

## Lecture 17

### HORMONAL CHANGES DURING PREGNANCY

#### III. PREGNANCY

(begins when fertilized ovum implanted in uterine endometrium)

1) ↑E & P inhibit GnRH secretion by hypothalamus → ↓LH & FSH

- a) no follicular development
- b) no ovulation
- c) no menstruation

2) prolactin

- a) maternal pituitary
- b) titers increase progressively & reach maximum at birth
- c) essential for E & P stimulation →  
maternal breast development & milk synthesis

3) relaxin

- a) hCG stimulates CL → relaxin 0-8 weeks
- b) after this time endometrium secretes
- c) relaxes pelvic ligaments in preparation of parturition (birth)
- d) with P inhibits uterine contraction → premature expulsion of fetus

4) insulin

- a) 3rd month from maternal pancreas
- b) maternal response → decreased sensitivity to insulin
- c) severe insensitivity → gestational diabetes  
temporary condition returns normal after birth

5) aldosterone

- a) maternal adrenal cortex
- b) maintain adequate Na<sup>+</sup> levels in maternal circulation
  - 1) Na<sup>+</sup> uptake by fetus
  - 2) Na<sup>+</sup>/water retention → ↑maternal/fetal plasma volumes

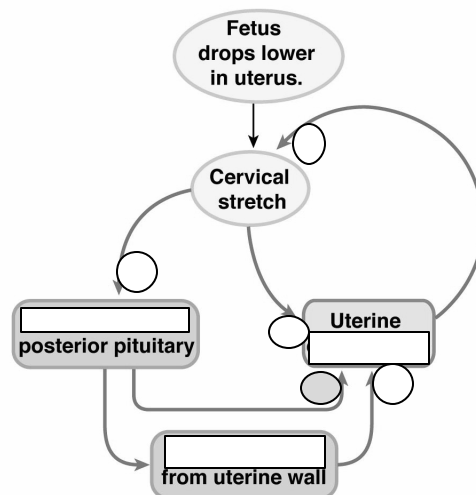
6) cortisol

- a) maternal adrenal glands
- b) ↑ free/protein bound cortisol during pregnancy
- c) E → maternal liver → cortisol binding globulin (CBG)
- d) ↑ maternal adipose tissue volume & development of mammary glands

7) thyroxine (T4) and triiodothyronine (T3)

- a) maternal thyroid gland increased size
- b) ↓ T4/T3 production
- c) ↓ basal metabolic rate
- d) ↓ resting pulse rate
- e) hormones ↓ maternal cardiopulmonary function  
    ↓ rate of delivery of O<sub>2</sub>/nutrients to developing fetus

**IV. PARTURITION (birth)**



1) oxytocin (Pitocin)

- a) stimulates contraction of uterine muscles
- b) dilation of cervix (cervical stretch) before delivery →  
afferent neural input to hypothalamus
- c) hypothalamus → *posterior* pituitary → oxytocin
- d) E & relaxin → I # of oxytocin receptors in uterus  
(I uterine sensitivity to oxytocin at end of pregnancy)

2) prostaglandins (PGF & PGE)

- a) stimulates contraction uterine smooth muscles
- b) oxytocin → uterus → prostaglandins →  
paracrine action → uterine contractions
- c) administer prostaglandins to induce labor & terminate pregnancy  
(almost any stage of gestation)

3) P

- a) inhibit uterine contractions
- b) decrease in P removes inhibition of uterine contractions
- c) ?? this P decreases have not been found in all women
- d) placenta secretes P-binding protein before delivery:

decrease P → recent studies

4) relaxin

- a) CL
- b) endometrium
- c) I # oxytocin receptors in uterus
- d) softens the cervix-pliable for facilitation of delivery
- e) relaxation pelvic ligaments → easing fetal passage thru birth canal

#### IV. DEVELOPMENT OF BREAST DURING PREGNANCY

- 1) E (ovary/placenta)
  - a) stimulates proliferation of glandular tissue & ducts of breast
  - b) stimulates prolactin release  
but blocks action of prolactin on breast
- 2) P (ovary/placenta)
  - a) stimulates proliferation of glandular tissue & ducts of breast
  - b) blocks action of prolactin on breast
- 3) hCG, hCS (placenta)-stimulates mammary growth
- 4) prolactin (anterior pituitary) → stimulates mammary growth
- 5) oxytocin (posterior pituitary)
  - a) no effect on mammary growth
  - b) sensitivity of myoepithelial cell to oxytocin ↑ during pregnancy

#### V. HORMONAL CONTROL OF LACTATION

breast alveolar cells extract from maternal circulation for milk production

glucose

amino acids

fatty acids

glycerol

1.5 liters of milk/day

- 1) major differences between human & cow milk
  - amount/type of proteins
    1. human protein (**lactalbumin**) lower casein-easier to digest
    2. cow-**casein** -forms sizable curds
      - heat
      - changes enzymes or pH

## 2) Contaminants

carrier-mediated diffusion/active transport from maternal during lactation

a) drugs: 2% of maternal dose enters breast milk

1. most pose no risk

2. some harmful: many sedatives:

lithium, reserpine; valium diazepam

symptoms: drowsiness; lethargy

3. anticoagulants-induce bleeding

4. narcotics-heroin painkiller Darvon-lead to addiction

b) caffeine

c) viruses

d) environmental pollutants

e) alcohol

## During Pregnancy

1) Fetal alcohol syndrome (FAS)

a) growth retardation & abnormalities of facial development

b) central nervous systems-hyperactivity, tremors,  
impairment of intellectual development

2) Smoking, drugs, malnutrition (other factors can contribute)

3) First trimester stop drinking-still risk of congenital abnormalities

a) spontaneous abortion, premature labor, and neonatal death

b) alcohol-impair transport of glucose/amino acids to fetus

-fetal acidosis/hypoxia thru blood constriction to fetus

## Conception

1) Heavy drinking → craniofacial deformity & impairment of CNS

### Chemical Termination of Early Pregnancy

- 1) Surgical intervention-risk of infection/postsurgical trauma
  - 2) Chemical → mifepristone (RU486)
    - a) synthetic steroid derivative with high affinity for P receptors → blocks action of P → antiprogesterone
    - b) CL secretes P during ovarian cycle & placenta after 6th week pregnancy
    - c) P stimulates
      1. growth & proliferation endometrial lining
      2. strongly inhibits uterine contraction
    - d) absence of P stimulation: endometrium undergoes hemorrhagic changes; outer layers of endometrium separate from uterus & discharged → onset of menstruation
    - e) RU486 together with prostaglandin induces uterine contractions & onset of menstruation (evacuation of uterine contents) whether or not a fertilized ovum is present
- in France authorized for clinical use (U.S.?)

### Menopause: cessation of menstruation: 45 - 50 years old

- 1) several years before onset of menopause- menstruation occurs less frequently & variable intervals
- 2) # of follicles in ovaries decline with age
- 3) ↓ estrogen secretion declines as well
- 4) follicles disappear: ovary stops E production
- 5) adrenal glands continue secrete E precursors → E at peripheral tissues
- 6) ↓ remaining follicles less sensitive to LH & FSH compensate by ↑ blood LH/FSH
- 7) ↓ E
  - a) loss of vaginal epithelium
  - b) decrease in breast mass
  - c) vascular flushing ("hot flashes")
  - d) rapid shifts in mood and emotion
  - e) ↑ in coronary vascular disease

- f) ↑ bone loss = menopausal osteoporosis  
(total bone mass/bone density)
1. loss of 1-2% bone mass/yr
  2. more bone eroded than replaced
  3. bones become more brittle & easily fractured
  4. bone pain: compression vertebrae fractures  
or long bone fractures
  5. spine curvature/x-ray bones appear transparent
  6. hormone replacement therapy (HRT): administer ↓E dose  
E associated with certain cancers
  7. HRT E accompany with dietary intake of ↑Ca (dairy products)
  8. ↑Ca intake limited  
50% absorption by GI tract: rest lost in feces & urine
  9. E in men but not prone to osteoporosis  
  
?? testosterone may protect from bone loss;  
men with osteoporosis: correlation with cases  
of impairment of gonadal function = hypogonadism

#### T & other androgens

- 1) secreted by the ovaries in low amounts
- 2) stimulate sexual drive
- 3) high titers at ovulation strongest urge in the menstrual cycle
- 4) high titers - oversecretion of adrenal glands/ovary  
enzymatic defects in adrenal cortisol metabolism →  
oversecretion/production → ovarian tumor
- a) hirsutism-excessive growth of hair where hair usually not present
  1. 10% of reproductive women
  2. incidence higher menopausal women
  3. degree (severity) of hirsutism not correlated  
with androgen production or titers of serum T
  4. unbound T enters through membrane →  
converted to DHT by enzyme  
5α-reductase
  5. DHT binds with cytoplasmic receptor: complex enters nucleus  
→ stimulates m-RNA → hair growth
  6. skin of hirsute women highly sensitive to available T:  
result of high 5α-reductase activity

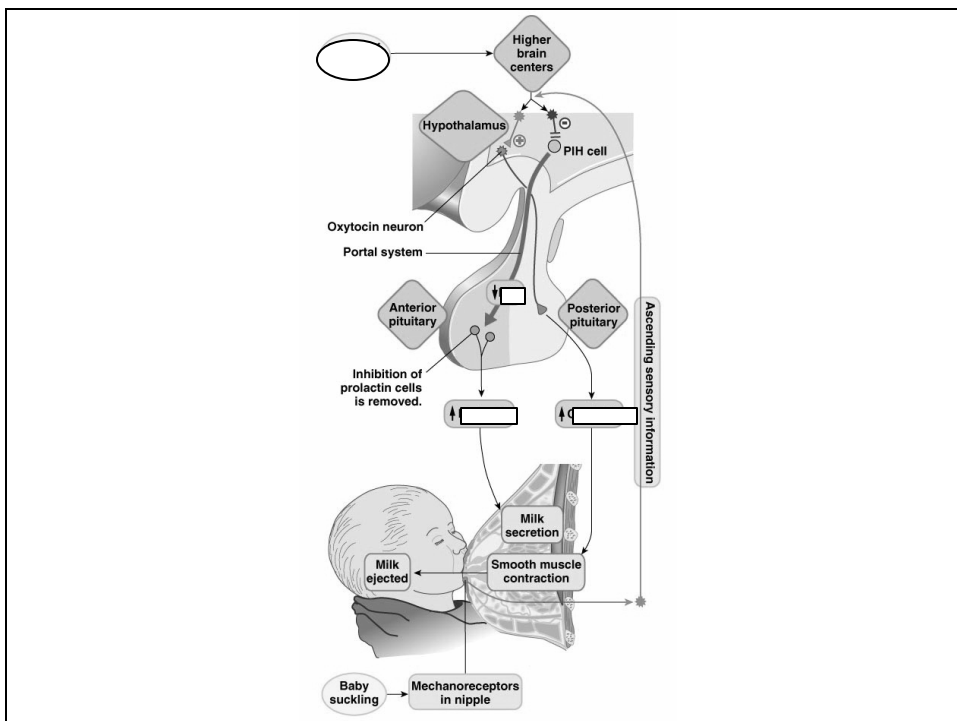
- 5) extremely high tiers
  - a) virilization-masculinization of external genitalia
  - b) lead to infertility
    1. T aromatized to estradiol in hypothalamus  
→disruption of LH/FSH secretion
    2. interference of follicular growth/maturation
    3. ↑ T inhibits ovarian LH/FSH receptor formation
    4. anovulation
      - a. oligomenorrhea (few menstrual cycles)
      - b. amenorrhea (absence of menstruation)
      - c. irregular menstrual cycles

### Hyperprolactinemia

- oversecretion of pituitary prolactin (PRL)
- excess milk production= galactorrhea
- amenorrhea/anovulation
- breast engorgement
- normal postpartum lactation fails to discontinue→  
(Chiari-Frommel syndrome)
- suckling of breast --normal stimulation of PRL
- stimuli afferent impulses in neuroendocrine reflex pathways →  
PRL secretion  
e.g. tight fitting garments, trauma, surgery,  
continued breast manipulation
- amenorrhea result of PRL? inhibition of  
hypothalamic GnRH secretion→block of FSH/LH
- ↑ PRL directly inhibit ovarian E production-resulting amenorrhea
- women ↑ PRL and decreased E bone demineralization/bone fractures



- 1) high E & P inhibit milk production  
prior to parturition by blocking milk-inducing prolactin after birth:  
placenta expelled: decrease E & P
- 2) prolactin
  - a) stimulates milk synthesis/release from breast
  - b) high E during pregnancy stimulate prolactin release  
from maternal pituitary gland
  - c) high prolactin levels at birth & then decrease
  - d) hypothalamus sensitive to neural signals from breasts
    1. suckling by newborn → afferent neurons → spinal cord →  
hypothalamus → anterior pituitary →  
(10 fold increase) prolactin for 1 hr then go down to normal
    2. single nursing episode → milk production for next nursing
    3. no nursing → no prolactin release → no milk secretion
    4. prolonged nursing → milk production within 7-9 months after birth
    5. breast production can still produce  
significant quantities of milk several years



- e) inhibits GnRH from hypothalamus:
  - inhibits LH/FSH release from pituitary
  - 1. breast feeding inhibit ovulation & reduce fertility
  - 2. large individual variation during which prolactin inhibits GnRH with prolonged nursing → unreliable method of birth control

### 3) oxytocin

- a) stimulates milk release (**milk let down**)
- b) stimulates contraction of myoepithelial cells surrounding outer walls of alveoli
- c) released episodically during nursing:
  - 1. breast stimulation similar to pathway of prolactin
  - 2. auditory stimuli (baby crying) release of oxytocin → milk ejection from breast