Hormones & Aging

Hormonal Senescence

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Aging VS. Diseases of Aging

- Aging: Syndrome of progressive, universal, often irreversible and deleterious changes

- Diseases of aging: diseases associated with older age group (e.g., Alzheimer, arthritis etc).
Changes in Body Composition with Aging

- Decreased lean mass
- Increased body fat mass
- Decreased bone mass
- Decline in functional capacity of most organs
Changes in Body Composition with Aging

Are undesirable:

1. Decreased lean mass
   - Decreased Aerobic work capacity
   - Decreased function capacity

2. Increased adiposity:
   - Hypertension
   - Glucose intolerance
   - Hyperlipidemia
Changes in Body Composition with Aging

**Potential Causes**

- Genetically programmed process
- Chronic illnesses
- Nutritional deficiencies
- Disuse atrophy
- Sedentary lifestyle
- Hormonal changes
Hormone Effects

- **Generalized/ multiple tissues**
  - Glucocorticoids
  - Thyroid Hormone
  - Testosterone
  - GH

**Biological/ Health Impact**
- Energy
- Well Being
- Body Weight
- Athletic Performance
- Body Habitus
- Sexual Function

**Specific**
- Mineralocorticoid Action: Na, K
- ADH Action: Water balance

*All are adversely affected by aging*

*Minimally influenced by aging*
Changes in Hormone Levels Throughout Life

- Variable
- Secretion of many hormones is age & gender dependent
- ?? Relation to the aging process
  - Prolactin
  - Melatonin
  - Thyroid hormone
  - Adrenal steroids
  - GH
  - Gonadal steroids
Prolactin Secretion

No significant changes throughout life

Elmlinger et al Clin Chem Lab Med 2003; 41:934
Melatonin

- Secreted by the Pineal gland
- Release is stimulated by darkness and inhibited by light

Biologic Effects:
- Hypnotic
- Control of circadian rhythm
- Possible role in cycle mood disorders
- ? Anti-aging: scavenger of free radicals/ anti-oxidant effects
Melatonin & Aging

- Inconsistent data: some show decrease & others show no change
- No good data on its use in the elderly
- Could have reasonable anti-aging effects:
  - Attenuation of cell damage by free radicals
  - Enhancement of the immune system
Hypothalamic Pituitary Thyroidal Function

Minimal; clinically insignificant changes
Function of the Adrenal Cortex

- Three Layers
- Distinct & different regulation
- Mineralocorticoid secretion
- Glucocorticoid secretion
- Adrenal androgens/estrogens
DHEA/ DHEA-S

- Mild/ weak androgens
- No specific cell receptor
- Secretion starts in fetal life with sudden surge around adrenarche
- Levels decline gradually with age
- Neuro-active in animals and humans
- Potential conversion into more potent androgens and estrogens
Somatotropin

*Growth Hormone*

- Levels decline gradually with increasing age
  - 14% / decade after age 20
  - Caused by a decline in GHRH secretion
- Parallel decline in IGF-1 levels

**GH deficiency in adults causes**

- Decreased lean body mass
- Increased body fat
- Decreased bone mass
Alterations in Gonadal Function in Aging Humans

- **Women:**
  - Relatively sudden decline at menopause
  - Often symptomatic
  - Replacement therapy beneficial

- **Men:**
  - Gradual, less dramatic (over 2-3 decades)
  - Subtle symptoms
  - Replacement therapy beneficial
Alterations In Gonadal Function In Aging Men

- Gradual decline in testosterone levels
  - Hypogonadism
  - Medications
  - Rise in SHBG
- Decline in sexual activity/Impotence
  - Medications
  - Illnesses
  - Vascular
  - Neuropathy
- Hypogonadism and impotence are common, independently distributed conditions
Changes in Body Composition with Aging

- Decreased lean mass
- Increased body fat mass
- Decreased bone mass
- Decline in functional capacity of most organs

- Parallel decline in:
  - GH
  - DHEA
  - Gonadal steroids

- ? Relation Vs. coincidence
Can Hormone Replacement Therapy Reverse some of the Aging Effects?

- Studies using DHEA
- GH therapy
- Androgen replacement therapy
Effect of DHEA Replacement in Aging Men & Women

- Mixed results:
  - Oral VS. vaginal cream
  - Duration of therapy
  - Biochemical findings:
    - Men; Slight inc in androstendione
    - Women: increased serum androgens (DHEA-S, androstendione, testosterone, DHT)
    - Increased free IGF-I
  - Clinical benefits: variable
    - Some improvement in well being
    - NO benefit
Growth Hormone Therapy
(Patients With Deficiency)

- Increased fat oxidation
- Increased nitrogen retention & protein synthesis
- Increased lean body mass
- Decreased body fat
- Improved sense of well being
- Dose-dependent rise in plasma IGF-1 levels
Effects of GH Therapy on Visceral Fat

Before GH  after GH
Side Effects of GH Administration In Adults

- Short-term: Dose dependent; reversible
  - Edema
  - Hypertension
  - Arthralgias
  - Carpal Tunnel Syndrome
  - Glucose intolerance
  - Gynecomastia

- Long-term: Largely Unknown; dose dependent
Androgen Supplementation in Otherwise Healthy Aging Men

- Increase in Lean weight
- No change in body fat
- Decrease in Urinary OH-proline

Tenover et al J CEM; 75:1092-
Adverse Effects of Androgen Replacement Therapy

- Weight gain/ fluid retention
- Acne/ Skin changes
- Aggressive behavior
- Gynecomastia
- Sleep apnea
- Atherogenic lipid profile
- Erythrocytosis
- Insulin resistance
- Prostate enlargement
- Liver disease
  - Cholestasis
Who Should be Considered for Hormone Replacement therapy??

- **GH:**
  - Documented deficiency; hypopituitarism

- **Testosterone:**
  - Documented deficiency with symptoms/ and/ or osteoporosis
  - No contraindications

- **DHEA:**
  - Small doses (25-50 mg/day) are probably OK in patients with adrenal insufficiency
Can Exercise Training and/or Nutritional Supplementation Reverse physical frailty In elderly Individuals??

“YES”

- High intensity resistance exercise with/without nutritional supplement in 100 elderly subjects (72-98 Yrs of age) over 10 weeks showed:
  - Increased muscle mass & strength
  - Improved stair-climbing power
  - Increased spontaneous physical activity
  - Increased gait velocity

Fiatarone et al ( N Engl J Med; 330:1769-
Anti Aging Business

Change Your Body and Be Admired

Anti-Aging Fitness