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Hormones and growth factors A.S. Cole B.Sc., Ph.D., J.E. Eastoe D.Sc., Ph.D., F.D.S.R.C.S., D.I.C.A.R.C.S., in *Biochemistry and Oral Biology (Second Edition)*, 1988

Synthesis of prostaglandins The enzyme primarily responsible for the synthesis of prostaglandins is cyclooxygenase which converts arachidonic acid into endoperoxide intermediates (PGG and PGH) which are the immediate precursors not only of prostaglandins PGE and PGF but also of thromboxane and prostacyclin (Figure 24.10).

Physiology G.F.M. Ball, in *Encyclopedia of Food Sciences and Nutrition (Second Edition)*, 2003

Prostaglandin Synthesis The prostaglandins (PG) are a group of hormone-like lipids formed in the body from derivatives of essential fatty acids, particularly arachidonic acid (20:4n-6). Decidua expresses both synthesizing and some metabolizing enzymes, but little overall change occurs in the capacity for prostaglandin synthesis with labor, and the levels of PGHS-2 and PGE isomerase are much lower in decidua compared with levels in amnion and chorion (451,453). In myometrial samples obtained from the lower segment, some workers reported that there was no significant change in the levels of PGHS-1 or PGHS-2 during labor at term or preterm (463,464), whereas others found that PGHS-2 mRNA expression increased with advancing gestation but did not change further with labor (461,462). The high PGDH activity in chorion trophoblasts forms a metabolic barrier preventing the passage of prostaglandins generated in the amnion or chorion from reaching the underlying decidua or myometrium. It should be noted that PGHS-2 is required for production of PGI₂ (an inhibitory prostaglandin), as well as PGE₂ and PGF₂, and PGI synthase expression was found to decrease in the myometrium with advancing gestation, although there was no change in the expression of PGES (90). Furthermore, if regional differences in prostaglandin synthase activity occur at the time of labor, measurements made on tissue obtained from the lower segment may not be representative of changes observed in the fundal region. Also, in vitro studies with isolated human myometrial cells indicate that stretch can upregulate expression of PGI synthase, resulting in increased PGI₂ levels, but had no effect on PGE₂ or PGF₂. Prostaglandins have, potentially, very important applications in a wide range of clinical conditions, e.g. in the treatment of hypertension and thrombosis, as well as for contraception, the induction of abortions and the relief of asthma and peptic ulcers. It has been proposed that this deficiency might allow prostaglandins generated in amnion or chorion to pass unmetabolized to the underlying decidua and myometrium and provoke uterine contractility (456). Taken together, these studies would be consistent with a decrease in production of the inhibitory PGI₂ and a decrease in metabolism of prostaglandins, resulting in increases in local levels of stimulatory prostaglandins, in the myometrium during labor. The functionally prevalent form of PGHS that increases with advancing gestation and with labor at term and preterm is PGHS-2 (457), although increased levels of PGHS-1 mRNA were also found in the chorion at these times.

Parturition William Gibb, ... John R.G. Challis, in *Knobil and Neill's Physiology of Reproduction (Third Edition)*, 2006

Prostaglandin Synthesis. The cPLA₂ enzyme with its specificity for arachidonic acid-containing phospholipids is the most extensively studied phospholipase in relation to parturition. The cPLA₂ enzyme is expressed in the placenta, amnion, chorion, and myometrium, with the highest levels in the fetal membranes (437-439). At term, if the prostaglandins produced in the amnion and chorion are to access the myometrium, the synthetic activity of

amnion/chorion would need to exceed the metabolic potential of chorionic trophoblasts. The synthesis of prostaglandins The rate of PG production seems to be determined by the concentration of free essential fatty acids (page 123), chiefly arachidonic acid. PG synthesis is inhibited by anti-inflammatory agents such as aspirin, indomethacin and acetaminophen which inhibit cyclooxygenase. This effect occurs over the physiological range of vitamin C concentrations and is desirable because PGE1 is an inhibitor of platelet aggregation. PGE1 is also required for T lymphocyte formation, regulation of collagen and cholesterol metabolism, and regulation of responsiveness to insulin. sPLA2 levels are also elevated in maternal plasma and amniotic fluid in patients delivering preterm (445,446). In one study, sPLA2 and cPLA2 in the myometrium were unchanged with term or preterm labor (439), but others found that sPLA2 mRNA, although not cPLA2 mRNA, expression increased with gestational age and term labor in both the upper and lower segment of the myometrium (449). There is also a decrease in PGDH expression during labor in the region of the chorion overlying the cervix, and this may enable prostaglandins from the amnion and chorion to access the cervix (458). Studies on prostaglandin synthesis in myometrium during gestation are confusing, in part because of the difficulty in obtaining appropriate tissue for examination. In the baboon, the earliest change occurs with increased expression of PGHS-2 mRNA in the lower uterine segment and the cervix (467).