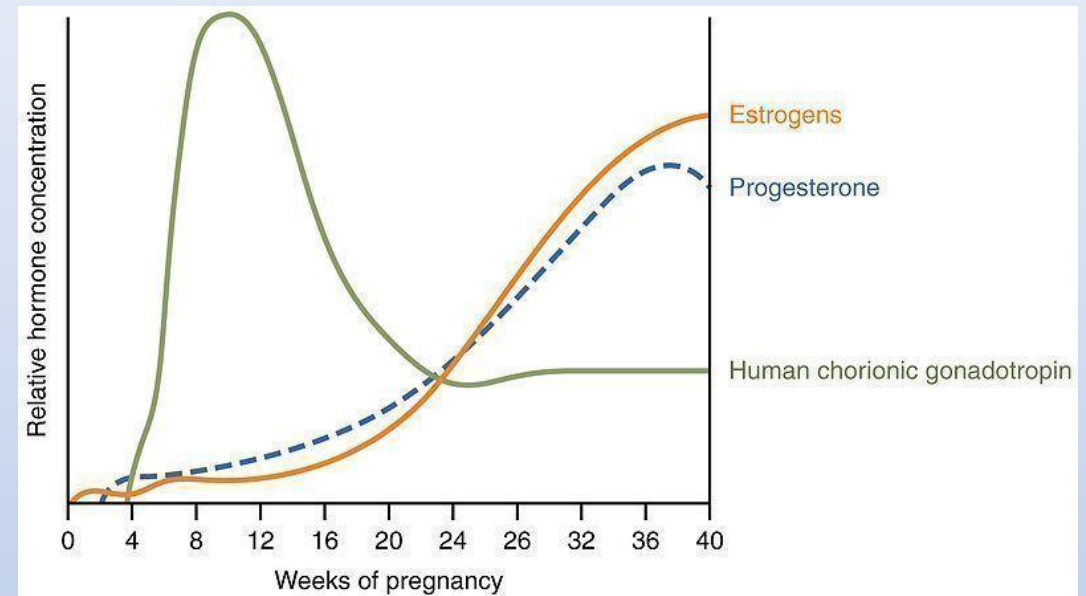


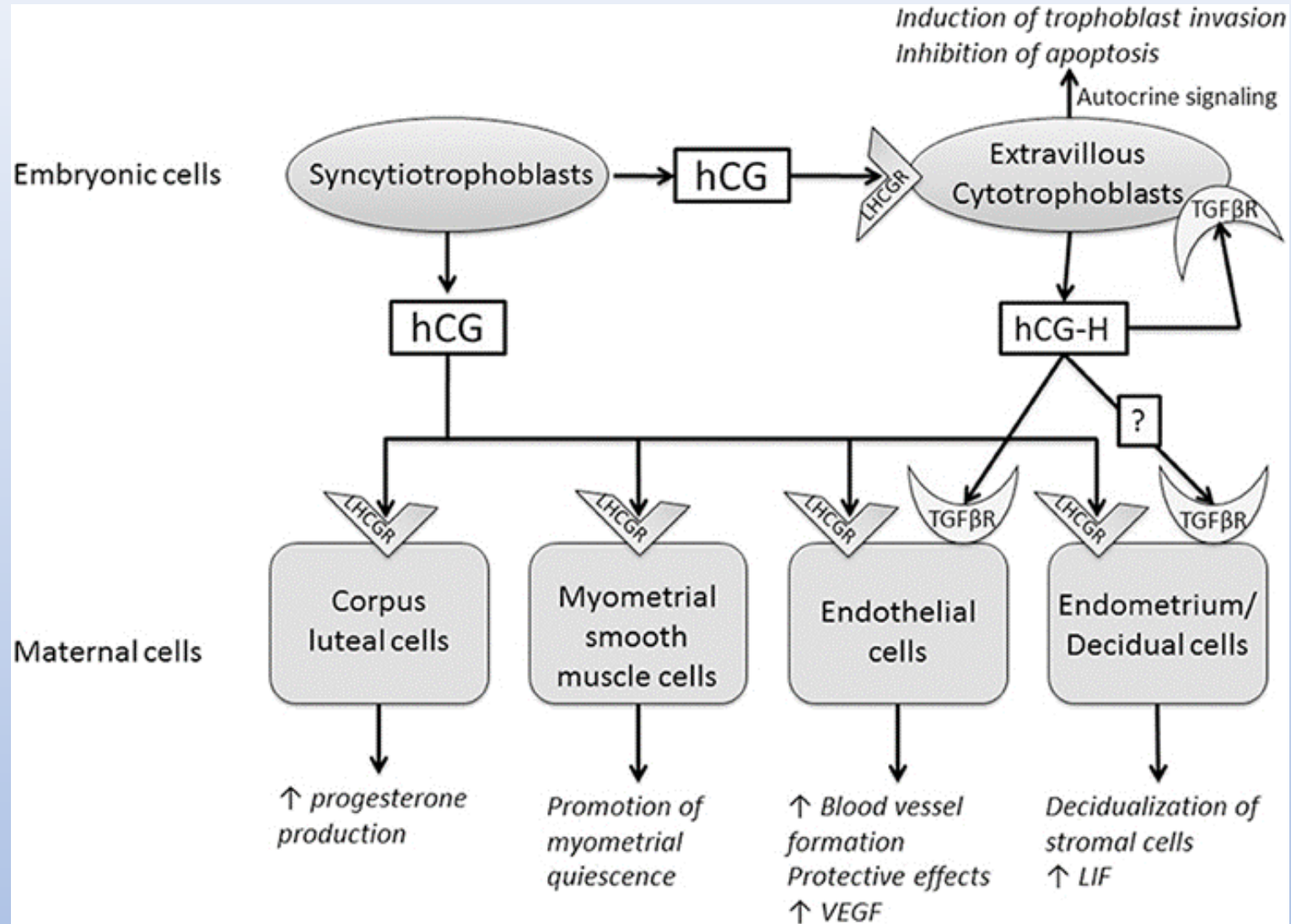
Parturition. Lactation.

Endocrine function of placenta - hCG

- Human chorionic gonadotropin
- First marker of trophoblast differentiation, first measurable product (blood plasma, 8 days after fertilization)
- Similarity with TSH, FSH, LH
- Functions:
 - Survival of the embryo
 - Progesterone secretion maintenance by the corpus luteum

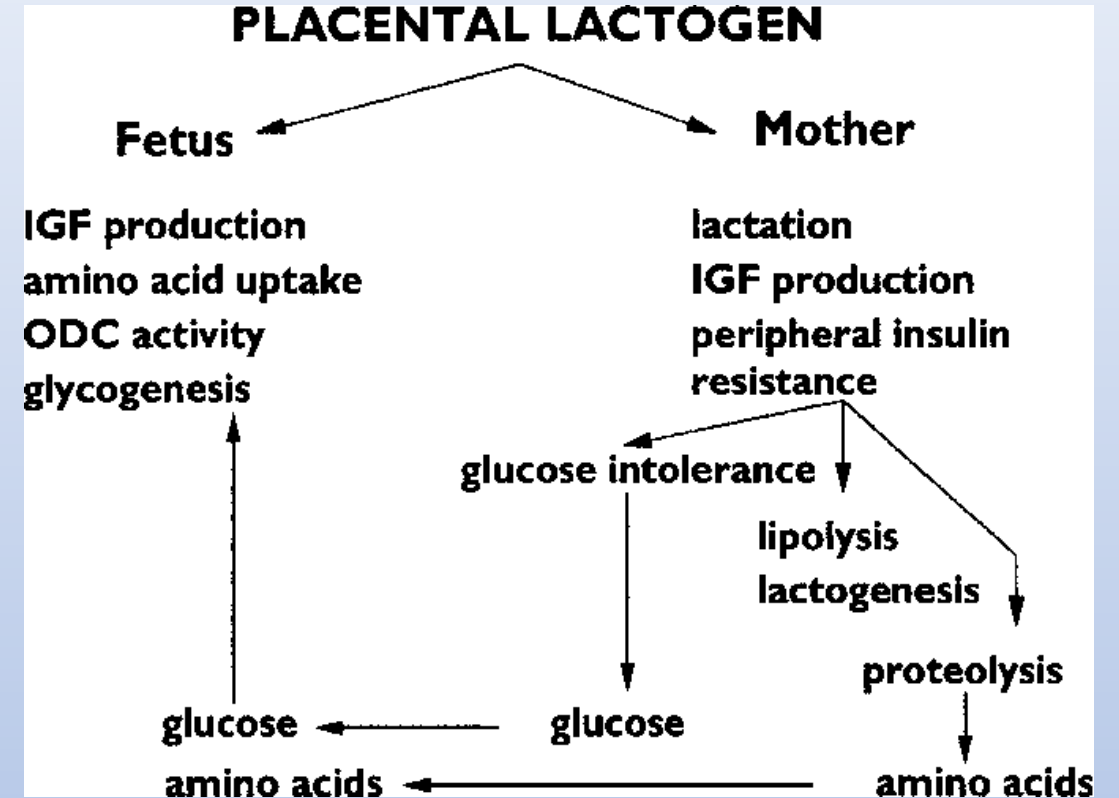


hCG - functions



Endocrine function of placenta - hPL

- Human placental lactogen (somatomammotropin)
- From 4 – 5 gestational weeks
- Similarity with GH and PRL
- Diabetogenic and lactogenic functions
- Minimal growth-promoting activity
- Secretion:
 - Prolonged fasting
 - HDL
 - Insulin-induced hypoglycemia
- Functions:
 - Maternal glucose metabolism (hyperglycemia)
 - Mobilization of FFA
 - Stimulation of insulin secretion
 - **Peripheral insulin resistance**



Endocrine function of placenta – placental growth hormone

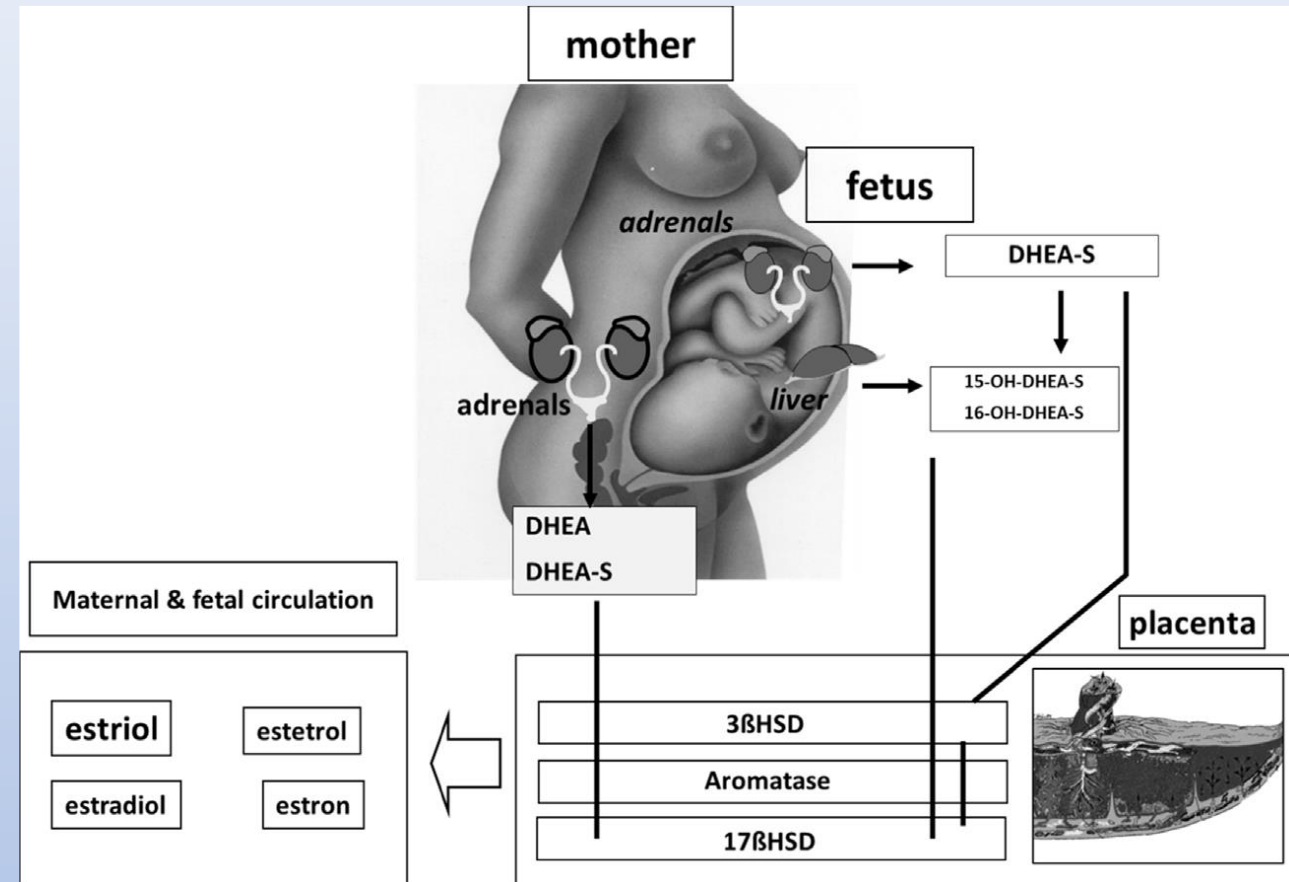
- Detectable at 15–20 gestation weeks
- Highest during third semester
- Secretion:
 - Hypoglycemia (+)
 - Leptin, insulin, cortisol (-)
- Functions:
 - GHR and PRLR
 - Enhancement of maternal IGF-1 synthesis
 - Metabolic regulations – promotion of gluconeogenesis, lipolysis and anabolism, increasing the nutrient availability for fetal nourishment

Endocrine function of placenta - progesterone

- Interconversions of steroids delivered from maternal or fetal precursors!
- Maternal cholesterol
- Establishment and maintenance of pregnancy
 - Attachement and implantation of embryo
 - Blocking effect on pro-proliferative estrogens
- Immunologic tolerance
- Inhibition of myometrium contractility
- Preparation of mammary gland to lactation
- Antagonization of PRL

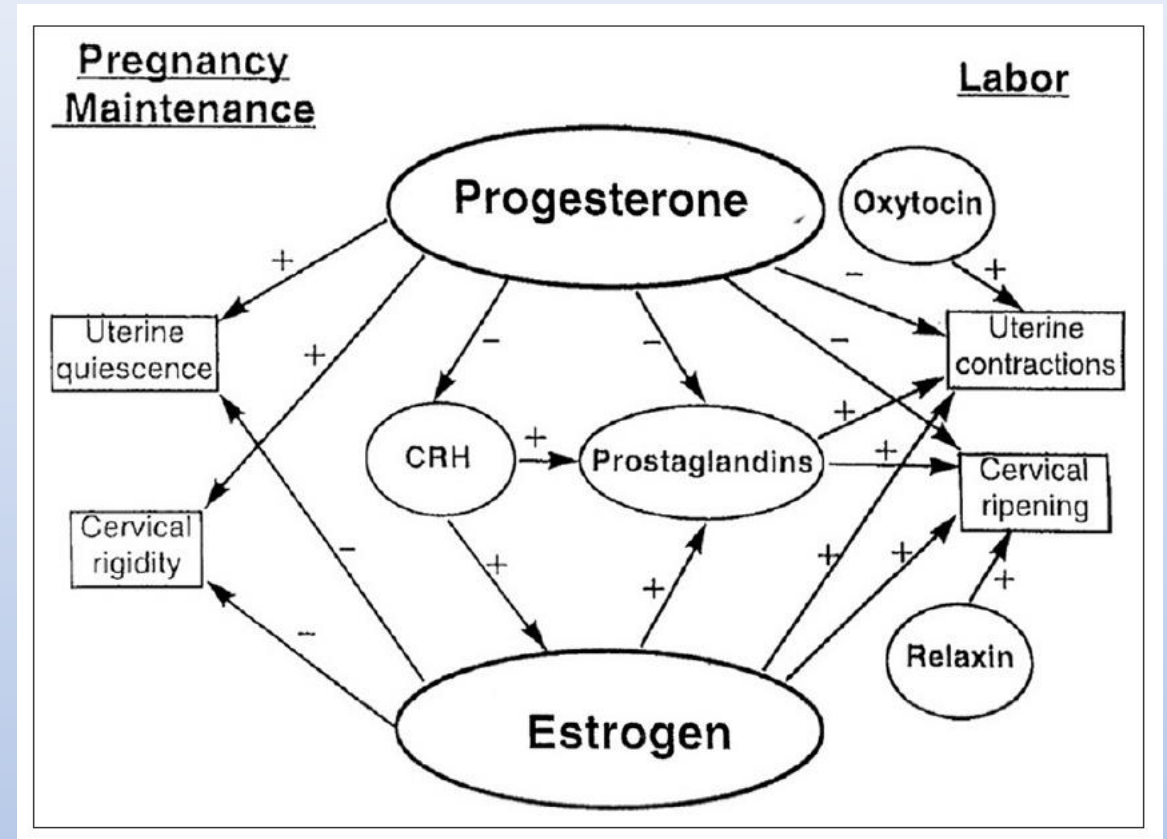
Endocrine function of placenta - estrogens

- Hyperestrogenic state during **pregnancy**
- Depends on circulating precursors – predominantly from fetal androgens (DHEA), regulatory function of CRH
- Estriol, estrone and estradiol
- First synthesis by corpus luteum, then placenta
- Increase the uteroplacental blood flow (estriol)
- Stimulation of endometrial growth and differentiation, angiogenesis and vasodilatation (estradiol)
- Stimulation of contraction of myometrial cells by increasing connexin-43 expression and OTR (estriol, estradiol)



Parturition

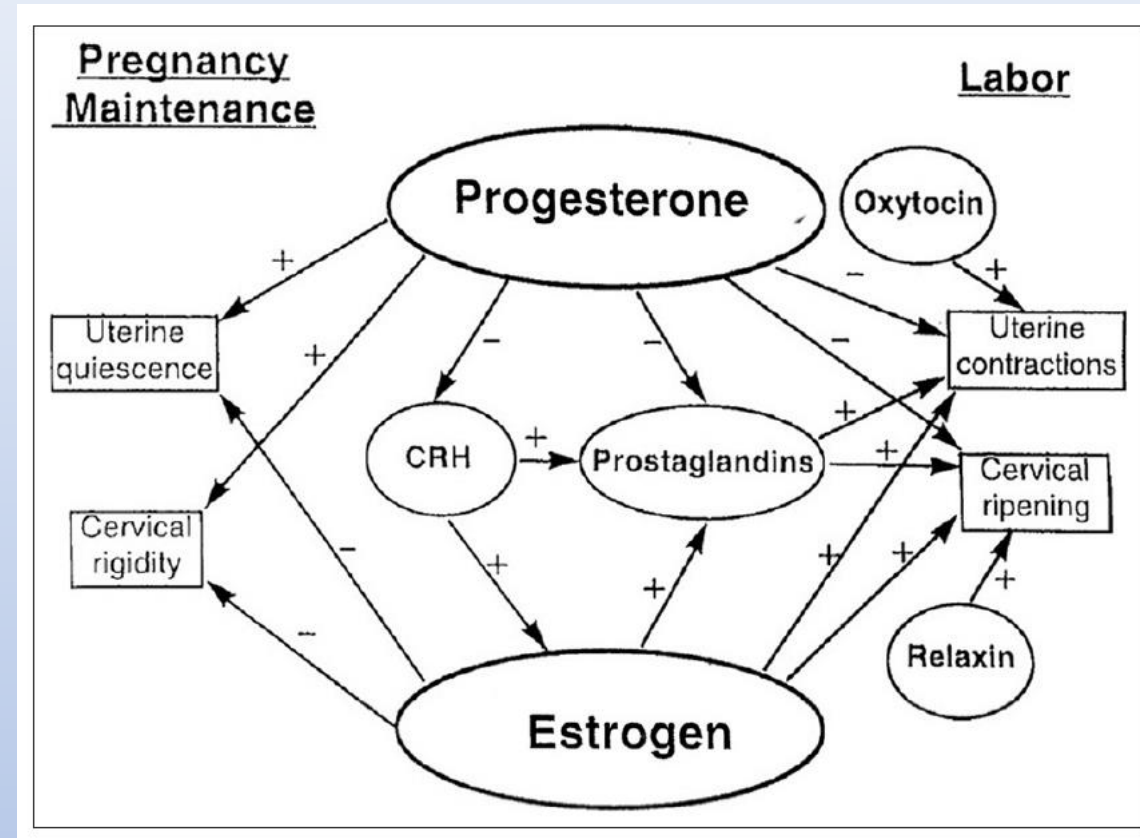
- Parturition = coordinated process of transition from a quiescent myometrium to an active rhythmically contractile state requiring complex interplay between placental, fetal and maternal compartments
- Functional progesterone withdrawal, increased estrogen availability, CRH, increased responsiveness of the myometrium to oxytocin



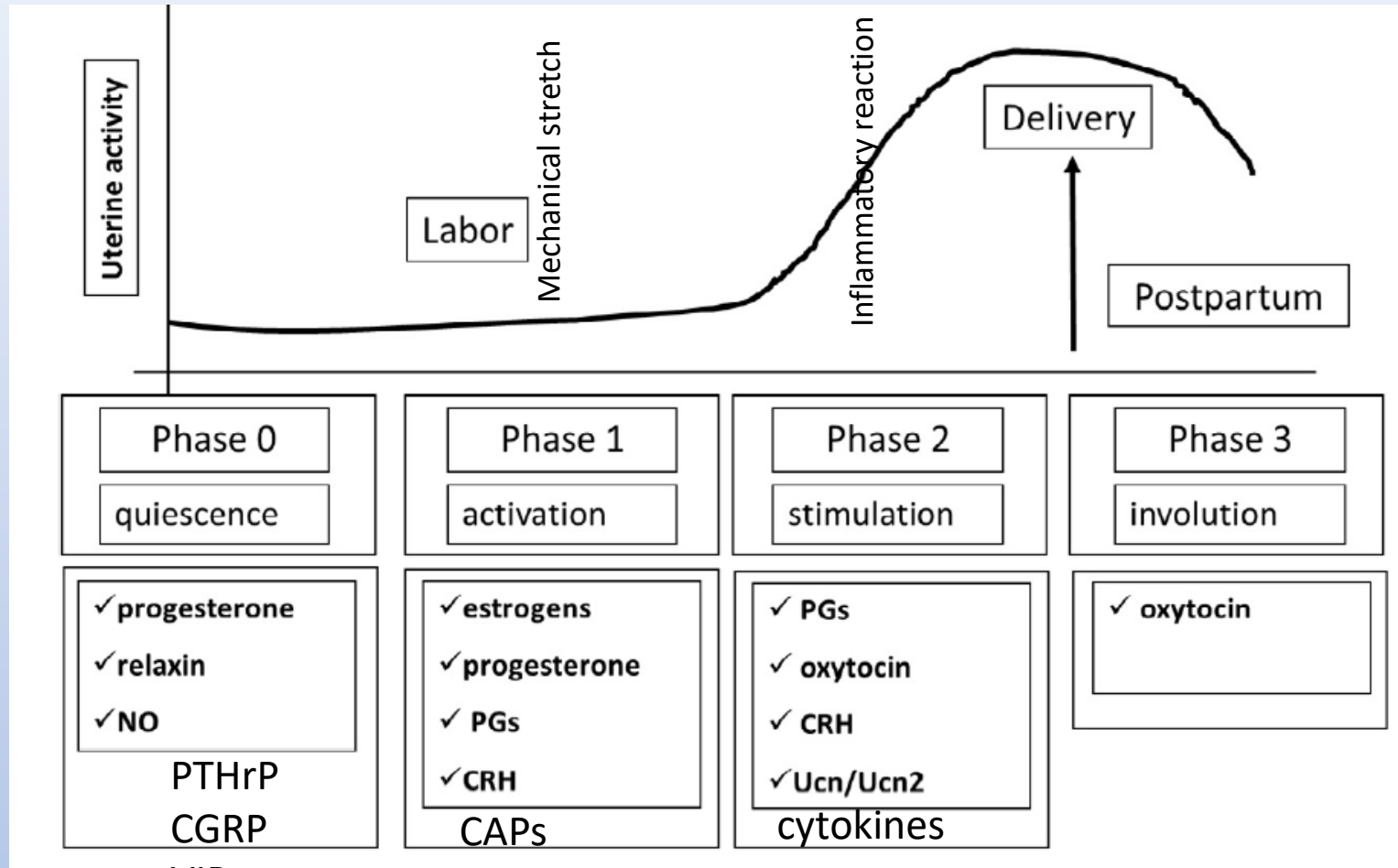
Estrogens, progesterone, oxytocin, PGS, relaxin, CRH

Parturition

- Uterus conversion from quiescent structure with dyssynchronous contractions to an active co-ordinately contracting organ
- Capability of cervical connective tissue and smooth muscle of dilatation to allow the passage of the fetus from the uterus
 - formation of gap junctions between myometrial cells
 - shift from progesterone to estrogen dominance
 - increased responsiveness to oxytocin by means of up regulation of myometrial oxytocin receptor
 - increased PG synthesis in uterus
 - increased myometrial gap junction formation
 - decreased nitric oxide (NO) activity
 - increased influx of calcium into myocytes
 - increased endothelin leading to augmented uterine blood flow and myometrial activity
 - activation of the fetal HPA axis
 - collagenolysis, and a decrease in collagen stabilization through metalloproteinase inhibitors = cervical softening and dilation



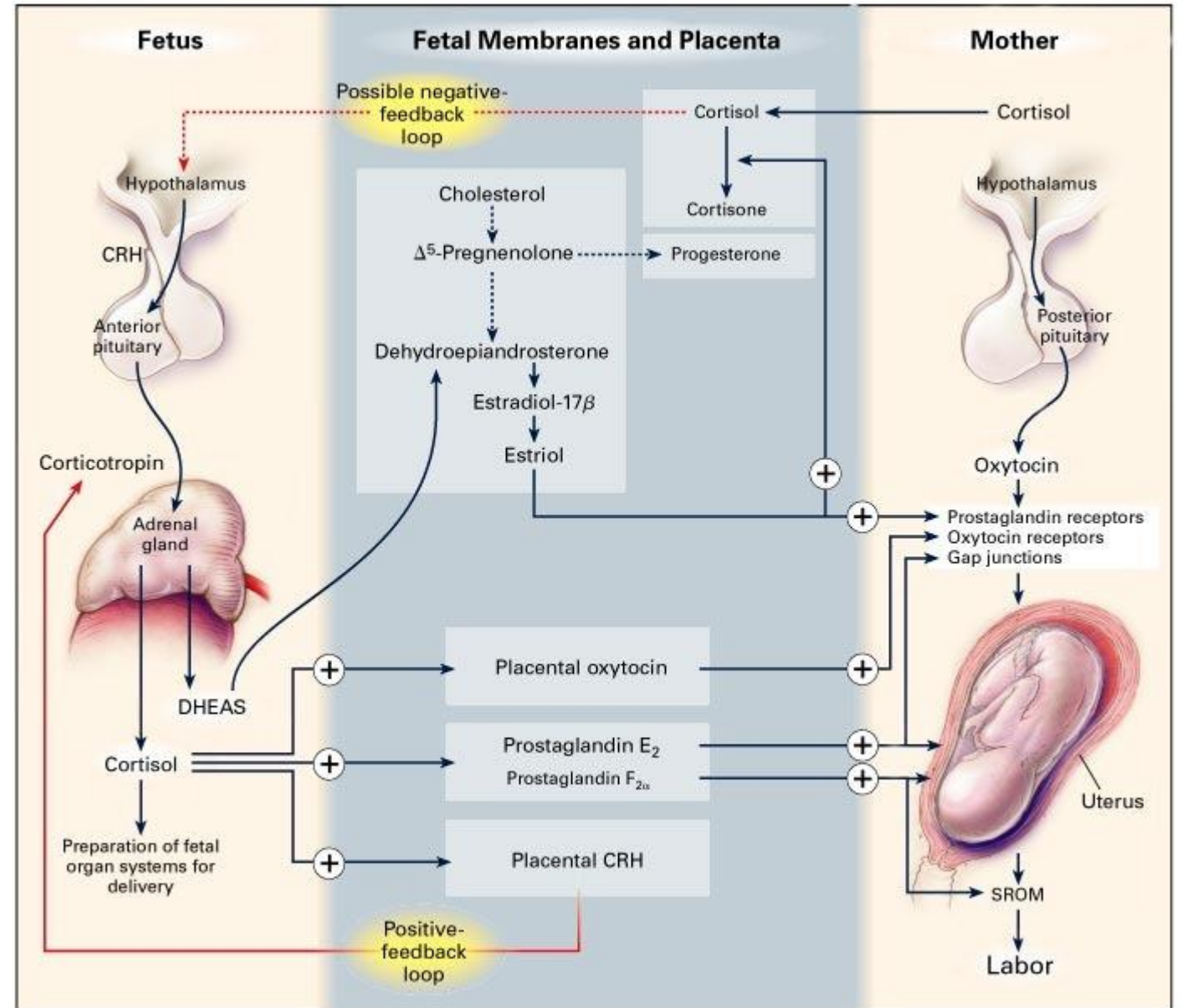
Phases of human parturition



Increased cAMP/cGMP = inhibition of calcium ions release

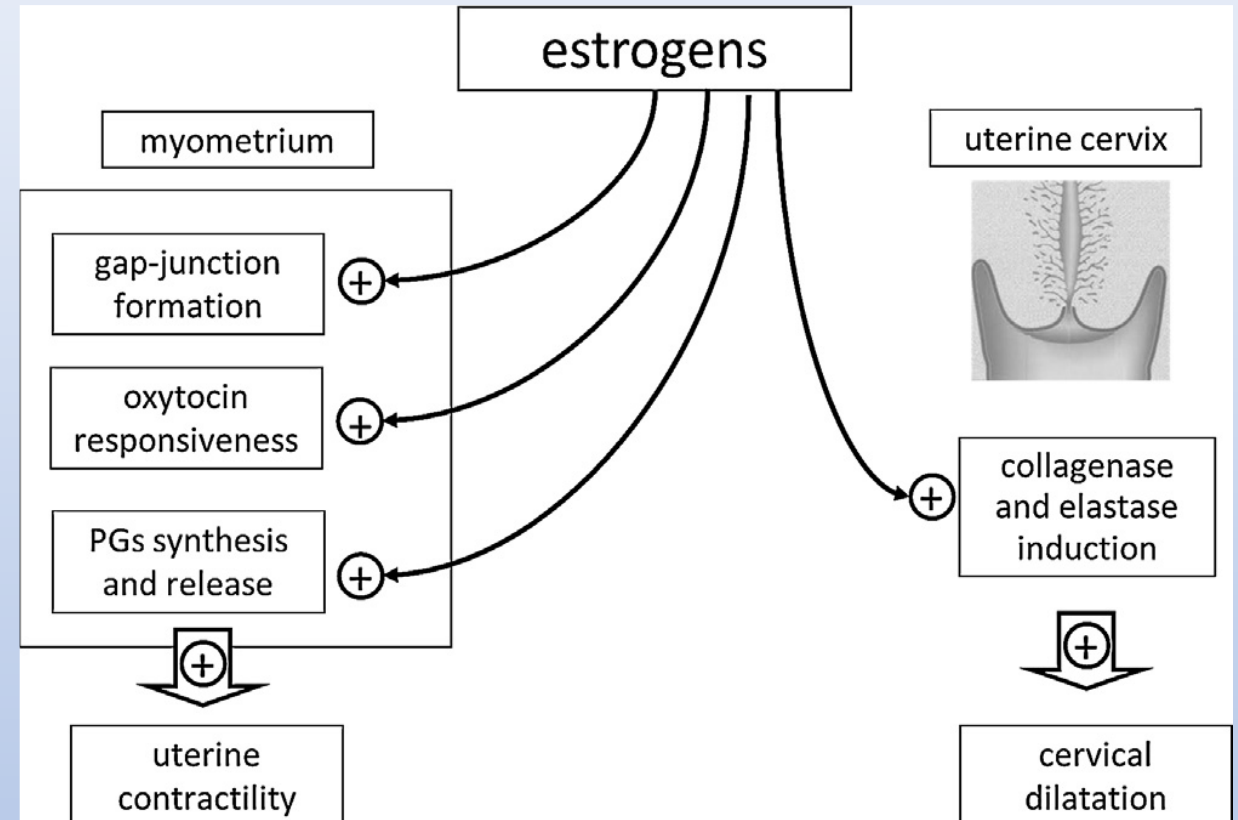
Labour induction

- CRH/cortisol (inflammation – PGs)
- Mechanoreceptors (mechanical distension)
- Inflammation, mechanical distension of the uterus in term of paracrine and autocrine signalling between feto-placental unit and mother promote initiation of parturition.



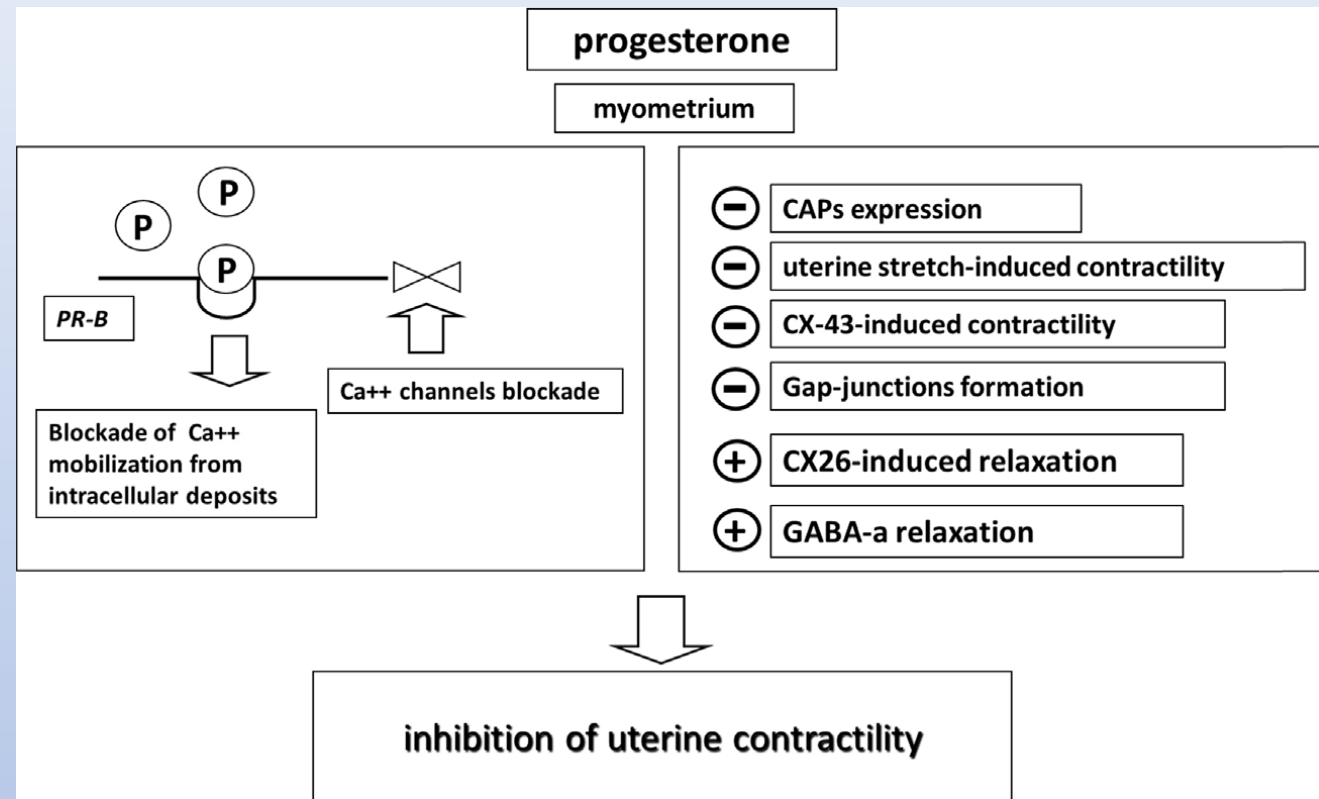
Estrogens and parturition

- Increase in the number of prostaglandin receptors, oxytocin receptors, and up-regulating the enzymes responsible for muscle contractions (myosin light chain kinase, calmodulin)
- Increase connexin 43 synthesis and gap junction formation in the myometrium
- Cervical ripening (rearrangement and realignment of collagen, elastin, and glycosaminoglycans, mediated by the induction of collagenase and elastase)

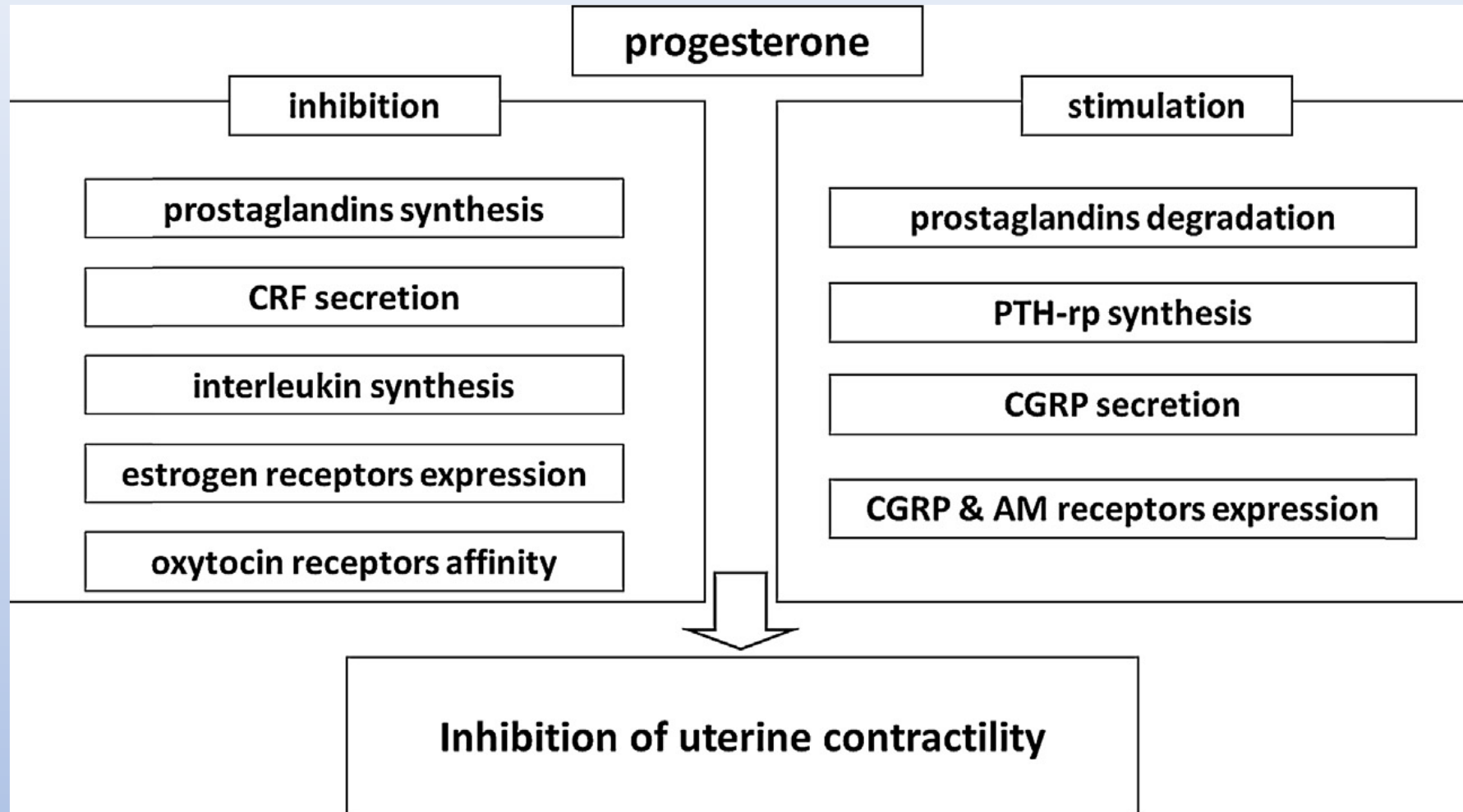


Progesterone and parturition

- Stimulation of the uterine NO synthetase
- Inhibition of myometrial gap junctions
- (-) prostaglandin production
- (-) development of calcium channels
- (-) OTR
- (-) collagenolysis
- Note – switch of balance between estrogens and progesterone
 - Change in the activities of enzymes involved in synthesis (17,20 hydroxysteroid dehydrogenase)
 - Decrease in progesterone receptors expression
 - Local metabolism of progesterone

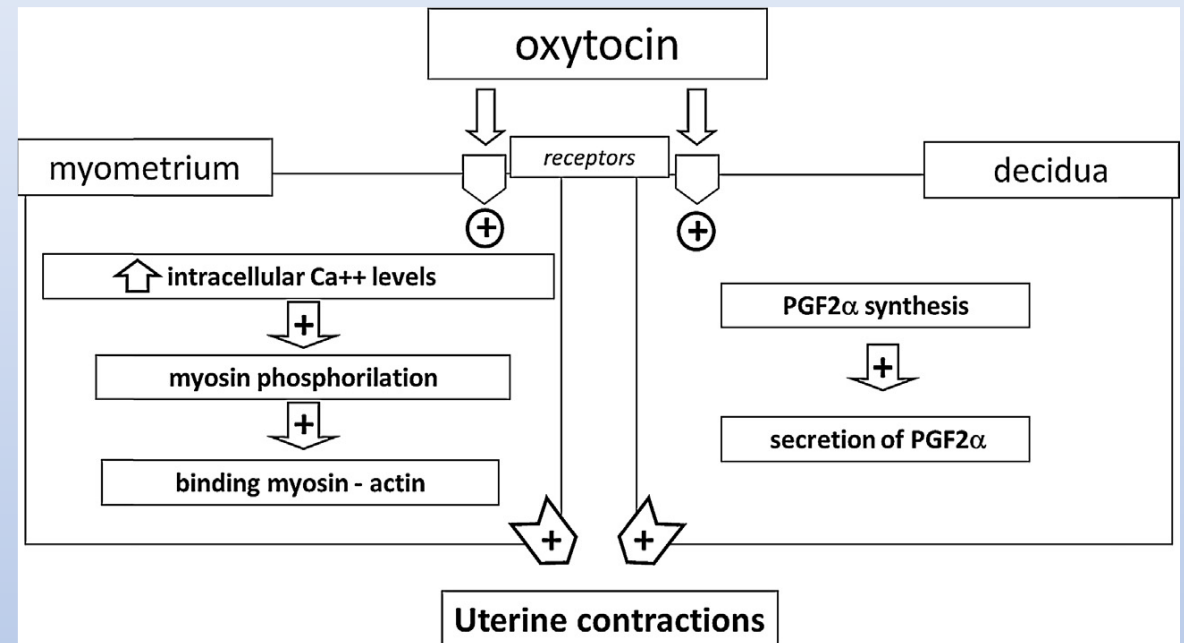


Progesterone and parturition



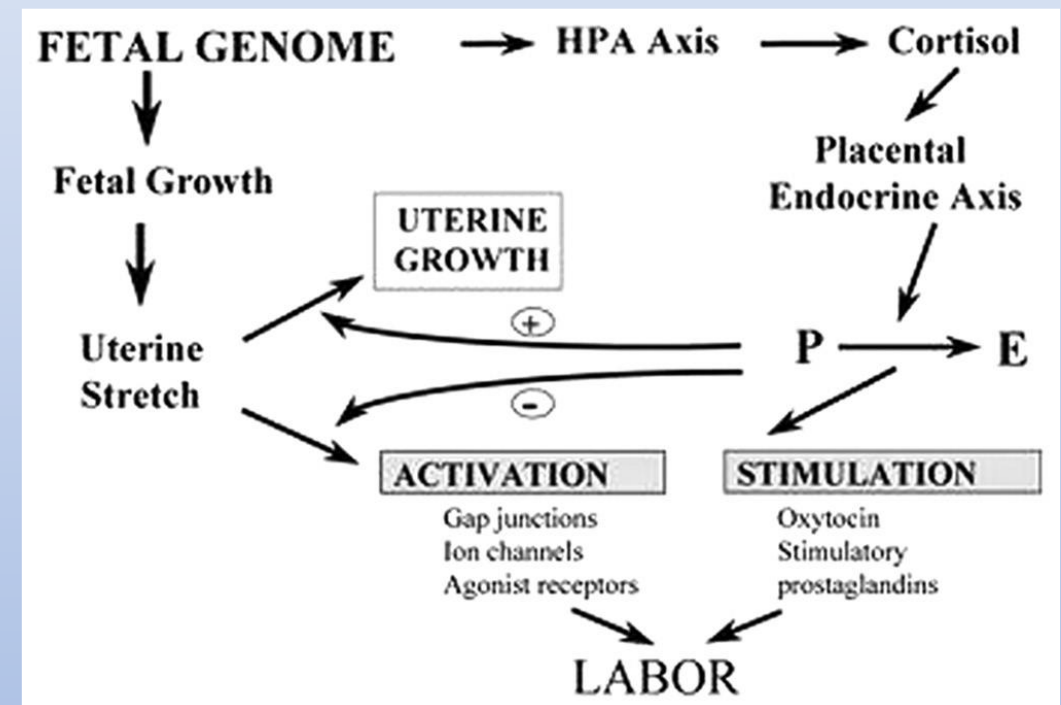
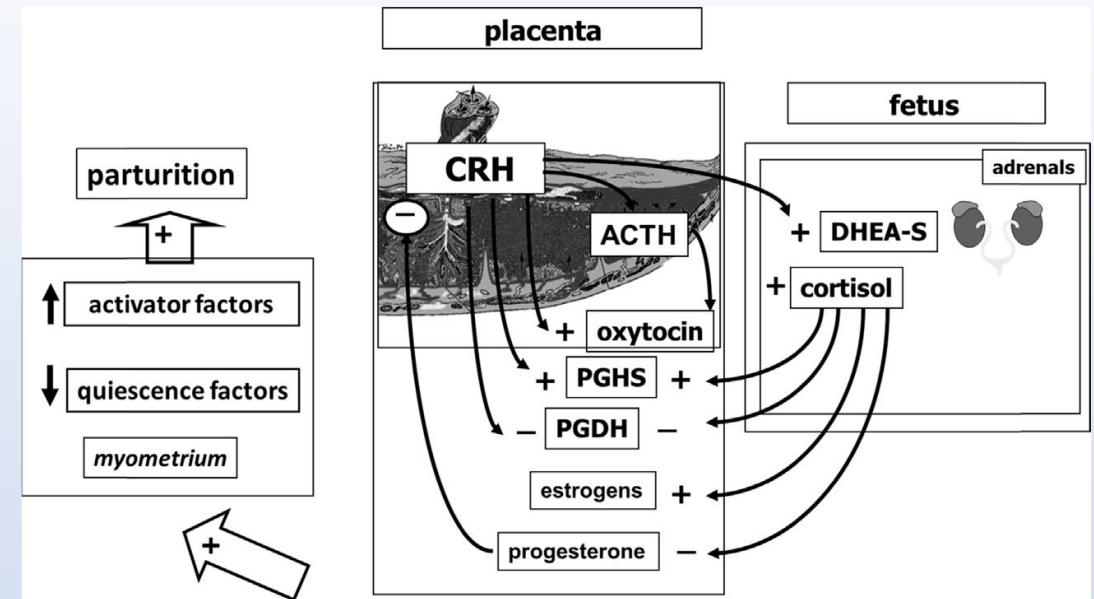
Oxytocin and parturition

- Increased OT production (pulses)
- Increased number of OTR at the end of pregnancy (estrogens, (-) progesterone)



CRH, urocortins and parturition

- CRH synthesis is stimulated by the produced fetal cortisol (positive feedback mechanism).
- Very rapid rise of CRH in late pregnancy – connection with estriol surge and critically altered P/E3 and estriol/estradiol (E3/E2) ratios = estrogenic environment
- Modulation of PGF production
- Vasodilation of feto-placental circulation (NOS)
- Stimulation of fetal DHEAS = fetal lung maturation and adaptive mechanisms in response to the stress of parturition
- CRH increases corticotropin production and, consequently, the synthesis of cortisol by the fetal adrenal gland and maturation of the fetal lungs



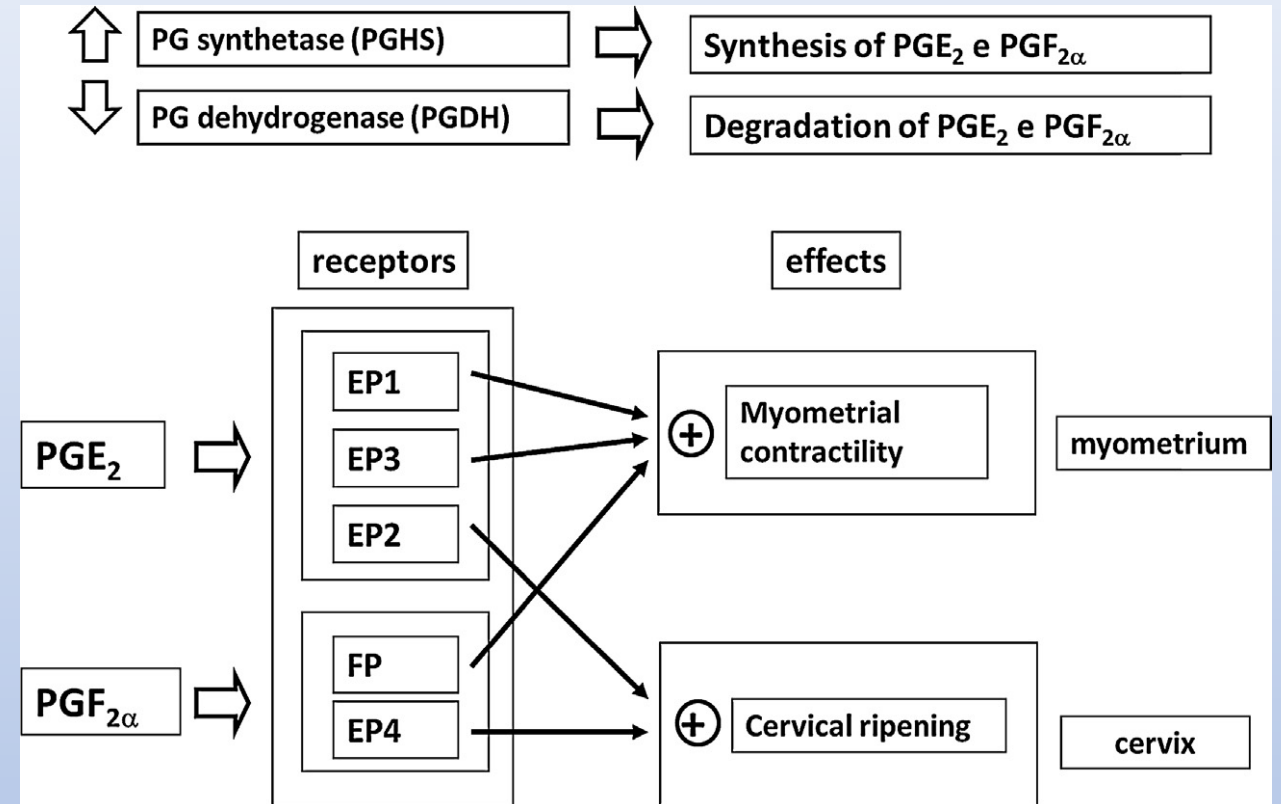
Relaxin and PGS and parturition

- PGS

- Increased levels before and during labor in the uterus and membranes
- Central role in parturition
- Stimulation of myometrial contractility
- Ripening the cervix
- Endpoint of the CRH cascade

- Relaxin

- Endometrial vascularization and remodelling of connective tissue
- loosening of joints and tendons as well as softening of the cervix in preparation for birth
- Corpus luteum, placenta, decidua



Endocrinology of the puerperium – uterine changes

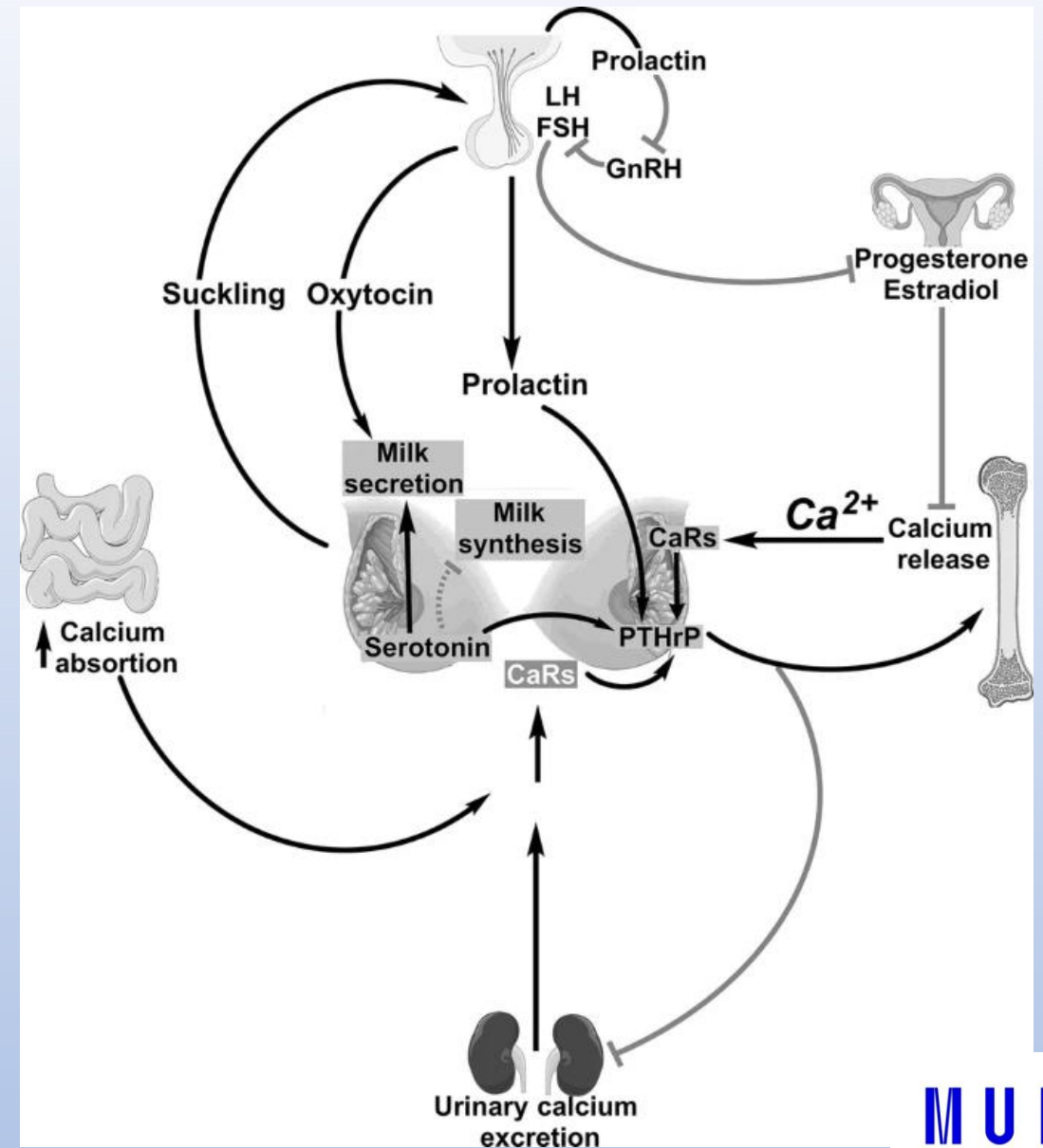
- Progressive involution (500 g/week)
- Palpable abdominally until about 2 weeks postpartum
- Nonpregnant size (60 – 70 g) after 6 weeks postpartum
 - Mechanism: decrease of volume of myometrial cells
- Rapid regeneration
 - 7th day = complete restoration of surface epithelium
- Longer regenerative changes – area of placental implantation

Endocrinology of the puerperium – endocrine changes

- Steroids
 - Rapid decrease (half-lives of minutes)
 - Progesterone
 - 24 h to luteal phase levels
 - Several days to follicular phase levels
 - Estradiol
 - 1-3 days to follicular phase levels
- Pituitary hormones
 - FSH and LH
 - suppression in early weeks of puerperium
 - normal levels by the 4th postpartum week
 - decreased sensitivity to GnRH
 - Prolactin
 - PRL rises during pregnancy
 - Fall with the onset of labor
 - Delivery = rapid surge in PRL
- Nonlactating women
 - Rapid fall over 7 to 14 days
 - Normal cyclic functions and ovulation within 3 months
 - Initial ovulation – 9-10 weeks postpartum
- Lactating women
 - PRL – anovulation, inhibition of GnRH secretion

Lactation

- Mammogenesis
 - Estrogen, progesterone, PRL, GH and glucocorticoids, hPL
- Lactation – enlargement of lobules, synthesis of milk constituents
 - PRL, insulin, adrenal steroids
- PRL
 - High levels during third semester
 - Blocking effect of estrogens
- Oxytocin
 - Milk ejection
 - Contractile response of smooth muscle cells
 - Visual, psychologic or physical stimuli)
- Suckling
 - Activation of neural arch



Lactation - overview

