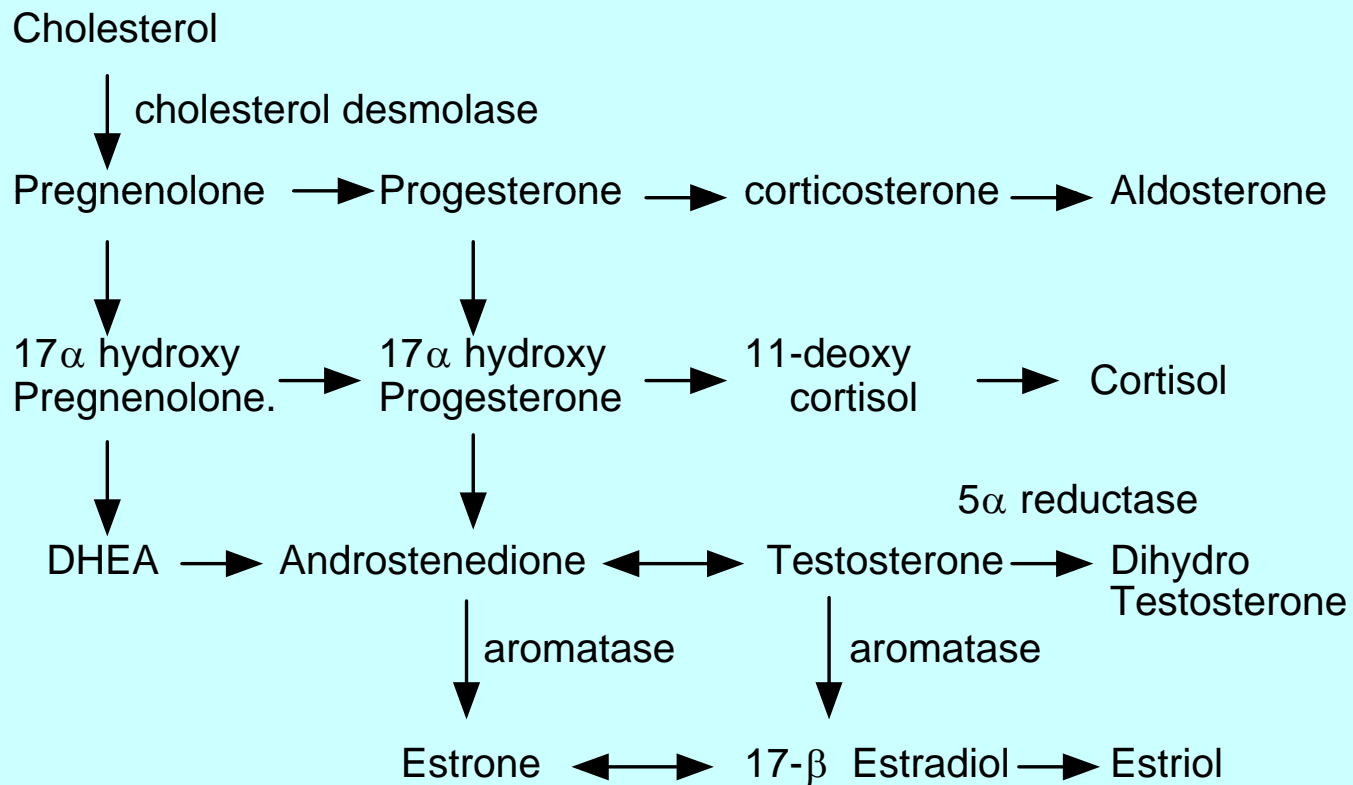


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Presents: Intro To Hormones 102
Salivary Hormone Testing
Part 4
Adrenal Function Assessment
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Salivary Adrenal Testing

- Cortisol and DHEA are the primary hormones produced by the adrenal glands
- Dehydroepiandrosterone sulfate (DHEAS) is the sulfated version of DHEA.
- DHEA levels naturally peak in the early morning hours, however, DHEAS levels show no diurnal variation.
- From a practical point of view, measurement of DHEAS is preferable to DHEA as levels are more stable and reflect body stores

Hormone Metabolism



Cortisol

- Cortisol is the most potent glucocorticoid produced by the human adrenal gland.
- Cortisol is synthesized from cholesterol.
- Its production is stimulated by pituitary adrenocorticotrophic hormone (ACTH), which is regulated by corticotropin releasing factor (CRF).
- ACTH and CRF secretions are inhibited by high cortisol levels in a negative feedback loop.
- In plasma a majority of cortisol is bound with high affinity to corticosteroid binding globulin (CBG or transcortin).

Diurnal Cortisol Rhythm

- Cortisol production has an ACTH-dependent circadian rhythm with peak levels in the early morning and a nadir at night.
- The factor controlling this rhythm is not completely defined and can be disrupted by a number of physical and psychological conditions.
- ACTH and cortisol are secreted independent of circadian rhythm in response to physical and psychological stress.

Cortisol Effects

- Promotes the conservation of glucose, and inhibits glucose utilization
- Promotes hepatic protein synthesis and gluconeogenesis
- Stimulates the release of fatty acids from adipose tissue via lipase
- Anti-inflammatory - down-regulates phospholipase A2
- Immunosuppressive

Cortisol Levels

- Elevated cortisol levels and a lack of diurnal variation have been identified with Cushing's disease (ACTH hypersecretion) and adrenal tumors.
- Low cortisol levels are found in primary adrenal insufficiency (e.g. adrenal hypoplasia, Addison's disease) and ACTH deficiency.
- Due to the normal circadian variation in cortisol levels, distinguishing normal from abnormally low cortisol levels can be difficult; therefore, several daily collections are recommended.

High Cortisol

- Stress stimulates ACTH secretion, which is referred to as the “Fight or Flight” response.
- High levels of cortisol at night interfere with REM sleep.
- High cortisol is correlated with high protein diets, and an inverse relationship with high carbohydrate diets
- Associated with calcium malabsorption and low bone mineral density
- Prolonged stress may result in decreased AM and increased PM levels (a “cortisol flip”)

Low Cortisol

- Addison's disease is a cortisol deficiency
- Low cortisol levels in the morning cause fatigue, and are associated with chronic fatigue syndrome
- Cortisol deficiency results in anorexia, weight loss, weakness, apathy, hypotension and an inability to withstand stress
- Cortisol deficiency associated with chronic illness, autoimmune and rheumatic disease

Cortisol Deficiency

- Vascular smooth muscle becomes unresponsive to NE and EPI (epinephrine used to be called adrenaline), eventually causing vascular collapse
- There is increased sensitivity to smells and taste
- Personality changes include irritability, apprehension, and an inability to concentrate
- An inability to excrete a water may cause water intoxication

Cushing's Disease

- Cushing's disease is caused by high cortisol levels in the blood
- Symptoms include: muscle weakness, obesity, weight gain, poor wound healing, easy bruising, renal calculi, Hirsutism, loss of libido and acne (androgens), psychiatric disturbances
- Signs include: ecchymoses (skin atrophy with purple striae), moon faces, buffalo hump, trunkal obesity with skinny extremities, osteoporosis, peptic ulcer, diabetes (glucose intolerance), hypertension, and edema

Cushing's Disease

Epidemiology

- Female:male – 5:1, occurs during childbearing years
- Ectopic ACTH is more common in men, and usually occurs later in life.

Addison's Disease

- Addison's disease is primary adrenal insufficiency
- Signs include: fatigue, weakness, weight loss, dizziness, syncope, lightheadedness, fainting, mental changes (nervous irritability, depression, apprehension), increased skin pigmentation, headache, palpitation, craves sweets, alcohol intolerance, alternating diarrhea/constipation, premenstrual tension, scanty perspiration
- Symptoms include: postural hypotension, hypotension, dry and thin skin, sparse hair
- Associations: allergies, hay fever, skin dermatitis

Glucocorticoids

Glucocorticoids:

- Cause connective tissue dissolution
- Have an anti-vitamin D effect
- Cause proteolysis of muscle
- Inhibit lymphocytes and monocytes
- Increase acid and pepsin secretion
- Increase gluconeogenesis

DHEA

- DHEA (dehydroepiandrosterone) is synthesized primarily in the adrenal glands from the steroid precursor pregnenolone, which is synthesized from cholesterol.
- DHEA is the main precursor for estradiol and testosterone.

DHEAS

- DHEA is the most abundant circulating steroid in humans
- In the blood, most DHEA is sulfated (DHEA-S04) providing a storage depot for DHEA, thereby prolonging its half life and providing a steady state source of DHEA for conversion to estrogens and androgens in the adrenal glands, ovaries, and testes.

Decreased DHEA

- Circulating levels are closely associated with aging, dropping nearly 5-fold from a peak at age 20-25 to a low at age 70-80.
- 17,20 desmolase, essential for synthesis of DHEA, is functionally reduced with aging
- The zona reticularis of the adrenal gland, where DHEA is made, atrophies with age

Diseases with Low DHEA

Various diseases have been associated with low circulating DHEA levels:

- Heart disease, cancer, diabetes, obesity, chronic fatigue syndrome, AIDS, Alzheimer's disease, systemic lupus erythematosus (SLE), rheumatoid arthritis, and multiple sclerosis

Functions of DHEA

DHEA has been associated with:

- The ability to stay thin and to make muscle
- Avoiding breast cancer (for women)
- Avoiding cardiovascular disease (for men)
- Improving memory and stress resistance
- Improving one's sense of "well-being"

DHEA and Insulin/Cortisol

- Insulin both inhibits the synthesis of DHEA and accelerates the breakdown of DHEA.
- High levels of DHEA are anabolic, have an anti-glucocorticoid activity, and balance cortisol

Increasing DHEA

- It has been suggested that measures which increase circulating DHEA levels such as exercise, proper diet, stress reduction, and/or supplementation can ameliorate some of the diseases associated with low DHEA levels, especially the generalized debilitation associated with aging.

DHEA Cautions

- Use caution in patients at risk for developing hormone-dependent cancers: prostate cancer in men and reproductive cancers in women.
- Doses above 1500 mg/day have been known to result in insulin resistance in humans.

Salivary Adrenal Stress Tests

- Salivary tests of Cortisol and DHEA are commonly referred to as Adrenal Stress Tests
- Cortisol is usually measured 4 times during a 24-hour period
- DHEA or DHEA-S is usually measured once.

Chronic Fatigue Syndrome

- CFS is characterized by persistent or relapsing debilitating fatigue for at least 6 months in the absence of any other definable diagnosis.
- Symptoms of CFS may include depression, hypotension, weight loss, and inability to endure stress.
- Researchers have proposed that CFS is actually a disease of the hypothalamic-pituitary-adrenal axis.
- CFS may be associated with excess cortisol secretion, or decreased cortisol in late stages when the adrenal glands become exhausted

Insomnia

- Normal sleep rhythms are associated with increased melatonin and decreased cortisol and DHEA
- Rapid eye movement (REM) sleep occurs primarily when cortisol levels are decreasing

Menstrual Disorders

- Excess cortisol is produced during stress
- A progesterone and estradiol deficiency can result from the accelerated conversion into cortisol
- Excess cortisol signals the body to lower production (inhibition feedback), which may cause over-production of testosterone, progesterone and/or estrogen,
- High cortisol levels have been measured in women with exercise-associated amenorrhea

Alzheimer's Disease

- DHEA levels were significantly lower in patients with early or late Alzheimer's disease compared to normal controls.
- DHEA may protect against oxidative stress in the hippocampal region of the brain, a critical area for memory function often damaged by Alzheimer's disease.

Immune Dysfunction

- DHEA protects the thymus gland (which produces T cells) from glucocorticoid-induced involution.
- DHEA has been shown to stimulate interleukin-2 (IL-2) activity and interferon-gamma production in T cells isolated from human donors.

HIV and AIDS

- DHEA inhibits RNA and DNA viral expression in animal studies, and also seems to suppress HIV replication.
- One recent investigation of HIV-positive patients showed that a reduction in serum DHEA and DHEA-S levels inversely correlates with the progression of AIDS, indicating that DHEA can provide some measure of protection against HIV infection.

Nutritional Support

- In this section, we will review the nutritional support for the adrenal glands

Vitamin B5

- Vitamin B5 (Pantothenic Acid) is required for the formation of some steroids via the action of CoA
- Vitamin B5 is useful for adrenal insufficiency and stress

Vitamin C

- The adrenal gland is among the organs with the highest concentration of vitamin C in the body.
- The adrenal glands secrete vitamin C in response to stress

Licorice

- Licorice supports the adrenal glands and was used for Addison's disease.
- Liquorice is an adaptogen which helps regulate the hypothalamic-pituitary-adrenal axis.
- Licorice contains isoflavones (phytoestrogens).

Licorice and BP

- Large doses of glycyrrhizinic acid and glycyrrhetic acid in liquorice extract can lead to hypokalemia and serious increases in blood pressure (apparent mineralocorticoid excess).
- As such, licorice is contraindicated in hypertension and pregnancy

Ashwagandha

- Ashwagandha (*Withania somnifera*) is a tonic and adaptogen
- alkaloids are sedative, reduce blood pressure and lower heart rate
- withanolides are anti-inflammatory and inhibit growth of cancer cells
- withanolides increase hemoglobin levels

Ginseng

- Siberian ginseng (*Eleutherococcus senticosus*) and Panax ginseng (ren shen) are adaptogens
- The adaptogenic properties of ginseng are believed to be due to its effects on hypothalamic-pituitary-adrenal axis, resulting in elevated plasma corticotropin and corticosteroids levels.

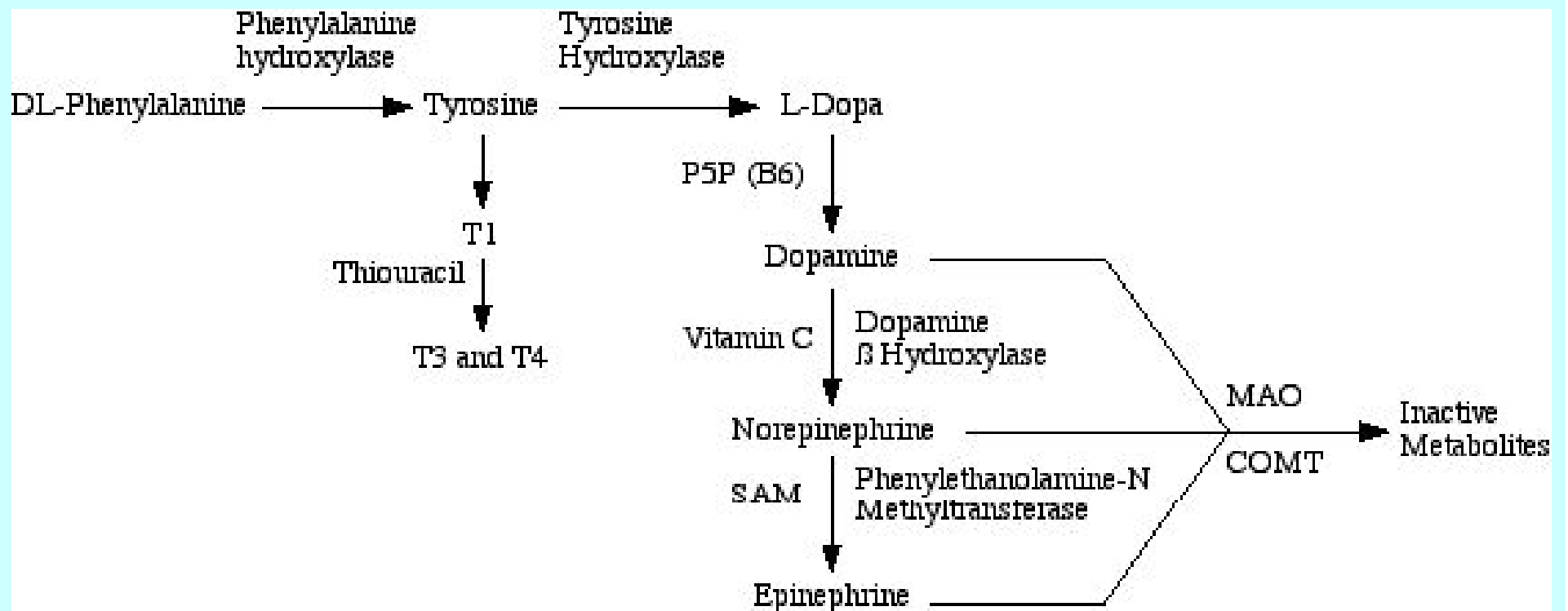
Blood Type O

- According to Dr. D'Adamo in "Eat Right for Your Blood Type", people with blood type O use B vitamins for energy
- Beef and liver, which they naturally crave, contain high amounts of niacin (vitamin B3)
- A high quality B complex with plenty of B5 may be beneficial

Catecholamines

- The chromaffin cells of the adrenal medulla are the body's main source of catecholamine hormones adrenaline (epinephrine) and noradrenaline (norepinephrine).
- Catecholamines are part of the fight-or-flight response initiated by the sympathetic nervous system.

Biochemistry



Tyrosine

- Notice the conversion of catecholamines
 - Phenylalanine
 - Tyrosine
 - Dopamine
 - Norepinephrine
 - Epinephrine (adrenaline)
- Those with phenylketonuria (PKU) don't convert phenylalanine into tyrosine

Summary

- In this section we briefly reviewed diseases associated with imbalances in adrenal function
 - Addison's and Cushing's Disease
 - Chronic Fatigue Syndrome
 - Insomnia
 - Menstrual disorders
 - Alzheimer's disease
 - Immune dysfunction
 - HIV and AIDS

Stress

- The adrenal gland presents a common link with several mechanisms of stress, including:
 - DHEA and Cortisol
 - Catecholamines (adrenalin/epinephrine)
 - Aldosterone (sodium and BP regulation)
 - Steroids (estrogen and testosterone)

Adrenal Support

- Nutritional support includes:
 - Vitamins B5 and C
 - Licorice (caution: may raise BP)
 - Ashwagandha
 - Ginseng