Prostaglandin production by the rabbit uterus and placenta \textit{in vitro}\textsuperscript{*}

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\textbf{Summary.} Endogenous concentrations of prostaglandin (PG) F-2\(\alpha\) in the rabbit uterus were higher on Day 17 of pseudopregnancy than on Days 4, 7 and 11 of pseudopregnancy and Day 17 of pregnancy. These differences are consistent with the findings reported previously that the output of PGF-2\(\alpha\) from the rabbit uterus is higher on Day 17 of pseudopregnancy than on earlier days of pseudopregnancy and Day 17 of pregnancy. Uterine homogenates synthesized PGs and, of the 3 PGs measured, 6-oxo-PGF-1\(\alpha\) was the major product. There were no differences in the amounts of any one PG synthesized during pseudopregnancy. 'Unstretched' uterine tissue from Day-17-pregnant rabbits produced quantities of PGs similar to those of uterine tissue from Day-17-pseudopregnant rabbits. However, 'stretched' uterine tissue from Day-17-pregnant rabbits produced more 6-oxo-PGF-1\(\alpha\) and PGE-2, but not PGF-2\(\alpha\), than did 'unstretched' tissue or pseudopregnant uterine tissue from Day-17 rabbits. PG production by the fetal placenta was higher than that by the maternal placenta. PGE-2 and 6-oxo-PGF-1\(\alpha\) were the major PGs produced by the fetal and maternal placentae, respectively. Metabolism of PGF-2\(\alpha\) required NAD\textsuperscript{+} and metabolism by the placenta was greater than that by the uterus. Compounds less polar and more polar than PGF-2\(\alpha\) were produced, although the production of more polar metabolites appeared to require a period of progesterone priming of the uterus.

\textbf{Introduction}

Prostaglandin (PG) F-2\(\alpha\) concentrations in the uterine venous plasma of rabbits increase on Day 17 of pseudopregnancy, and the PGF-2\(\alpha\) released probably contributes to luteolysis (Lytton & Poyser, 1982). In pregnant rabbits, PGF-2\(\alpha\) concentrations in uterine venous plasma do not increase on Day 17 which may be beneficial for the maintenance of the corpora lutea (Lytton & Poyser, 1982). PGE-2 concentrations in the uterine venous plasma remain low throughout pseudopregnancy, but increase greatly after Day 11 in pregnant rabbits (Venuto, O'Dorisio, Stein & Ferris, 1975; Meese, Fischer, Hoffman & Frolich, 1980; Lytton & Poyser, 1982). In the present study, PG concentrations in and production \textit{in vitro} by the uterus on selected days of pseudopregnancy and on Day 17 of pregnancy have been measured, since such measurements in other species have indicated some of the biochemical processes which control PG production by the uterus (see Horton & Poyser, 1976). PG production by the Day 17 placenta, and metabolism of PGF-2\(\alpha\) by the uterus and placenta have also been investigated.

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Materials and Methods

Experiments

Experiment 1. New Zealand White rabbits (5 groups of 4 animals) received an intravenous injection of 0.5 ml saline (9 g NaCl/l, Group 1) or 500 i.u. hCG (Organon Laboratories, Morden, U.K.; Groups 2–5) between 15:00 and 15:30 h, the day of injection for Groups 2–5 becoming Day 0 of pseudopregnancy. Group 1 (control) rabbits were killed, by stunning and incising the neck, the day after injection, and rabbits in Groups 2, 3, 4 and 5 were killed on Days 4, 7, 11 and 17 of pseudopregnancy, respectively. Immediately after killing the uterus and ovaries in each rabbit were exposed, and the ovaries were inspected for the presence of corpora lutea. The two uterine horns were removed and were placed in ice-cold Krebs' solution (for composition see Mitchell, Wilson & Poyser, 1977). Each uterine horn was opened longitudinally and cut into ~1 g segments. Three segments taken at random were blotted dry and weighed; the remaining tissue was used in Exp. 4.

Segment 1 was homogenized in 15 ml absolute ethanol, and the prostaglandins extracted as described for the rat uterus (Poyser & Scott, 1980). Segments 2 and 3 were each homogenized in 15 ml Krebs' solution and incubated in the absence (segment 2) or presence (segment 3) of 75 µg exogenous arachidonic acid for 90 min at 37°C. Prostaglandins formed were extracted with ethyl acetate and then stored as described previously (Mitchell et al., 1977; Fenwick, Jones, Naylor, Poyser & Wilson, 1977). The amounts of PGF-2α, PGE-2 and 6-oxo-PGF-1α in all extracts were measured.

Experiment 2. Four female New Zealand White rabbits (Group 6) of proven fertility were mated with fertile male rabbits, the day of mating becoming Day 0 of pregnancy. The rabbits were killed on Day 17 and the two uterine horns were removed as in Exp. 1. Each uterine horn was opened longitudinally and the number of fetuses noted. The placental and fetal tissues in each horn were removed, and the placental tissue was placed in ice-cold Krebs' solution for use in Exps 3 and 4. The uterine tissue appeared to be of two types: tissue which had surrounded the fetus had a 'stretched' appearance and an apparently thin layer of endometrium, while uterine tissue from between the fetuses appeared 'unstretched' and had a thicker endometrium. There was no apparent difference in the thickness of myometrium between the two locations. The uterine tissue was therefore divided into 'stretched' and 'unstretched' types. After blotting dry and weighing, one segment of each type was homogenized in 15 ml absolute ethanol. A second segment of each type was homogenized in 15 ml Krebs' solution and incubated, without addition of exogenous arachidonic acid, for 90 min at 37°C. PGs were extracted and assayed as in Exp. 1.

Experiment 3. Placentae from rabbits in Exp. 2 were freed of uterine tissue and the embryonic sac with its contents. Two segments of placenta from each rabbit were treated as in Exp. 2. In 3 rabbits, there was sufficient placental tissue for segments consisting solely of maternal and fetal types to be obtained. Two segments of each placentical type were treated as in Exp. 2. PGs were extracted and assayed as in Exp. 1.

Experiment 4. Segments of uterus and, when pregnant, of whole placenta from rabbits in Exps 1 and 2 were blotted dry, weighed and each homogenized in 15 ml Krebs' solution. Nicotinamide-adenine dinucleotide (NAD⁺; 2 mM), 0.5 µCi [3H]PGF-2α (sp. act. 160 Ci/mmoll; Amersham International, U.K.) and 10 µg PGF-2α were added to each homogenate, and all homogenates were incubated for 90 min at 37°C. Additional homogenates of uterus and of placenta were prepared and treated as above except that no NAD⁺ was added. After incubation, all homogenates were extracted as in Exp. 1. Each dried extract was dissolved in 0.2 ml methanol and analysed by thin-layer chromatography by methods previously described (Maule Walker & Poyser, 1978). The percentage metabolism of [3H]PGF-2α by rabbit uterus and placenta was calculated as for the guinea-pig uterus (Poyser, 1979).
A reference plate onto which had been spotted 10 \( \mu g \) of each of PGF-2\( \alpha \), 15-oxo-PGF-2\( \alpha \) and 13,14-dihydro-15-oxo-PGF-2\( \alpha \) was similarly analysed and the \( R_F \) values of these compounds were calculated.

**Assay procedures**

PGF-2\( \alpha \), PGE-2 and 6-oxo-PGF-1\( \alpha \) were measured by radioimmunoassays using antibodies raised in this department and whose cross-reactivities have been reported elsewhere (Dighe, Emslie, Henderson, Rutherford & Simon, 1975; Dighe, Jones & Poyser, 1978; Poyser & Scott, 1980; Lytton & Poyser, 1982). The PGF-2\( \alpha \) antibodies do not distinguish between PGF-2\( \alpha \) and PGF-1\( \alpha \), but have low cross-reactivities with other PGs. The limit of detection was 24 pg PGF-2\( \alpha \)/tube. The PGE-2 antibodies cross-react significantly with PGE-1 (100\%) and PGB-2 (260\%), but have low cross-reactivities with other PGs. The detection limit was 40 pg PGE-2/tube. The 6-oxo-PGF-1\( \alpha \) antibodies have low cross-reactivities with all PGs. The limit of detection was 50 pg 6-oxo-PGF-1\( \alpha \)/tube.

For each assay, two different volumes of each extract were assayed in triplicate. The intra-assay coefficients of variation, calculated from the triplicate results obtained, were 7.8\% (PGF-2\( \alpha \)), 8.5\% (PGE-2) and 9.0\% (6-oxo-PGF-1\( \alpha \)). The inter-assay coefficients of variation, calculated from the results obtained by incorporating 250 pg PGF-2\( \alpha \), 350 pg PGE-2 or 200 pg 6-oxo-PGF-1\( \alpha \) into the respective assays, were 7.9\% (PGF-2\( \alpha \)), 8.7\% (PGE-2) and 12.0\% (6-oxo-PGF-1\( \alpha \)).

**Analysis by gas chromatography and mass spectrometry**

After assaying the samples in Exp. 1 by RIA, sufficient material remained for further qualitative analysis by gas chromatography and mass spectrometry (GC–MS). Extracts of uterus incubated in the absence or presence of added arachidonic acid were pooled separately so as to produce two combined extracts. Authentic and extracted PGs were converted into methyl ester butyloximes (for keto group-containing PGs only), trimethylsilyl ethers as described by Fenwick et al. (1977). Then 500 ng \(^{3}H\)6-oxo-PGF-1\( \alpha \) were added to each sample of authentic or extracted PG before derivatization as an internal standard. The instrument, the conditions used and the analysis of the extracts for PGF-2\( \alpha \), PGF-1\( \alpha \), PGE-2, PGE-1, PGD-2 and 6-oxo-PGF-1\( \alpha \) were the same as described previously (Lytton & Poyser, 1982). Each extract was also analysed a second time for the presence of PGB-2 by monitoring the ions at \( m/\ell \) values of 321 and 349, and for PGE-2 by monitoring the ion at 295.

**Statistical tests**

The results for PG concentrations in and production by the uterus during pseudopregnancy were analysed by Duncan's multiple range test. However, the variances of the results for the concentrations of PGF-2\( \alpha \) and PGE-2 in the uterus on Day 17 were significantly higher, by the variance ratio (F) test, than the respective overall variance of the results on the other days. Consequently, these PGF-2\( \alpha \) and PGE-2 results for Day 17 were omitted from the multiple range test, and were compared with the PGF-2\( \alpha \) and PGE-2 results for the other days separately by the Wilcoxon rank sum test.

The effect of adding exogenous arachidonic acid on PG production by the uterus was analysed by the paired \( t \) test. All other comparisons were performed using Student's \( t \) test, after checking for homogeneity of variance by the variance ratio (F) test. If the variances were unequal, a modified \( t \) test was used (see Steel & Torrie, 1980).
Results

Experiment 1

Inspection of the ovaries from rabbits in Groups 2–5 showed that corpora lutea were present in both ovaries of all rabbits, confirming that these rabbits were pseudopregnant. The analysis by GC-MS of extracts of uterine tissue incubated in the absence or presence of added arachidonic acid showed that both pooled extracts contained PGF-2α, PGE-2, 6-oxo-PGF-1α and PGD-2. PGB-2, PGE-1 and PGF-1α were not detected.

The endogenous concentrations of PGF-2α in the uterus (i.e. the amounts in the ethanolic extracts) were slightly but significantly higher ($P < 0.05$) in Group 4 (Day 11) and Group 1 (non-pseudopregnant) than in Group 2 (Day 4) and Group 3 (Day 7). However, the endogenous concentration of PGF-2α was much higher in the uterus of Group 5 (Day 17) rabbits than in the uterus of rabbits in the other 4 groups ($P < 0.05$; Text-fig. 1). The endogenous concentrations of PGE-2 in the uterus showed no significant variation amongst the rabbits in the 5 groups, although the mean value for Day 17 (Group 5) was higher than for the other days.

The endogenous concentrations of 6-oxo-PGF-1α in the uterus were significantly higher ($P < 0.05$) in Groups 1 (non-pseudopregnant) and 5 (Day 17) than in Group 2 (Day 4), but were not significantly different from Groups 3 (Day 7) and 4 (Day 11). The major endogenous PG present in the uterus was 6-oxo-PGF-1α, except for Group 5 (Day 17) in which PGF-2α was present in the greatest quantities.

Text-fig. 1. Mean ($\pm$ s.e.m., $n = 4$) endogenous concentration in or production by the rabbit uterus (ng/100 µg tissue) of prostaglandin (PG) F-2α, PGE-2 and 6-oxo-PGF-1α from non-pseudopregnant controls (Group 1), Days 4, 7, 11 and 17 of pseudopregnancy (Groups 2–5, respectively) and Day 17 of pregnancy (Group 6). (See text for significant differences.)
Uterine tissue from all rabbits, incubated in the absence of exogenous arachidonic acid, synthesized PGs, and 6-oxo-PGF-1α was the major PG formed (Text-fig. 1). The amounts of PGF-2α, PGE-2 and 6-oxo-PGF-1α formed per unit weight of tissue did not vary significantly among the 5 groups of rabbits, except that PGF-2α production was significantly higher \((P < 0.05)\) in Group 5 (Day 17) than in Group 1 (non-pseudopregnant). The addition of exogenous arachidonic acid did not affect PG production by the rabbit uterus, except for significant increases \((P < 0.05)\) in PGF-2α, PGE-2 and 6-oxo-PGF-1α production in Group 1 (non-pseudopregnant) and in PGF-2α production in Group 2 (Day 4).

**Experiment 2**

Uterine tissue in Exp. 1 did not produce PGB-2, and it is therefore probable that pregnant uterine tissue also did not produce PGB-2, especially as no biosynthetic pathway for the conversion of arachidonic acid to PGB-2 has been reported. It was therefore assumed that PGB-2 was not interfering with the assay of PGE-2 in this experiment or in Exp. 3.

The endogenous concentrations of PGF-2α, PGE-2 and 6-oxo-PGF-1α did not differ between ‘stretched’ and ‘unstretched’ uterine tissue from Day-17-pregnant rabbits (Group 6, Text-fig. 1). The endogenous concentration of PGF-2α, but not of PGE-2 or 6-oxo-PGF-1α, in both types of uterine tissue from pregnant rabbits (Group 6) was significantly lower \((P < 0.05)\) than that in tissue from Day-17 pseudopregnant animals (Group 5). Homogenates of pregnant uterine tissue of both types synthesized PGs during incubation, with 6-oxo-PGF-1α being the major PG formed (Text-fig. 1). PGF-2α production by ‘stretched’, ‘unstretched’ and Day-17-pseudopregnant uterine tissue did not differ significantly. PGE-2 and 6-oxo-PGF-1α production by ‘unstretched’ and Day-17-pseudopregnant uterine tissue also did not differ significantly. However, production of PGE-2 and 6-oxo-PGF-1α was significantly higher \((P < 0.05)\) from ‘stretched’ than from ‘unstretched’ or Day-17-pseudopregnant uterine tissue.

**Experiment 3**

Endogenous concentrations of PGF-2α, PGE-2 and 6-oxo-PGF-1α in Day 17 whole placenta were low, with PGE-2 being present in the greatest quantities (Table 1). Homogenates of whole placenta synthesized PGs, and PGE-2 was synthesized in significantly greater quantities \((P < 0.05)\) than PGF-2α or 6-oxo-PGF-1α.

**Table 1.** Mean \((±\text{ s.e.m., } n = 3 \text{ or } 4)\) endogenous concentration in or production by the placenta of prostaglandin (PG) F-2α, PGE-2 and 6-oxo-PGF-1α from Day-17-pregnant rabbits (see text for significant differences).

<table>
<thead>
<tr>
<th>Tissue</th>
<th>PGF-2α</th>
<th>PGE-2</th>
<th>6-oxo-PGF-1α</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endogenous</td>
<td>Produced</td>
<td>Endogenous</td>
</tr>
<tr>
<td>Whole placenta</td>
<td>3.4 ± 0.7</td>
<td>79.9 ± 8.0</td>
<td>8.0 ± 2.2</td>
</tr>
<tr>
<td>Maternal placenta</td>
<td>1.5 ± 0.4</td>
<td>31.8 ± 4.4</td>
<td>9.6 ± 3.7</td>
</tr>
<tr>
<td>Fetal placenta</td>
<td>2.7 ± 0.1</td>
<td>264.4 ± 77.7</td>
<td>51.6 ± 12.9</td>
</tr>
</tbody>
</table>

The endogenous concentrations in and productions by the maternal placenta of PGF-2α, PGE-2 and 6-oxo-PGF-1α were significantly lower \((P < 0.05)\) when compared to the fetal placenta (Table 1). In both tissue types, the endogenous concentrations of PGE-2 were significantly higher \((P < 0.05)\) than the endogenous concentrations of PGF-2α or 6-oxo-PGF-1α. PGE-2 was produced by homogenates of fetal placenta during incubation in significantly
greater amounts ($P < 0.05$) than were PGF-2α or 6-oxo-PGF-1α, whereas 6-oxo-PGF-1α was produced in significantly greater amounts ($P < 0.05$) by the maternal placenta. On average, the fetal placenta produced 18 times more PGE-2, 8 times more PGF-2α and twice as much 6-oxo-PGF-1α than did the maternal placenta.

Experiment 4

The $R_F$ values of authentic PGF-2α, 15-oxo-PGF-2α and 13,14-dihydro-15-oxo-PGF-2α were 0.33, 0.51 and 0.57, respectively.

Uterine homogenates from pseudopregnant and pregnant rabbits metabolized [3H]PGF-2α, in the presence of NAD+, into two less polar metabolites having the same $R_F$ values as 15-oxo-PGF-2α and 13,14-dihydro-15-oxo-PGF-2α. Due to their close proximity, these metabolites were not separated for counting purposes. Pseudopregnant uteri from Day 7 onwards, and Day-17-pregnant uteri also converted [3H]PGF-2α into a more polar metabolite of $R_F$ value 0.16. Total metabolism of [3H]PGF-2α by the uterus, in the presence of NAD+, was 30–40%, but as the percentage metabolism to the more polar metabolite increased, the percentage metabolism to the less polar metabolites decreased (Table 2).

<table>
<thead>
<tr>
<th>Group</th>
<th>% Production of metabolites at $R_F$ value</th>
<th>Total metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.16</td>
<td>0.24</td>
</tr>
<tr>
<td>1</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>3</td>
<td>13.5 ± 2.1</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>27.2 ± 12.9</td>
<td>n.d.</td>
</tr>
<tr>
<td>5</td>
<td>19.5 ± 1.0</td>
<td>n.d.</td>
</tr>
<tr>
<td>6 (uterus)</td>
<td>16.0 ± 3.0</td>
<td>n.d.</td>
</tr>
<tr>
<td>6 (placenta)</td>
<td>14.2 ± 0.2</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

n.d., not detectable.

* Significantly different from other values in this column ($P < 0.05$).

Total metabolism of [3H]PGF-2α by the whole placenta was significantly greater ($P < 0.05$) than that by the uterus (Table 2). The same metabolites were produced, except that an additional more polar metabolite of $R_F$ value 0.24 was produced by the placenta.

Homogenates of uterus and placenta to which no NAD+ was added failed to metabolize [3H]PGF-2α since all the radioactivity was recovered as a single compound of $R_F$ value 0.33.

Discussion

Towards the end of the oestrous cycle in the sheep, guinea-pig and cow and of pseudopregnancy in the rat, the concentrations of PGF-2α in the uterus increase (Wilson, Cenedella, Butcher & Inskeep, 1972; Poyser, 1972; Shemesh & Hansel, 1975; Doebler, Wickersham & Anthony, 1981), and are coincident with an increase in PGF-2α concentrations in the uterine venous drainage (Bland, Horton & Poyser, 1971; McCracken, Carlson, Glew, Goding, Baird, Gréen & Samuelsson, 1972; Blatchley, Donovan, Horton & Poyser, 1972; Shemesh & Hansel, 1975; Weems, 1979). Similarly, the present study has shown that the concentration of PGF-2α in
the pseudopregnant rabbit uterus is higher on Day 17 than on earlier days of pseudopregnancy, and that this increase is coincident with the increase in PGF-2α concentrations in the uterine venous plasma (Lytton & Poyser, 1982). In addition, the PGF-2α concentration in the Day 17 pregnant rabbit uterus is lower than that in the Day-17-pseudopregnant rabbit uterus, reflecting the low output of PGF-2α from the pregnant uterus at this time (Lytton & Poyser, 1982).

Metabolism of PGF-2α by the uterus and placenta was not detected in the absence of NAD+. As the same enzymes and co-factors are involved in the metabolism of other PGs, PG production during the incubation of uterine and placental tissue reflects PG synthesis. In the guinea-pig (Poyser, 1972; Wlodawer, Kindahl & Hamberg, 1976) and sheep (Alwachi, Bland & Poyser, 1979; Huslig, Fogwell & Smith, 1979), the increase in uterine venous plasma concentration and uterine tissue concentration of PGF-2α are associated with an increase in uterine PG synthetase levels. However, in the present study, PG production by the uterus was no higher on Day 17 than on earlier days of pseudopregnancy, indicating that PG synthetase levels in rabbit uterus, like those in the rat (Fenwick et al., 1977), do not increase at the end of pseudopregnancy. These differences may be related to the fact that hysterectomy prolongs the life-span of the corpus luteum to a much greater extent in cyclic sheep and guinea-pigs than in pseudopregnant rabbits and rats (see Anderson, Bland & Melampy, 1969). Failure of luteal regression, due to an underproduction of PGF-2α by the uterus, would therefore more seriously affect subsequent fertility in sheep and guinea-pigs than in rabbits and rats, and the increase in the PGF-2α synthesizing ability of the uterus in sheep and guinea-pigs makes this failure less likely to occur.

The major PG synthesized by the uterus was 6-oxo-PGF-1α (reflecting PGI-2 production). A similar finding has been reported for uterine tissue of rats, sheep and women (Fenwick et al., 1977; Jones, Poyser & Wilson, 1977; Abel & Kelly, 1979), although it is probable that, in the rabbit, the myometrium is the major source of 6-oxo-PGF-1α and the endometrium the major source of PGF-2α, as in the three species above (Williams, Dembinskakiec, Zmuda & Gryglewski, 1978; Abel & Kelly, 1979; Alwachi, Bland & Poyser, 1980). The specific increase in the endogenous concentration of PGF-2α in the rabbit uterus on Day 17 of pseudopregnancy is therefore probably due to a specific increase in PGF-2α synthesis by the endometrium.

‘Stretched’ and ‘unstretched’ pregnant uterus and the pseudopregnant uterus from Day 17 rabbits synthesized similar quantities of PGF-2α. However, ‘stretched’ uterine tissue synthesized more PGF-2α and 6-oxo-PGF-1α than did ‘unstretched’ or pseudopregnant uterine tissue on Day 17. These increases may be related to the close proximity of ‘stretched’ uterine tissue to the developing fetus, but the reason for differences in PG production by different areas of tissue in the pregnant uterus is not known.

Homogenates of whole placenta synthesized PGE-2, PGF-2α and 6-oxo-PGF-1α in the ratio of 3:5:1:1. However, the fetal and maternal components of the placenta had a different spectrum of PG production. PGE-2, PGF-2α and 6-oxo-PGF-1α were synthesized in the ratios of 5:3:2:5:1 and 1:1:2 by the fetal and maternal placentae, respectively. Total production of these 3 PGs by the fetal placenta was 7 times higher than that by the maternal placenta. PGE-2 concentrations in the uterine venous blood of pregnant rabbits increase after Day 11 and are positively correlated with the number of fetuses in the uterine horn (Lytton & Poyser, 1982). The fetal placenta may be the source of this PGE-2 because, of the tissues investigated, this had the highest capacity to synthesize PGE-2, although the increase in PGE-2 production by ‘stretched’ uterine tissue may also be of importance in this respect. The relatively high endogenous concentration of PGE-2, compared to those of the two other PGs in the maternal placenta, may indicate that the maternal placenta is also producing PGE-2 in vivo, or, more likely, is indicative of large quantities of PGE-2 passing from the fetal side to the maternal side of the placenta. Rabbits immunized against PGE-2 and made pregnant die after mid-pregnancy (Elzayat & Stylos, 1974). The effect of the antibodies is on the placenta, which indicates the importance of PGE-2, probably produced locally, in placental function.
Whole placental tissue metabolized about 65% of the added [3H]PGF-2α, in the presence of NAD⁺, and 4 metabolites were formed. The two less polar metabolites had RF values corresponding to 15-oxo-PGF-2α and 13,14-dihydro-15-oxo-PGF-2α. The two more polar metabolites of PGF-2α at RF values of 0.16 and 0.24 were almost certainly 20-hydroxy-PGF-2α and 13,14-dihydro-15-oxo-20-hydroxy-PGF-2α (Powell & Solomon, 1978; Powell, 1980).

Total metabolism of [3H]PGF-2α by the uterus was approximately half that by the placenta. Uteri from non-pseudopregnant and early pseudopregnant rabbits only produced the less polar metabolites; uteri from animals later in pseudopregnancy and pregnancy also metabolized PGF-2α into 20-hydroxy-PGF-2α. As the proportion of this more polar metabolite formed increased, the proportion of the less polar metabolites formed decreased. The enzyme responsible for the conversion of PGF-2α to 20-hydroxy-PGF-2α is induced in rabbit lungs by pseudopregnancy and by progesterone administration (Powell, 1978, 1980). Progesterone secreted during pseudopregnancy and pregnancy may be responsible, therefore, for the induction of 20-hydroxylase PG activity in the uterus. The significance of the conversion of PGF-2α to 20-hydroxy-PGF-2α by the uterus and its control by progesterone is not known.

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References


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