The menopause and the andropause

Aging of the human reproductive system
Developmental transitions in reproductive system

• Both males and females transition from reproductive immaturity into puberty
• The change is initiated by the maturation of a brain mechanism that includes gonadotropin pulse generator (GNRH)
Preprogrammed actions of reproductive hormones

- At puberty, secretion of
  - hypothalamic gonadotrophin releasing hormone increases
  - pituitary gonadotrophins increases
  - secretion of gonadal steroids increases
  - GH secretion increases in part in response to increased gonadal steroids
Preprogrammed actions of reproductive hormones

- Puberty is initiated by nocturnal increases in LH secretion.
Growth spurt, growth cessation and puberty are connected

- Mean weight
  - needed to initiate growth spurt is 30 kg
  - at peak growth velocity is 39 kg
  - at the onset of puberty is 47 kg
  - for all these events is the same in early and late maturing girls
Developmental transitions in reproductive system

- Males and females transition from reproductive maturity into reproductive senescence differently
- Females undergo complete cessation of reproductive function upon the onset of menopause at around 51 years
- Males undergo a gradual diminution of reproductive function as they age
Menopause

• Permanent cessation of reproductive and hormonal cycles (menses)
• Transition into menopause is initiated by
  – changes in the ovary
  – changes in the brain
• Transition is characterized by large and irregular hormonal swings
Characteristics of mature ovarian function

- Egg develops within a follicle
- Granulosa and theca cells
- Number of follicles fixed
  - 2 million at 5 mos
  - cca 250,000 involved
  - most follicles perish through atresia
  - starvation slows atresia
- Depletion of follicles initiates menopause
Progression to menopause

- Total number of ova in the ovary declines
- Number of ova per cycle declines
- Increased abnormalities in eggs
- Disruption in hormonal environment
- Fertilization abnormalities
  - delayed fertilization
  - chromosomal abnormalities
Reproductive cycle in the female

- Hormonal and endometrial changes during a menstrual cycle
  - follicular phase
  - ovulation
  - corpus luteum (CL) secretes estrogen and progesterone
  - luteal phase
  - menstruation to hormone withdrawal
Brain changes contributing to menopause

- Brain control of reproductive cycles becomes irregular
- Brain structures responsible for cyclicity are estradiol dependent and become less responsive
- Prolonged exposure to estrogens (like cortisol) may be neurotoxic
- Neurotransmitter changes
At menopause hormonal cycles become irregular
Environmental influences on the onset of menopause

- Nutrition (-)
- Parity
- Smoking (-)
- Contraception (+)
Hormonal changes in menopause

• Plasma estradiol declines (620 to 40 pM/L)
• Extraovarian tissues convert androgens to estrone by aromatization
• Sex-hormone binding globulin declines
• Failure of ovarian progesterone production
• Ovary and adrenal synthesize androgens
  – testosterone
  – androstenedione
  – dehydroepiandrosterone
• DHEA(S) declines with age
Consequences of hormonal changes in menopause

- Reproductive organ atrophy
  - oviducts
  - uterus and cervix
  - vagina and vulva
  - mammary glands
Consequences of hormonal changes in menopause

• Loss of vaginal epithelial glycogen
  – reduced lactobacilli populations
  – rise in vaginal pH
  – increase in UTIs
  – antibiotics increase yeast infestation and vaginitis

• Urinary (and GI) tract changes
  – stress and urge incontinence due to loss of contractile tissue
  – reduced autonomic sphincter control
Consequences of hormonal changes in menopause

- Circulatory (autonomic) instability
  - hot flashes (flushes)
  - tachycardia (palpitations)
  - anxiety
  - sweating
  - paresthesia (“creepy” sensations)
Consequences of hormonal changes in menopause

- CNS changes
  - headaches
  - insomnia
  - depression
  - irritability
  - mood swings
Consequences of hormonal changes in menopause

• Skin changes
  – thinning due to reduced collagen production
  – water loss
  – loss of elasticity
  – wrinkling

• Masculinization
  – hirsutism
  – voice changes
Consequences of hormonal changes in menopause

- Metabolic changes
  - abdominal fat distribution
  - insulin resistance
  - hypertension
  - autoimmune disease
Consequences of hormonal changes in menopause

• Cardiovascular health
  – Increased plasma lipids
    • LDL
    • HDL
    • TG
  – Increased atherosclerosis
  – Increased risk of CHD
Andropause

- Is andropause analogous to menopause?
- Transition is gradual
- Functional impairments are gradual
Hormonal control of male fertility

- Testicular cell types
  - Leydig cells secrete testosterone
  - Sertoli cells participate in spermatogenesis
Hypothalamic control of male fertility

- Pulsatile LH secretion stimulates Leydig cells
- FSH production stimulates spermatogenesis
- Testosterone may be converted to
  - DHT
  - Estradiol
Aging-associated changes in male reproductive system

- Reduced pituitary response to GNRH
- Decreased secretion of androgens
- Increased opioid action
- Reduced androgen receptor sensitivity
- Reduced DHEAS release
- Insulin resistance
- Decreased TSH secretion
- Decreased GH-IGF-I secretion
Aging-associated changes in male reproduction

- Reduced spermatogenesis due to fewer Sertoli cells
- Reduced libido
- Reduced erectile function
  - spontaneous
  - stimulated
Consequences of aging-associated changes in male reproductive hormones

• Reduced spacial cognition
  – spatial attention
  – visual perception
  – object identification
  – visual memory

• Changes in mood
  – depression
  – agitation
Consequences of hormonal changes in menopause

• Musculo-skeletal changes
  – increased bone resorption
  – decreased bone formation
  – osteoporosis
  – osteoarthritis
  – loss of type IIb muscle fibers
  – loss of muscle strength
Hormone replacement treatment of menopause and andropause

• Justification for treatment
  – relief of symptoms
  – prevention and treatment of osteoporosis
  – reduction of risk of CHD morbidity and mortality
Hormone replacement treatment of menopause and andropause

• Estrogens
  – esters or conjugated
  – pills, creams, or patches
  – effectiveness (BMD, cognitive)
  – uterine cancer problem

• Estrogens opposed by progesterone

• Estrogen-testosterone combination
Hormone replacement treatment of menopause and andropause

• Testosterone
  – prostate cancer
  – hair loss
  – gynecomastia
  – skeletal BMD