The CL was excised by blunt dissection and immediately placed in Ham's F-10 medium (Sigma Chemical Co., St. Louis, MO) at 4°C for transport to the laboratory. One CL, which was used to characterize PG production over time, was collected following superovulation with human menopausal gonadotropin (Pergonal; Serono Labs., Milan, Italy) and human CG (hCG, APL; Ayerst Labs., Rouses Point, New York). These compounds were administered in a regimen similar to that used by Stouffer et al. (1986). PG production over time was similar between this CL and the other two CL used for this characterization. Dispersed luteal cells were prepared by a combination of 0.25% collagenase (Worthington Biochemical, Freehold, NJ)/0.02% DNAse (Sigma) digestion and gentle

mechanical agitation in a manner similar to that of Stouffer et al. (1976). Cell viability, as determined by trypan blue exclusion, was >95%. Suspensions of dispersed luteal cells were incubated in a gyratory shaker bath at concentrations of 50, 100, and 200 × 10^3 cells per 250 μl Ham's F-10 medium at 37°C in an atmosphere of 95 O_2:5 CO_2. Incubation times of 0 (no incubation) 1, 2, 3, 6, 9, 12, 18 and 24 h were tested.

After characterization of incubation conditions, putative stimulators/inhibitors of luteal synthesis of PGs were tested. CL from 3–4 monkeys were used to evaluate each compound. hCG, estradiol-17β, and progesterone were used to examine their effects on luteal PG production. Testosterone was also tested since it is a precursor of estradiol-17β. To differentiate between an androgenic and an estrogenic effect, a nonaromatizable androgen, dihydrotestosterone (DHT), was tested for its ability to modulate luteal synthesis of PGs. To test the effect of endogenous estrogens on luteal PG production, we attempted to block luteal synthesis of estrogens with the aromatase inhibitor, 1,4,6-androstatriene-3, 17-dione (ATD) (Brodie et al., 1976).

Purified hCG (CR 125; 11,900 IU/mg, NIADDK) was added to luteal cells to achieve concentrations of 0, 1, 10, 100, 1000 and 10,000 ng/ml in a total of 250 μl/tube. The estrogen synthesis inhibitor, ATD, and the ovarian steroids, estradiol-17β and progesterone, were added to cells to achieve concentrations of 0, 0.1, 1, 10, 100, and 1000 ng/ml. The androgens, testosterone and DHT, were added to the cells to achieve concentrations of 0, 1, 10, 100, 1000, and 10,000 ng/ml. All steroids were obtained from Steraloids Inc. (Wilton, NH). The ethanol content (solvent for steroids) was less than 0.2% for all additions. A PG synthesis inhibitor, indomethacin (Sigma), was added to cells to achieve concentrations of 0, 1, 10, 100, and 1000 ng/ml. Calcium ionophore (A23187, Sigma), a stimulator of prostaglandin synthesis (Laychock and Putney, 1982), was added to cells to achieve concentrations of 0, 0.05, 0.1, 0.5, 1.0, 5.0, and 10.0 μM. The content of the solvent for calcium ionophore, dimethyl sulfoxide, was less than 0.06% for all additions. For most studies, cells and medium were frozen at −20°C after incubation. Cells and medium were separated by centrifugation at 160 × *g*. This separation preceded freezing for studies with calcium ionophore. Concentrations of progesterone, PGE_2, $PGF_{2\alpha}$, and 6-keto-$PGF_{1\alpha}$ (the stable metabolite of PGI_2) in the medium were estimated by RIA. Data were analyzed after log transformation using analyses of variance for a randomized complete block design, with individual CL as the block.

Validation of RIA

RIAs were developed to measure concentrations of progesterone and PGs ($PGF_{2\alpha}$, PGE_2, and 6-keto-$PGF_{1\alpha}$) in serum and/or F-10 medium incubated with dispersed luteal cells. Specific and proven antibodies for $PGF_{2\alpha}$ and 6-keto-$PGF_{1\alpha}$ were donated by Dr. Richard Fertel, Department of Pharmacology, Ohio State University. The antibody for PGE_2 was donated by Dr. Harold Behrman, Department of Obstetrics and Gynecology, Yale University, and the antibody for progesterone was donated by Dr. Gordon Niswender, Department of Physiology and Biophysics, Colorado State University. Cross-reactivities of PG antibodies with eight similar compounds has been reported to be <0.1%, except for the $PGF_{2\alpha}$ antibody, which cross-reacts 15% with $PGF_{1\alpha}$ (Fertel et al., 1981). Advanced Magnetics (Cambridge, MA) donated the PG standards, and other reagents were purchased.

Concentrations of progesterone in monkey serum and medium were quantified as described by Hild-Petito et al. (1987). PGs in medium were measured according to the protocol of Fertel et al. (1981), with some modifications. Unextracted F-10 medium was assayed with 100 μl of sample per assay tube. The antisera for $PGF_{2\alpha}$, 6-keto-$PGF_{1\alpha}$, and PGE_2 were used at the following dilutions, respectively: 1:600, 1:300, and 1:400.

To validate these RIAs, we first established standard curves with slopes of ~2.20 when using a log/logit transformation. When various volumes of samples of medium from incubated cells or spiked pools of medium were assayed for progesterone, PGE_2, $PGF_{2\alpha}$, and 6-keto-$PGF_{1\alpha}$, values were parallel to the standard curves. Slopes for standard curves and increasing volumes of medium (10–100 μl), respectively, were as follows: progesterone assay, −2.01 and −2.01; PGE_2 assay, −2.07 and −2.29; $PGF_{2\alpha}$ assay, −2.28 and −2.29; and 6-keto-$PGF_{1\alpha}$ assay, −2.22 and −2.12. Thus, these assays were valid over a range of volumes of medium. Generally, exogenous treatments did not interfere with the RIAs over the range of doses used in these studies. However, the highest doses of steroids interfered with the progesterone assay. Thus, concentrations of progesterone in tubes with the highest concentration of steroid treatment

were excluded from analyses. Coefficients of variation within and between assays were as follows: progesterone assay, 8.72 and 10.95%; PGE_2 assay, 8.50 and 14.58%; $PGF_{2\alpha}$ assay, 11.20 and 13.60%, and 6-keto-$PGF_{1\alpha}$ assay, 9.57 and 15.59%.

RESULTS

Figures 1 and 2 illustrate the mean concentrations of PGs and progesterone in medium following a 6-h incubation of increasing numbers of dispersed luteal cells. PGs were detectable at all cell concentrations tested. Concentrations of PGs and progesterone increased as a function of cell number ($p<0.05$). The lowest cell concentration (50,000 cells/tube) was chosen for subsequent work to maximize the number of tests that could be performed with each CL.

Figures 3 and 4 show concentrations of PGs and progesterone in medium as a function of duration of cell incubation. Concentrations of $PGF_{2\alpha}$, PGE_2, and progesterone in medium were relatively low prior to incubation (0 h), increased linearly ($p<0.05$) within the first 6–12 h, and plateaued during the remaining 24 h. A similar pattern was observed for concentrations of 6-keto-$PGF_{1\alpha}$. The pattern of concentrations in medium of 6-keto-$PGF_{1\alpha}$ includes only one CL because concentrations in medium generated by the other two CL were nondetectable until 24 h. Since incubation times of 6–12 h generally yielded measurable concentrations of PGs, these times were deemed suitable for future studies.

The steroids tested (estradiol, progesterone, ATD, testosterone, and DHT) did not appreciably alter concentrations of PGs during the 6-h incubation period at any of the doses tested. Similarly, estradiol, ATD, testosterone, and DHT did not affect luteal production of progesterone. The acute effect of exogenous progesterone on luteal progesterone production was not examined.

hCG stimulated progesterone production in a dose-dependent manner ($p<0.05$, Fig. 5), but did not alter concentrations of PGs in medium (not shown). Maximum stimulatory effect appeared when the final concentration of hCG was 100 ng/ml in the incubation medium. Indomethacin had no effect on progesterone production (not shown), but reduced ($p<0.05$) concentrations of PGs in medium in a dose-dependent manner (Fig. 6). Concentrations of PGs in the medium of tubes containing the highest doses of indomethacin did not exceed PG concentrations in medium collected prior to incubation (n=2). Thus, these high doses of indomethacin appeared to totally block synthesis of all three PGs.

Calcium ionophore increased concentrations of PGE_2 ($p<0.01$) and 6-keto-$PGF_{1\alpha}$ ($p<0.05$) in a dose-dependent manner (Figs. 7 and 8). Although calcium ionophore elevated concentrations of $PGF_{2\alpha}$ (Fig. 8) by 150–250% in all CL tested, variability in

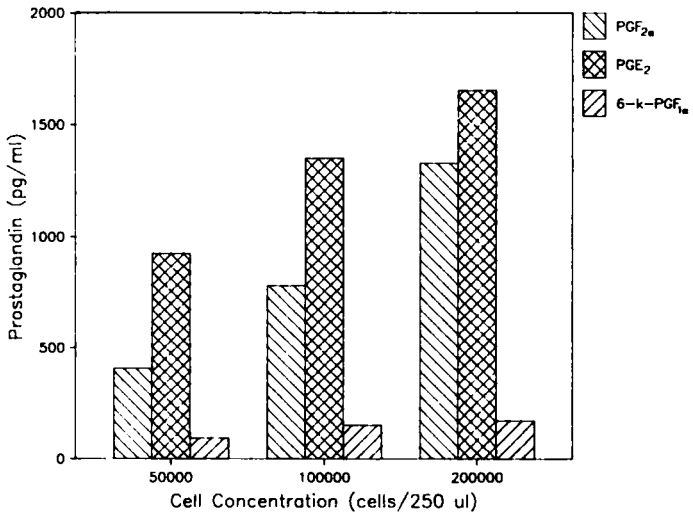

FIG. 1. Concentrations of prostaglandins (PGs) in medium as a function of cell number. Luteal cells were incubated at 37°C for 6 h at various cell concentrations (n=3). The standard errors for the means from the models used to analyze the data were 7.43 for $PGF_{2\alpha}$ concentrations, 134.18 for PGE_2 concentrations, and 15.91 for 6-keto-$PGF_{1\alpha}$ concentrations. PGs in the medium were detectable at all cell concentrations tested. Concentrations of $PGF_{2\alpha}$, PGE_2, and 6-keto-$PGF_{1\alpha}$ rose with increasing cell number ($p<0.05$).

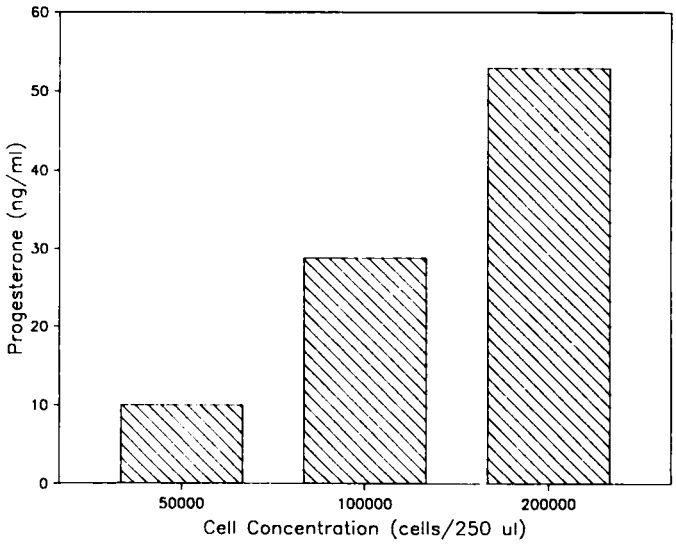

FIG. 2. Concentrations of progesterone in medium as a function of cell number. Luteal cells were incubated at 37°C for 6 h at various cell concentrations (n=3). The standard error of the means from the model used to analyze the data was 6.26. Progesterone rose linearly with increasing cell number ($p<0.05$).

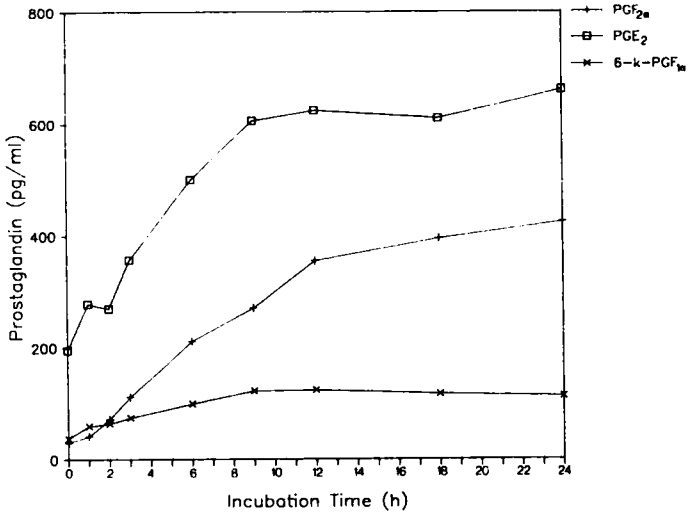

FIG. 3. Concentrations of prostaglandins (PGs) in medium as a function of time. Luteal cells (50,000 cells/tube) were incubated at 37°C for times of 0–24 h (n=3). The standard errors of the means from the models used to analyze the data were 110.59 for $PGF_{2\alpha}$ concentrations and 57.91 for PGE_2 concentrations. There was a linear increase in $PGF_{2\alpha}$ ($p<0.05$), PGE_2 ($p<0.05$) and 6-keto-$PGF_{1\alpha}$ within the first 6–12 h, and a plateau for the remaining 24 h. The pattern of 6-keto-$PGF_{1\alpha}$ includes only one corpus luteum because concentrations generated in medium by the other two were nondetectable until 24 h.

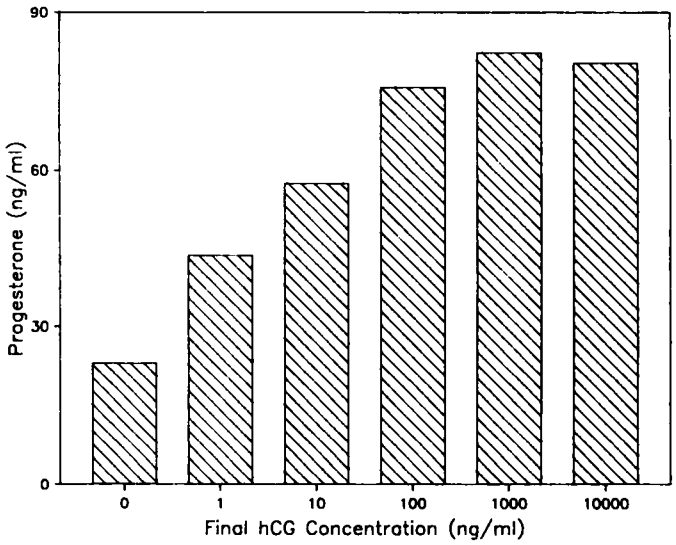

FIG. 5. Concentrations of progesterone in medium as a function of dose of human chorionic gonadotropin (*bCG*). Luteal cells (50,000 cells/tube) were incubated at 37°C for 6 h in the presence and absence of various doses of hCG (n=3). The standard error of the means from the model used was 20.93. Progesterone production increased in a dose-dependent manner ($p<0.05$). Maximal response was achieved at a final concentration of 100 ng/ml hCG.

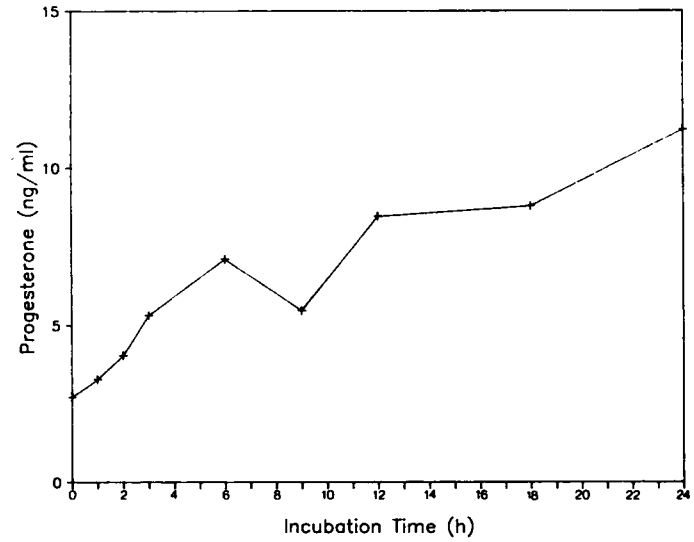

FIG. 4. Concentrations of progesterone in medium as a function of time. Luteal cells (50,000 cells/tube) were incubated at 37°C for times of 0–24 h (n=3). The standard error of the means from the model used to analyze the data was 2.44. Concentrations of progesterone increased ($p<0.05$) linearly the first 6–12 h and plateaued for the remaining 24 h.

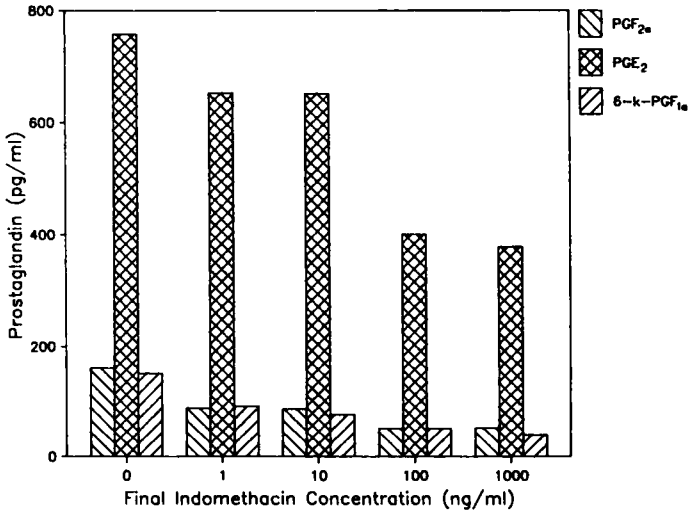

FIG. 6. Concentrations of prostaglandins (PGs) in medium as a function of dose of indomethacin. Luteal cells (50,000 cells/tube) were incubated at 37°C for 6 h in the presence and absence of various doses of indomethacin (n=3). The standard errors of the means from the models used to analyze the data were 17.68 for $PGF_{2\alpha}$ concentrations, 79.66 for PGE_2 concentrations, and 35.50 for *6-keto-*$PGF_{1\alpha}$ concentrations. Indomethacin decreased concentrations of PGs in a dose-dependent manner ($p<0.05$). Concentrations of PGs in tubes containing the highest doses of indomethacin did not exceed those at Time 0 (i.e. prior to incubation, n=2).

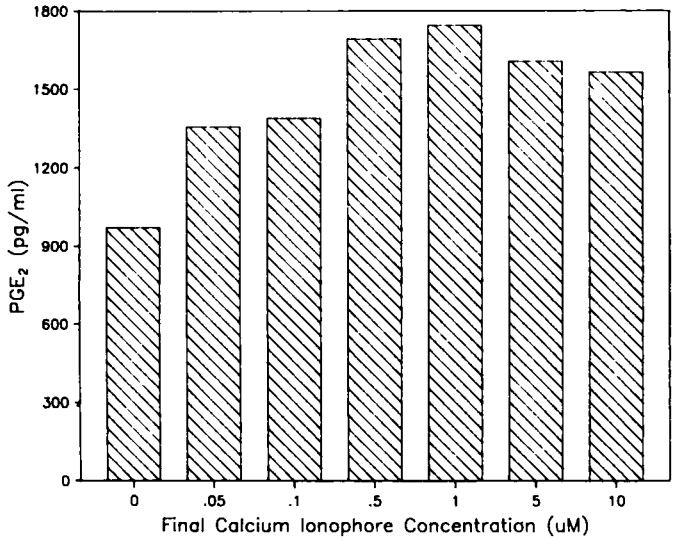

FIG. 7. Concentrations of prostaglandin (PG) E_2 in medium as a function of dose of calcium ionophore. Luteal cells (50,000 cells/tube; n=4) were incubated at 37°C for 8 h with increasing concentrations of calcium ionophore (A23187). The standard error of the means from the model used to analyze the data was 125.15. Calcium ionophore increased concentrations of PGE_2 in a dose-dependent manner ($p<0.01$).

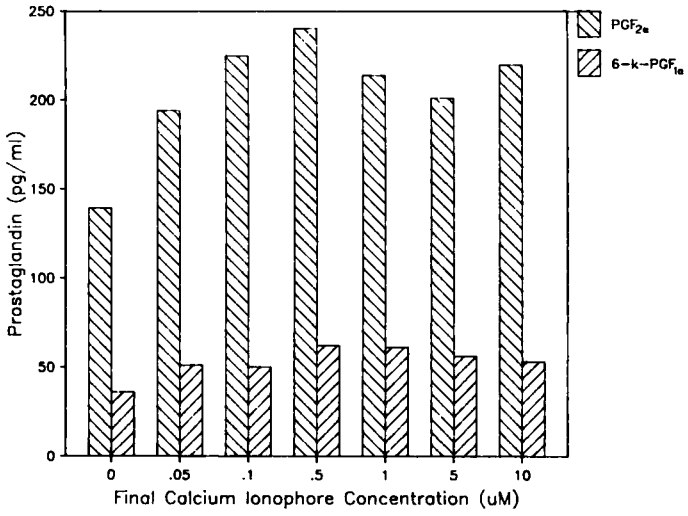

FIG. 8. Concentrations of prostaglandin (PG) $F_{2\alpha}$ and 6-keto-$PGF_{1\alpha}$ in medium as a function of dose of calcium ionophore. Luteal cells (50,000 cells/tube; n=4) were incubated at 37°C for 8 h with increasing concentrations of calcium ionophore (A23187). The standard errors of the means from the models used to analyze the data were 37.10 for $PGF_{2\alpha}$ concentrations and 6.06 for 6-keto-$PGF_{1\alpha}$ concentrations. Calcium ionophore increased concentrations of $PGF_{2\alpha}$ and 6-keto-$PGF_{1\alpha}$ ($p<0.05$) in a dose-dependent manner.

dose-response patterns prevented the demonstration of statistically significant differences ($p<0.05$) between treatments.

DISCUSSION

In the present study, the conditions that permit quantification of PG production by CL of rhesus monkeys have been established. Conditions detailed include the concentrations of luteal cells suitable for evaluating the synthesis of PGs and the incubation time required for production of measurable amounts of PGs. Our observations of the luteotropic effect of hCG in the current study, as well as the pattern of progesterone production by luteal cells over time, agree with the results of others (Stouffer et al., 1976; Hoyer and Niswender, 1985). These similarities support the validity of the incubation system used here.

Since cells and medium were frozen after incubation, probably causing substantial cell lysing, the value at time 0 (0 h) essentially represented the content of PGs and progesterone in cytoplasm and medium. The significant increase in concentrations of PGs and progesterone in medium during incubation suggested that the dispersed cells were producing these compounds. In addition, the inhibitory effect of indomethacin upon PG production was clearly evident in our study. Prostaglandin $F_{2\alpha}$, PGE_2, and 6-keto-$PGF_{1\alpha}$ concentrations all decreased with increasing doses of indomethacin (Fig. 6). The higher doses of indomethacin prevented any increase in concentrations of PGs above the levels prior to incubation. Since indomethacin is a known inhibitor of PG synthesis, this observation further substantiates the notion that actual synthesis occurred.

Incubation of luteal cells in the presence of calcium ionophore elevated concentrations of PGs in medium. Since calcium ionophore has been shown to stimulate PG synthesis by other cell types (Laychock and Putney, 1982), the increase in PGs in medium was probably due to an elevation in luteal synthesis of PGs. Thus, this observation solidifies the idea that PGs are produced by the macaque CL. Indeed, the actions of known inhibitors and stimulators of PG production were verified in this system. This supports the notion that we examined production of bona fide PGs and not other immunoreactive substances.

Production of $PGF_{2\alpha}$ by the mid-luteal phase CL used in the current study was generally higher than that of 6-keto-$PGF_{1\alpha}$, and production of PGE_2 was highest of all. Similarly, concentrations of PGE_2 were higher than those of $PGF_{2\alpha}$ in medium incubated with young CL from rhesus monkeys, although this difference had diminished by the mid-luteal phase

and was reversed in older CL (Balmaceda et al., 1979). In addition, PGE_2 production by human luteal tissue was higher than that of $PGF_{2\alpha}$ (Challis et al., 1976). Thus, the current data are consistent with similar measurements of primate luteal PGs in other studies. Primate CL differ from those of other species in this regard. Production of PGF by mid-luteal phase porcine CL predominated over that of PGE (Guthrie et al., 1978), and production of 6-keto-$PGF_{1\alpha}$ by mid-luteal phase bovine CL predominated over that of $PGF_{2\alpha}$ (Milvae and Hansel, 1983).

The lack of an acute effect of various steroids on PG production may be partially attributed to the short amount of exposure of the luteal cells to these hormones in vitro. Chronic exposure to progesterone in sheep, for example, is necessary to increase uterine $PGF_{2\alpha}$ production (Ottobre et al., 1984). In addition, progesterone modulates PG synthesis by bovine luteal cells in a long-term culture system (Pate, 1987). With regard to the role of estrogen on luteal function, there is increasing doubt that estrogen acts directly on the CL of the rhesus monkey (Hutchison et al., 1987). An acute and direct action of estrogen on the macaque CL is also argued against in the current study. Estrogen, testosterone (a substrate for estrogen synthesis), and ATD (an estrogen-synthesis inhibitor) were without effect on luteal production of PGs and progesterone. The lack of effect of estrogen at the level of the macaque CL is further corroborated by the absence of luteal estrogen receptors in this species (Hild-Petito et al., 1988).

When considering the potential role of luteal PGs in the regulation of luteal function, it is helpful to evaluate progesterone production in the presence and absence of a blockade of luteal PG synthesis. Progesterone production was unaltered during treatments with indomethacin, suggesting that blocking luteal PG synthesis does not alter luteal progesterone production acutely. Similarly, Pate and Condon (1984) found no acute effect of indomethacin on progesterone production by cultured bovine luteal cells. After a few days of culture with indomethacin, however, progesterone production by luteal cells was elevated. This elevation was blocked with $PGF_{2\alpha}$. Thus, the effects of luteal PGs on function of the CL may be difficult to demonstrate in acute studies. In in vivo studies, orally administered indomethacin did not alter progesterone production during the luteal phase of nonpregnant rhesus monkeys (Manaugh and Novy, 1976), but luteal infusion of meclofenamic acid, another PG-synthesis inhibitor, resulted in premature luteolysis (Sargent and Stouffer, 1987). Thus, chronic inhibition of luteal PG synthesis may reduce production of luteotropic and/or luteolytic PGs. The nature of such effects may be dependent on the species tested and on the age of the CL at the time of treatment.

In summary, these studies substantiate that CL of rhesus monkeys are capable of synthesizing PGs. The steroids tested (estradiol-17β, testosterone, dihydrotestosterone, 1,4,6-androstatriene-3, 17-dione, and progesterone) and hCG did not influence PG production acutely. Further studies are necessary to identify and define the roles that luteal PGs may play in the regulation of the primate CL.

ACKNOWLEDGMENTS

The authors would like to acknowledge the technical and scientific contributions of Brenda Houmard. We also extend our thanks to Michelle Vernier for her help in preparing the manuscript.

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