Aging and the Female Reproductive System

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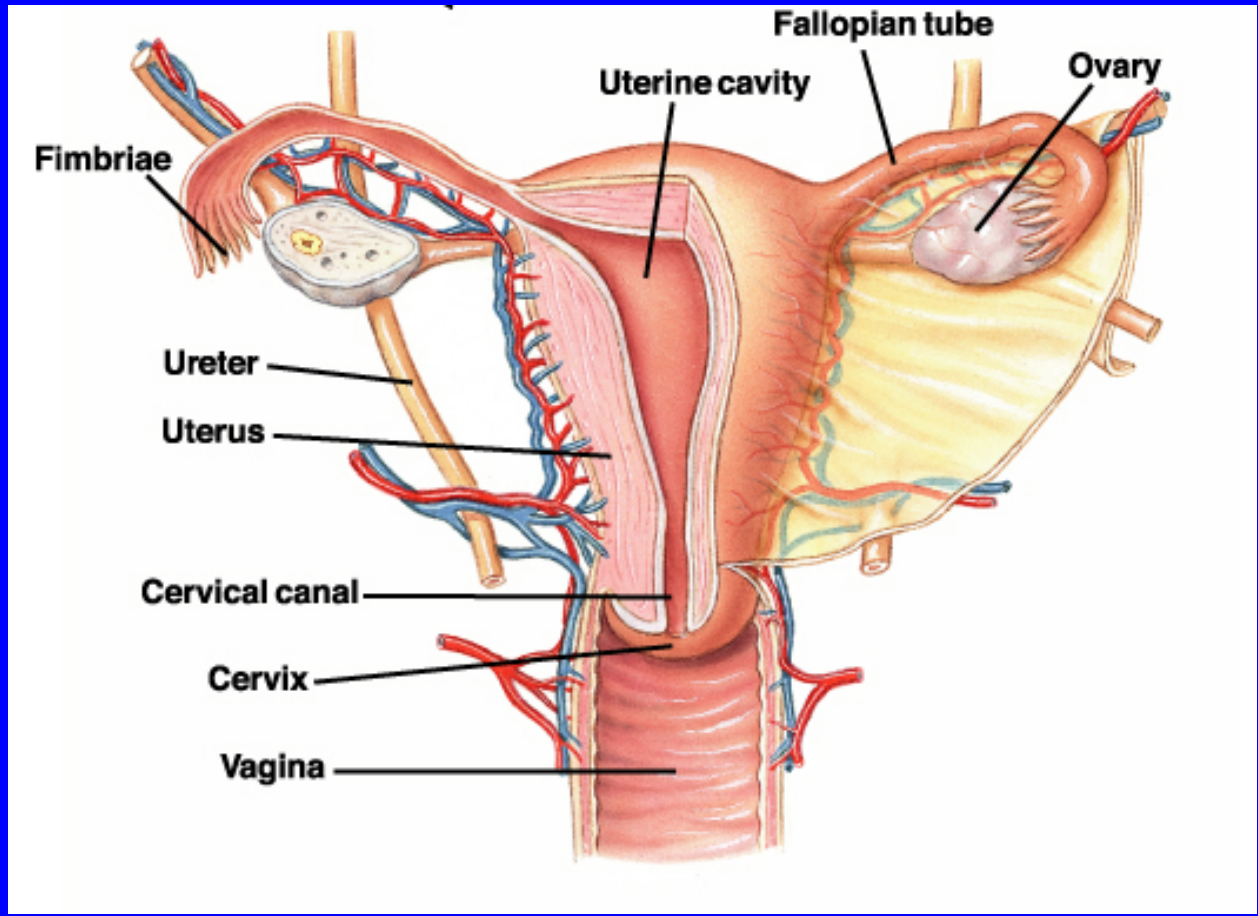
Why Menopause?

- Antagonistic Pleiotropy
  - Evolutionary value of an individual depends on its ability to produce surviving offspring
  - Selective pressures favor survival of young reproductively active individuals
  - Due to the increase in life span, women are living beyond a point where the reproductive system is designed to function
  - Menopause may be a pleiotropic effect of genes that had value earlier in life
- Menopause may carry advantage for survival of species
  - Beneficial to have non-reproducing species members to care for young

Terminology

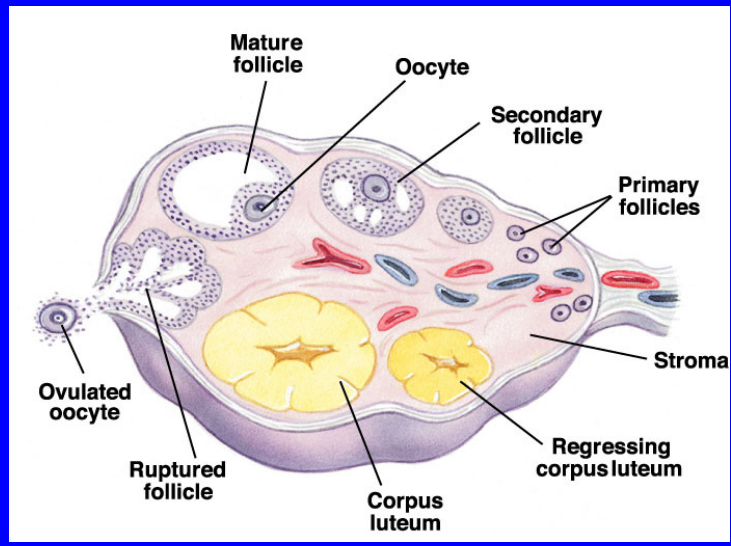
- Menopause
  - Permanent Cessation of Menstruation Associated With Loss of Ovarian Follicular Activity
- Perimenopause
  - Period Immediately Prior to and at Least 1 Year After Menopause
  - Characterized by Physiological and Clinical Features of Altered Ovarian Function
- Postmenopause
  - Period of Life After Menopause
- Premenopause
  - The Reproductive Period Prior to the Menopause

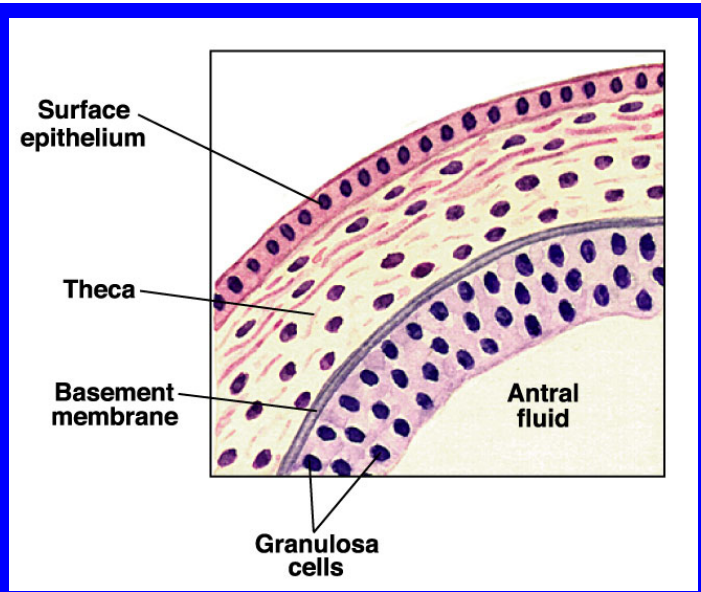
Anatomy:
Female Reproductive Tract



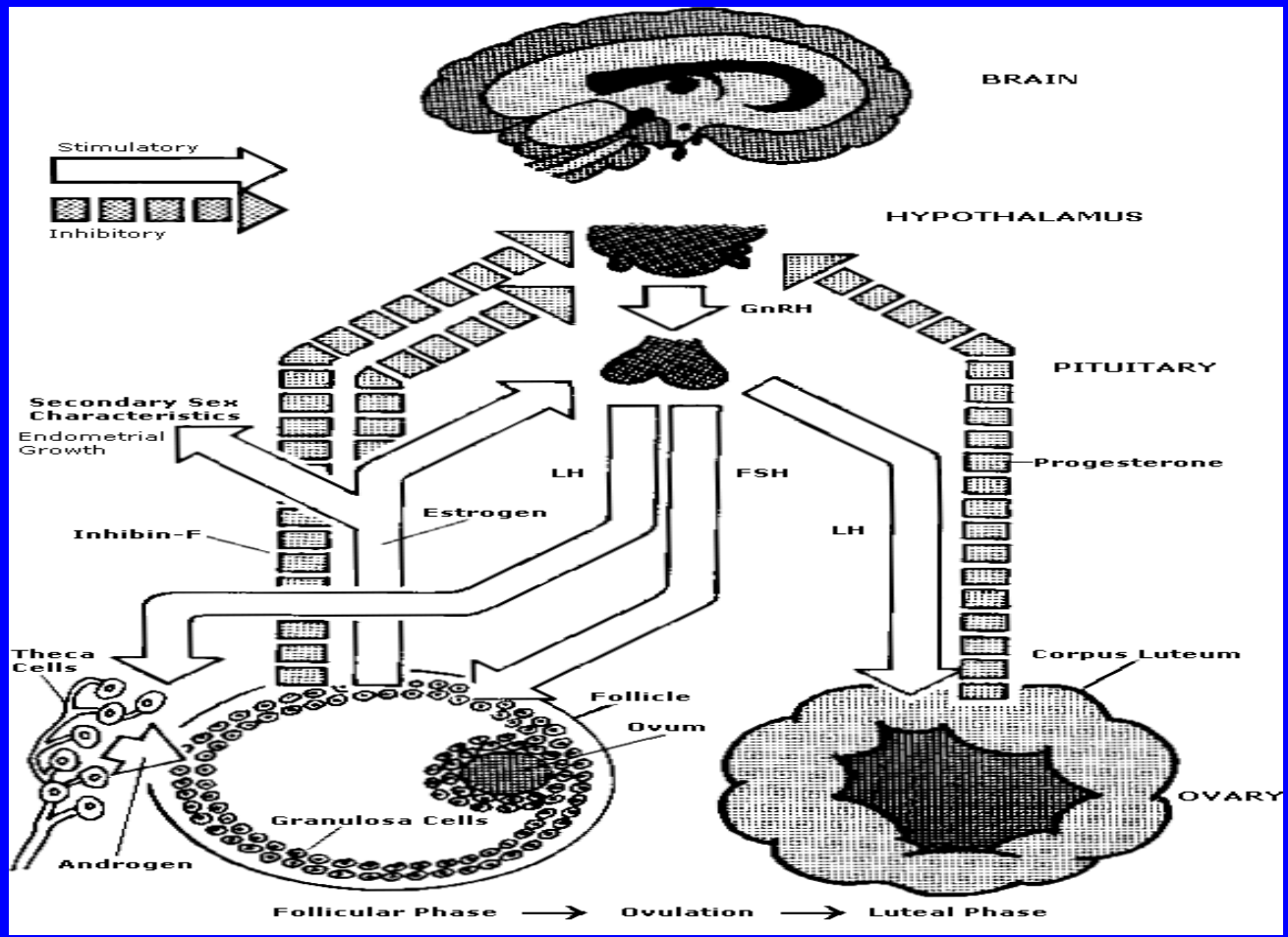
Ovary Characteristics

- Ovaries
  - Contain germinal cells
  - Contain endocrine producing cells
    - Granulosa
    - Thecal
  - Determine secondary structures and sexual characteristics

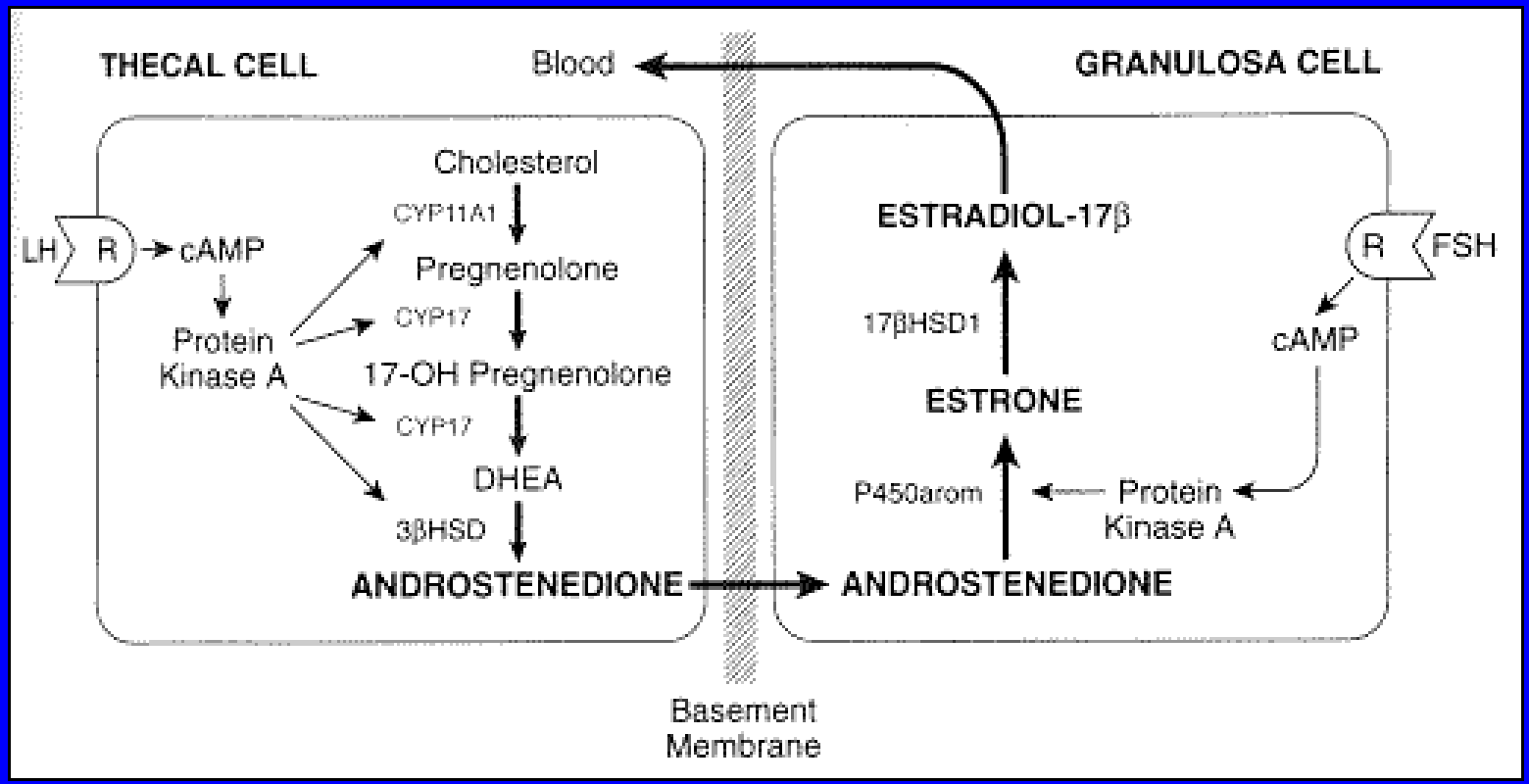




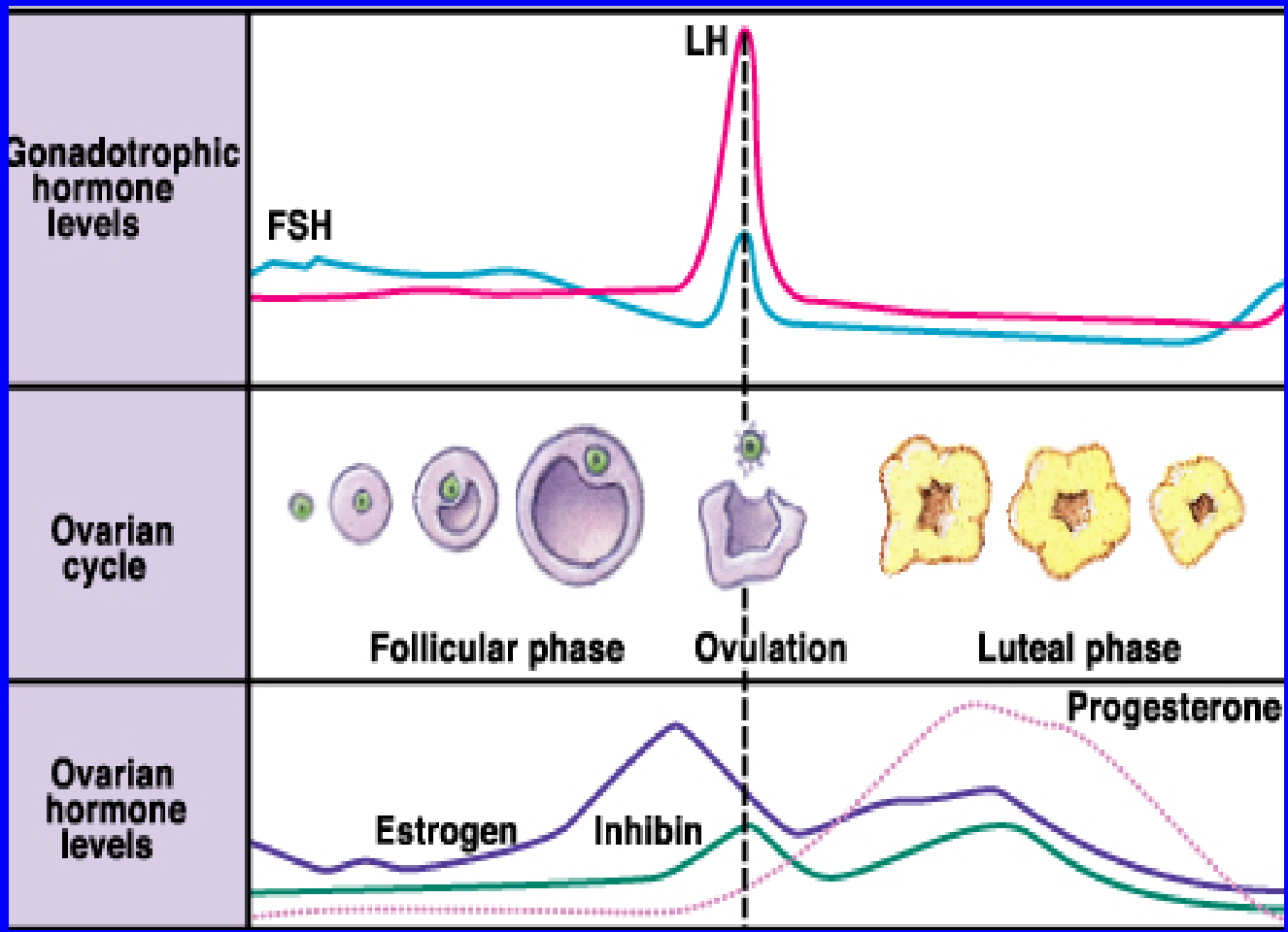
Hypothalamo-Pituitary-Gonadal Axis (H-P-G)



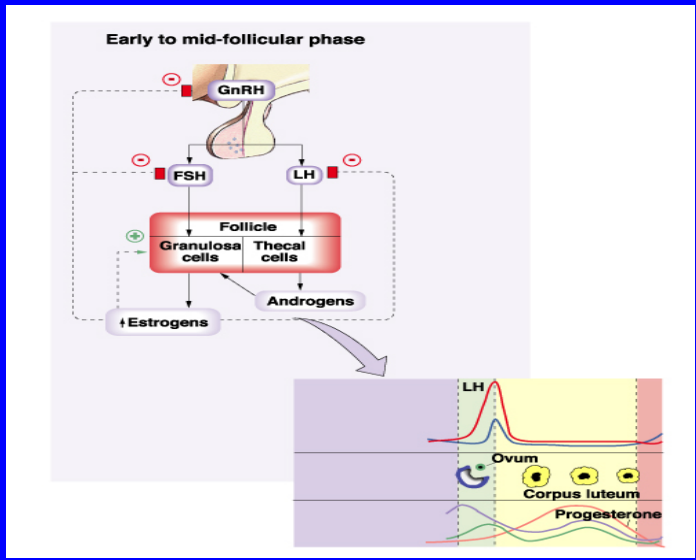
Gonadotropin Action

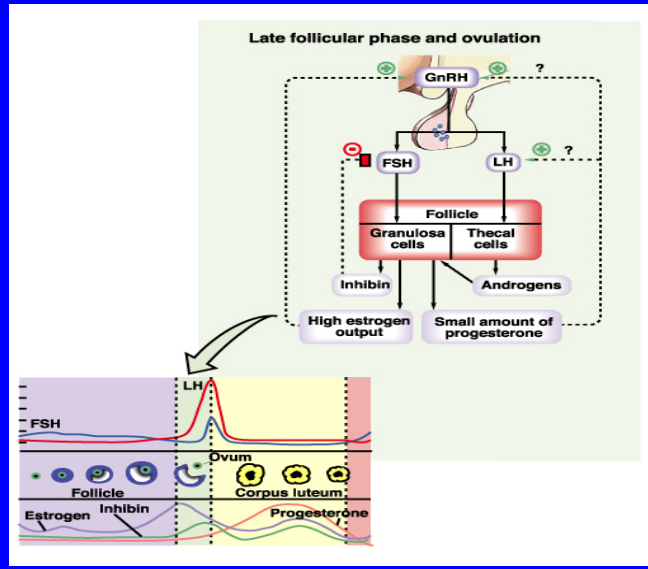


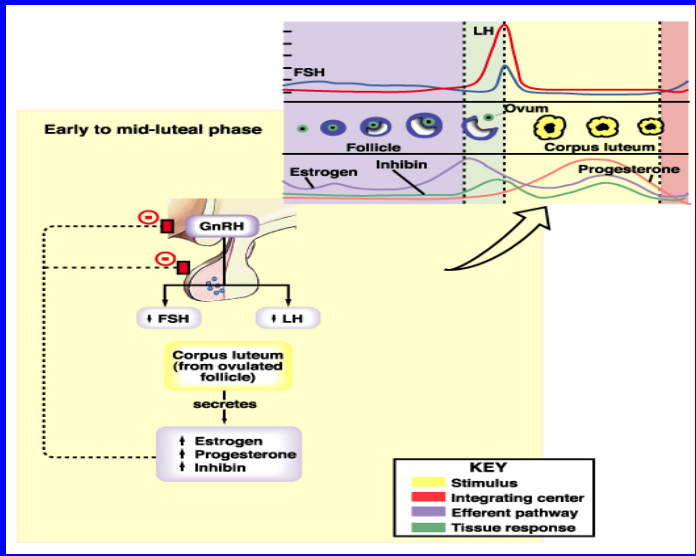
Normal Female Hormone Patterns

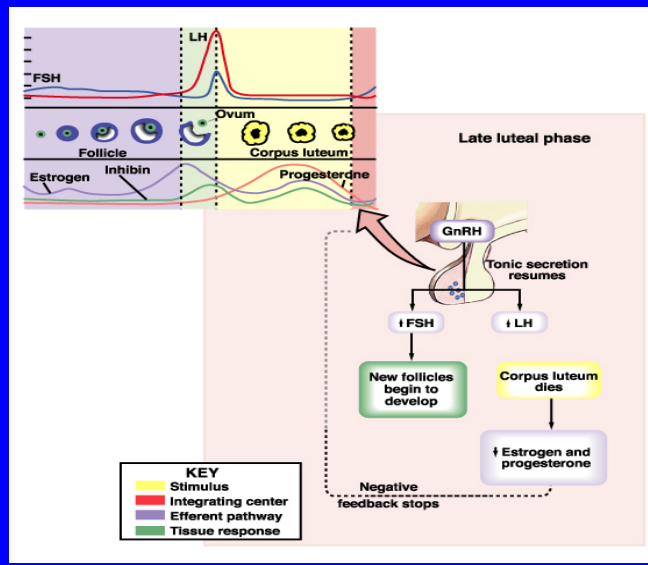


Hormone Patterns









Hormonal Changes From Aging

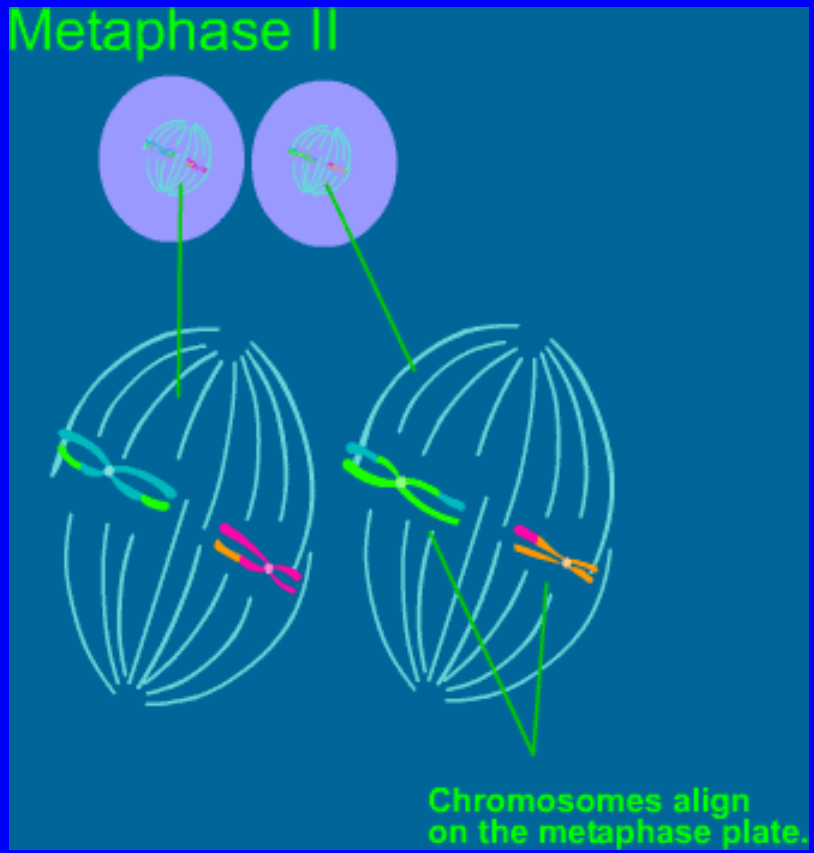
- Gonadotropins:
  - LH
    - Change occurs mid-follicular
    - Change to pulsatile pattern: ↑Duration, ↓Frequency
    - Possibly results in decreased responsiveness in feedback to estrogen
  - FSH
    - "Monotropic" FSH ↑
    - Evident during entire cycle
    - 1st Noticed prior to any change in cycle length
- Ovarian Steroidal Hormones
  - Estrone levels ↑ early in the cycle in older ovulatory women
    - Possible due to LH/FSH alterations
  - Luteal phase becomes shortened and Progesterone in insufficient to maintain corpus luteum
  - Eventually, H-P-G axis is unable to generate LH surge needed for ovulation

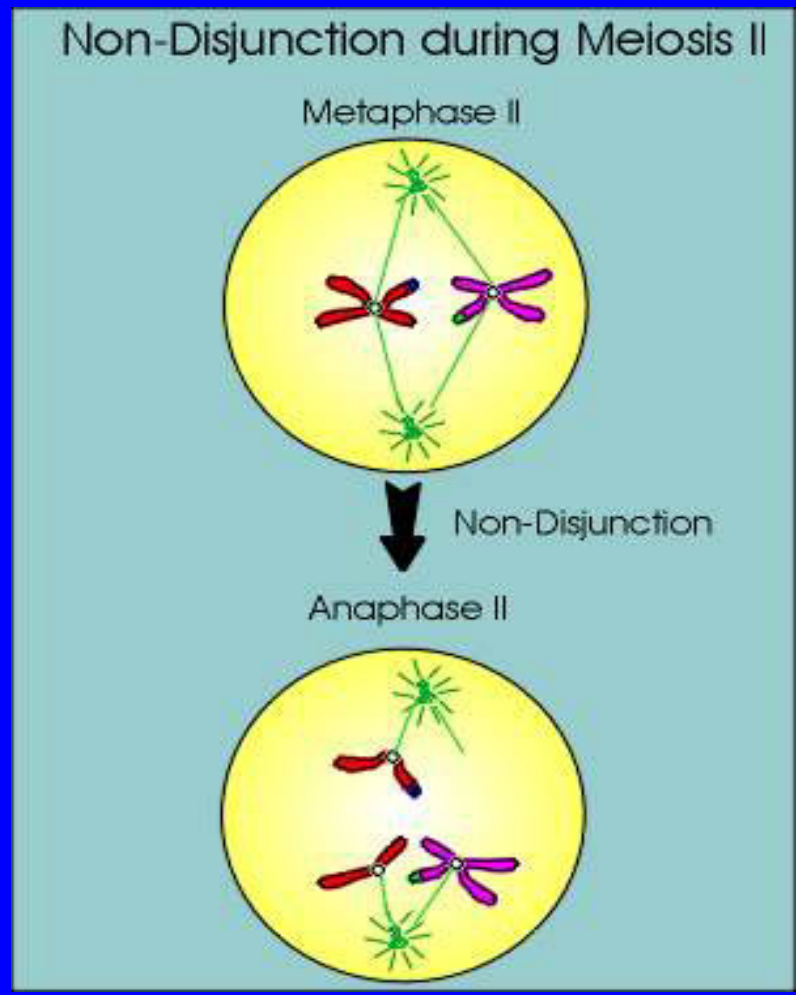
Fertility Changes and Perimenopause

- Fertility and Fecundity Decrease
  - Ovulatory cycle continues after onset of perimenopause
  - Cycle length becomes more variable
    - Shortening of follicular phase
    - No change in luteal phase
  - Peak fecundity occurs at 24, with a gradual decrease to 35, and a rapid decrease after 35

Ovarian Structural Changes

- Abnormalities in Older Oocyte
  - Change in microtubule and chromosome placement at the second metaphase of meiosis
  - May be linked to increased aneuploidy seen in offspring of older women
- Declining Follicular Reserve
  - 2 Million Primordial Follicles during fetal development
  - Declines to 1 million at birth and 250,000 by puberty
  - Primordial Follicles develop to primary and secondary follicles independent of hormone status
  - In the absence of LH/FSH, follicles undergo atresia
  - Once follicles are depleted, ovarian hormone production declines


Metaphase II
Chromosomes align
on the metaphase plate.


Non-Disjunction during Meiosis II
Metaphase II
Non-Disjunction
Anaphase II

Menopause Symptoms

- Hot Flashes
  - Most common reported symptom
  - 70-80 % of women report signs of hot flashes
  - This rate increases in women with oopherectomy and thin women that smoke
  - Asian women have much lower rate
    - 10-25 % Reported
    - Possibly due to genetics, diet, lack of reporting

Physiological Characteristics of Hot Flashes

- Sweating
- Increased Skin Conductance
- Increased Core Body Temperature
- Increased Metabolic Rate
- Increased Skin Temperature
- Hot flashes appear to be the result of noradrenergic control independent of estrogen regulation
  - However, ERT alleviates the symptoms of hot flashes

Menopause Effects on the Reproductive Tract

- Reproductive targets for steroidal hormones experience atrophy following menopause
- In addition, these more specific changes are seen:
  - Vagina
    - Dryness
    - Decreased Vascularity
    - Decreased Secretions
    - Increased Risk of Infections
  - Ovaries
    - Become more fibrotic as follicles diminish
  - Uterus
    - Loses Weight and Volume

Effects on Non-Reproductive Steroidal Targets

- Skin
  - Thinning of epidermis
  - Atrophy of sebaceous glands
  - Increased sensitivity to temperature, humidity, and trauma
- Bladder
  - General Atrophy
    - Results in urinary incontinence
- Hair
  - Body hair undergoes redistribution

Menopause and Non-reproductive Targets

- Skeletal System
  - Osteoporosis (Lecture May 3)
    - Decreased bone mass following menopause that appears to be the result of declining estrogen level
- Central Nervous System
  - Psychological
    - Anxiety/Depression
  - Cognition/Memory
- Cardiovascular System
- All of these will be further discussed in the context of HRT during Wednesday's Lecture