What You Must Know About Women’s Hormones

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References


THE STEROIDIODGENIC PATHWAY
WITH ENZYMATIC STEPS

Enzymatic Steps:
1. 20 α-hydroxylase, 22 hydroxylase & 20,22 desmolase
2. 3β-hydroxysteroid dehydrogenase & Δ5 - Δ4 isomerase
3. 17 α-hydroxylase
4. 17,20 desmolase (17,20-lyase)
5. 21-hydroxylase
6. 11 β-hydroxylase
7. 18-hydroxylase
8. 18-hydroxydehydrogenase
9. 17 β-hydroxysteroid dehydrogenase
10. aromatase
11. 3β-hydroxysteroid sulfotransferase
Hormone response is as unique to each person as their own fingerprints.

Hormone replacement should not be considered without a thorough understanding of how all of the body’s hormones interact with each other.

The normal age to go through menopause ranges from 35 to 55.

Therefore, a woman may live one half of her life without a menstrual cycle.

Cycling after the age of 55 increases a women’s risk of breast cancer.
Synthetic HRT: Other Problems

- It is estimated that one-half of women quit taking their synthetic hormone replacement therapy after one year because they are unable to tolerate the side effects.
- Synthetic hormones waste energy by giving incomplete messages to cells which then fail to produce a balanced hormonal response.
Why Consider HRT

- Relief of symptoms
- Prevention of memory loss
- Heart health
- Bone production
- Growth and repair
Hormones That Regulate Growth and Repair

- Insulin
- Growth hormone
- Testosterone
- Estrogens
- DHEA
Symptoms of Menopause

- Hot flashes
- Night sweats
- Vaginal dryness
- Anxiety
- Mood swings
- Irritability
- Insomnia
- Depression
Symptoms of Menopause (Cont.)

- Loss of sexual interest
- Hair growth on face
- Painful intercourse
- Panic attacks
- Weird dreams
- Urinary tract infections
- Vaginal itching
- Lower back pain
- Bloating
Symptoms of Menopause (Cont.)

- Flatulence
- Indigestion
- Osteoporosis
- Aching ankles, knees, wrists, shoulders, heels
- Hair loss
- Frequent urination
- Snoring
- Sore breasts
Symptoms of Menopause (Cont.)

- Palpitations
- Varicose veins
- Urinary leakage
- Dizzy spells
- Panic attacks
- Skin feeling crawly
- Migraine headaches
- Memory lapses
- Weight gain
Estrogen

- Estrogen has 400 functions in the body, including the following:
Functions of Estrogen

- Stimulates the production of choline acetyltransferase, an enzyme which prevents Alzheimer’s disease
- Increases metabolic rate
- Improves insulin sensitivity
- Regulates body temperature
- Helps prevent muscle damage
- Helps maintain muscle
- Improves sleep
Functions of Estrogen (Cont.)

- Reduces risk of cataracts
- Helps maintain the elasticity of arteries
- Dilates small arteries
- Increases blood flow
- Inhibits platelet stickiness
- Decreases the accumulation of plaque on arteries
- Enhances magnesium uptake and utilization
- Maintains the amount of collagen in the skin
Functions of Estrogen (Cont.)

► Decreases blood pressure
► Decreases LDL and prevents its oxidation
► Helps maintain memory
► Increases reasoning and new ideas
► Helps with fine motor skills
► Increases the water content of skin and is responsible for its thickness and softness
► Enhances the production of nerve-growth factor
Functions of Estrogen (Cont.)

- Increases HDL by 10 to 15%
- Reduces the overall risk of heart disease by 40 to 50%
- Decreases lipoprotein(a)
- Acts as a natural calcium channel blocker to keep arteries open
- Enhances energy
- Improves mood
- Increases concentration
- Maintains bone density
- Helps prevent glaucoma
Functions of Estrogen (Cont.)

- Increases sexual interest
- Reduces homocysteine
- Decreases wrinkles
- Protects against macular degeneration
- Decreases risk of colon cancer
- Helps prevent tooth loss
- Aids in the formation of neurotransmitters in the brain such as serotonin which decreases depression, irritability, anxiety, and pain sensitivity
Symptoms of Estrogen Excess

- Cervical dysplasia
- Depression with anxiety or agitation
- Increased risk of uterine cancer
- Weight gain (abdomen, hips, thighs)
- Water retention
- Headaches
- Poor sleep
- Panic attacks
- Swollen breasts
Symptoms of Estrogen Excess (Cont.)

➤ Heavy periods
➤ Increased risk of breast cancer
➤ Increased risk of auto-immune diseases
➤ Hypothyroidism
➤ Fatigue
➤ Irritability/mood swings
➤ Uterine fibroids
➤ Bloating
Causes of Excess Estrogen in The Body

- Taking too much estrogen
- Impaired elimination of estrogen
- Lack of exercise
- Diet low in grains and fiber
- Environmental estrogens
- Elevation of 16–OH estrone
Synthetic Estrogen

- Synthetic estrogen is not the same chemical structure of estrogen that the patient’s body is born with.
- Most common synthetic estrogen available worldwide.
  - Estrone
  - Sodium equilin sulfate
  - Concomitant components
    - 17 alpha–dihydroequilin
    - 17 alpha–estradiol
    - 17 beta–dihydroequilin
Natural Estrogen

- Medically, natural estrogen means that it is the same chemical structure that the patient is born with.
- It may or may not come from a plant.
- Natural estrogen helps to protect against endothelial dysfunction by increasing endothelial nitric oxide.
Endothelial nitric oxide synthase is a crucial enzyme involved in the production of nitric oxide in endothelial cells.

Study showed that compared to natural estrogen, gene transcription of endothelial nitric oxide synthase was 30 to 50% lower in response to equine estrogens.

Natural Estrogens (Cont.)

- E1 called estrone
- E2 called estradiol
- E3 called estriol
Estrone (E1)

- Is the main estrogen the body makes postmenopausally
- High levels many researchers believe may increase a women’s risk of breast cancer
Estradiol (E2)

- Increases HDL
- Decreases LDL and total cholesterol
- Decreases triglycerides
- Helps maintain bone structure
- Increases serotonin
- Decreases fatigue
- Works as an antioxidant
- Helps maintain memory
- Helps absorption of calcium, magnesium, zinc
Estriol (E3)

- Is 80 times weaker than E2 so has a lesser stimulatory effect
- Considerable evidence exists to show that it protects against breast cancer
- Experimentally E3 is being used in breast cancer patients
- It does not have the bone, heart, or brain protection of estradiol.
Functions of E3 in the Body

- Helps maintain pregnancy
- Benefits the vaginal lining
- Blocks E1 by occupying the estrogen receptor sites on the cells of the breasts
- Controls symptoms of menopause
- Decreases LDL
- Increases HDL
Functions of E3 in the Body (Cont.)

► Helps reduce pathogenic bacteria
► Helps restore the proper pH of the vagina, which prevents urinary tract infections
► Helps the GI tract maintain a favorable environment for the growth of lactobacilli
Estrogen Receptor Sites

- Estrogen has two main receptor sites that it binds to in the body
  - Estrogen receptor alpha
    - Increases cell growth
  - Estrogen receptor beta
    - Decreases cell growth
    - Helps prevent breast cancer development
Estrogen Receptor Sites (Cont.)

- E2 equally activates estrogen–receptors alpha and beta
- E1 activates estrogen–receptor alpha selectively in a ratio of 5:1 which increases cell proliferation
- E3 binds preferentially to estrogen–receptor beta in a 3:1 ratio which may be the reason that E3 may help prevent breast cancer
After menopause, the metabolism of estrogen can change. Consequently a woman may respond differently to estrogen replacement.
Estrogen Metabolism

Two major competing pathways

- 2-OH estrone
- 16-OH estrone
Estrogen Metabolism

- One minor pathway
  - 4-OH estrone
2-OH Estrone/Methylation

- Good estrogen. It does not stimulate the cell growth.
- Blocks action of stronger estrogen products that may be carcinogenic.
- 2-OH estrone is protective against cancer when methylated by catechol-O-methyltransferase (COMT) into 2-methoxyestrone. The ratio of 2-methoxyestrone to 2-hydroxyestrone can be measured in the urine and is a good gauge of the body’s ability to methylate.
Another way of evaluating the body’s ability to methylate is by measuring the homocysteine level.

Low ratios of 2/16 hydroxy estrogen are also associated with an increased rate of developing lupus.
Factors That Support Methylation

- SAMe
- Methionine
- B2, B6, B12
- Folic acid (also as folinic acid, 5-formyl THF, or 5-methyltetrahydrofolate--MTHF)
- TMG (betaine)
- Reducing catecholamine production by decreasing stress
16-OH Estrone

- Has significant strong estrogenic activity and studies show it may be associated with an increased risk of breast cancer.
- High levels are associated with obesity, hypothyroidism, pesticide toxicity (organochlorines), omega-6-fatty acid excess, and inflammatory cytokines.
4–OH Estrone

- Studies show it may directly damage DNA and cause mutations. Therefore, it is proposed to enhance cancer development.
- Equine estrogens, such as Premarin, increase metabolism into 4–OH estrones.
- Is present in greater quantities there is a deficiency of methionine and folic acid
- People who have uterine fibroids also may have increased levels of 4–OH estrone.
How Can You Raise 2-OH Estrone?

- Moderate exercise
- Cruciferous vegetables
- Flax
- Soy
- Kudzu
- Broccoli derivatives: indole-3-carbinol taken as a supplement. Daily dose is 200 to 300 mg. Other derivatives of broccoli that have been shown to be effective are DIM (diindolylmethane, a breakdown product of I-3-C) and sulforaphane glucosinolate
How Can You Raise 2-OH Estrone? (Cont.)

- Omega-3-fatty acids
- B6, B12, and folate
- MTHF
- TMG
- Rosemary, turmeric
- Weight loss
- High protein diet
There are other factors that affect estrogen metabolism.
Obesity Affects Estrogen Metabolism

- Decreases 2-OH estrone and increases 16-OH estrone
- Estrogen production and storage occurs in fat cells
- Concentrations of sex hormone binding globulin (SHBG) are decreased
There are 50 chemicals that imitate estrogen that are toxic to the body.

- Pesticides
- Synthetic hormones fed to animals
- Plastics
- Cosmetics
Alcohol interferes with the body’s ability to detoxify estrogen and increases E2 levels and the risk of breast cancer.

Antibiotics found in food may be associated with an elevated risk of breast cancer by changing the gut flora involved in the enterohepatic circulation of estrogens.
Common comments I hear from patients are the following:

- “I think that I am losing my mind.”
- “I feel like my body is divorcing itself.”
- “I have lost the ability to spell.”
- “I am always losing my keys.”
- “I may be getting Alzheimer’s disease.”
Estrogen and the Brain (Cont.)

- Increases blood flow
- Increases glucose and oxygen to the neurons
- Protects neurons
- Increases neurotransmitters
- Keeps the blood–brain barrier working
- Increases sensitivity to nerve growth factor
- Decreases neuronal generation of Alzheimer’s beta amyloid peptides
Estrogen and the Brain (Cont.)

- Is a natural antioxidant
- Increases manual speed and dexterity
- Increases availability of acetylcholine
- Boosts by 30% NMDA receptors to maintain strength and durability of synapse connections involved in creating long-term memories
- Decreases distractability
- Turns on progesterone receptors
Estrogen deficiency has been suggested to be a state of accelerated aging.

Estrogen Replacement

- Always give estrogen transdermally!
Estrogen Given By Mouth Can

- Increase blood pressure
- Increase triglycerides
- Increase estrone
- Cause gallstones
- Elevate liver enzymes
- Increase SHBG (decreases testosterone)
- Interrupt tryptophan metabolism and consequently serotonin metabolism
- Lower growth hormone
- Increase prothrombic effects
- Increase CRP
- Increase carbohydrate cravings
Compounded by a pharmacy

- Dose is individualized
- Can use any mix of different percentages of E2 and E3 (biest)
- Only method of obtaining E3 in North America
- Individualized therapy
- Do not use triest
In a 2013 study: researchers estimated that over the past decade between 18,600 to 91,600 postmenopausal women, ages 50–59 years old, who had had a hysterectomy may have died prematurely because they did not take estrogen.

Another study which was a meta-analysis from 27 published studies showed a 28% reduction in mortality in menopausal women under age 60 who used hormone replacement therapy and the participants also had improved quality of life.

Nolvadex and Raloxifene

- Do not have the same positive affects on the brain that natural hormone replacement does.
- They decrease total cholesterol by 5% and LDL by 10% but unlike natural hormone replacement are not very effective in lowering triglycerides and do not increase HDL.
New Research

- Presented at the American College of Cardiology Scientific Session, March 2017 in Washington D.C. by Yoav Arnson, M.D.
- He looked at coronary artery calcium scanning between 1998 and 2012 of postmenopausal women.
- “HRT results in lower atherosclerosis and improved survival for all age groups and for all levels of coronary calcium.”
Progesterone
Symptoms of Progesterone Loss

- Anxiety
- Depression
- Irritability
- Mood swings
- Insomnia
- Pain and inflammation
- Osteoporosis
- Excessive menstruation
Symptoms of Progesterone Loss (Cont.)

- Hypersensitivity
- Nervousness
- Migraine headaches before cycles
- Weight gain
- Decreased libido
- Decreased HDL
Causes of Low Progesterone

- Impaired production
- Low LH
- Increased prolactin production
- Stress
- Antidepressants
- Excessive arginine consumption
- Sugar
- Saturated fat
- Deficiency of vitamins A, B6, C, zinc
- Decreased thyroid hormone
Called progestins
Progestins do not reproduce the same actions of natural progesterone
Side Effects of Progestins

- Increases appetite
- Weight gain
- Fluid retention
- Irritability
- Depression
- Headache
- Decreases energy
- Bloating
- Breast tenderness
- Decreases sexual interest
Side Effects of Progestins (Cont.)

- Acne
- Hair loss
- Nausea
- Insomnia
- Interferes with the body’s own production of progesterone
- Does not help balance estrogen
- Remains in the body longer
- Can cause spasm of coronary arteries
Progestins increase breast cell replication and growth due to the stimulation of estrogen receptors by progestins.


Progestins increase the risk of breast cancer.

Stop the protective effects estrogen has on the heart
May make the symptoms of progesterone loss worse
Increases LDL
Decreases HDL
Protects only the uterus from cancer
Counteracts many of the positive effects of estrogen on serotonin
Natural Progesterone Effects Not Seen with Progestins

- Helps balance estrogen
- Leaves the body quickly
- Improves sleep
- Natural calming effect
- Lowers high blood pressure
- Helps the body use and eliminate fats
- Lowers cholesterol
Natural Progesterone Effects Not Seen with Progestins (Cont.)

- Increases scalp hair
- Helps balance fluids in the cells
- Increases the beneficial effects of estrogen on BV
- Increases metabolic rate
- Natural diuretic
- Natural antidepressant
- Is anti-inflammatory
Stimulates the production of new bone
Enhances the action of thyroid hormones
Improves libido
Helps restore proper cell oxygen levels
Induces conversion of E1 to the inactive E1S form
Promotes Th2 immunity
Is neuroprotective, promoting myelination

Studies have shown that progesterone does NOT induce estrogen–stimulated breast cell proliferation.

References

References

Natural progesterone has been shown to decrease the risk of developing breast cancer.

A study looked at 80,000 postmenopausal women for 8 years using different kinds of HRT.

- It found that women who used estrogen in combination with synthetic progestin had a 69% increased risk of developing breast cancer when compared to women who never took HRT.
- Women who used progesterone in combination with estrogen had no increased risk in developing breast cancer compared to women that did not use HRT and also had a decreased risk in developing breast cancer compared to the women that used progestin.
Reference

Another study done by the same researchers found a 40% increased risk of developing breast cancer in women who used estrogen with progestin.

In women who used estrogen combined with progesterone there was a trend toward a decreased risk of developing breast cancer.

Estrogen/Progesterone Ratio
Prolonged Use of Progesterone Without Adequate Estrogen

- Increases weight gain
- Increases total cholesterol
- Decreases HDL
- Increases LDL
- Increase triglycerides
- Causes depression
- Causes fatigue
- Decreases libido
- Increases insulin resistance
- Increases fat storage
Effects of Too Much Progesterone Even with Adequate Estrogen (Cont.)

► Elevates cortisol
► Increases insulin resistance
► Increases appetite and carbohydrate cravings
► Relaxes the smooth muscles of the gut: can cause bloating, fullness, and constipation. It can also contribute to gallstones.
► Causes incontinence
► Decreases growth hormone
► Causes ligaments to relax and can cause backaches, leg aches, and achy hips
► Suppresses the immune system
Adrenaline interacts with progesterone.

Adrenaline surges that occur with stress can block progesterone receptors. This can prevent progesterone from being used effectively in the body.
Treatment

► Compounded progesterone as a cream or as a capsule
► If the patient has insomnia as symptom then choose P.O. which affects the GABA receptors.
► Experts on HRT now suggests that for peri-menopausal women and menopausal women: progesterone PO helps prevent breast cancer better than transdermally applied progesterone.
► Prometrium-- advantages and disadvantages
Progestosterone and Breast Cancer Prevention

- Study measured blood levels of progesterone in almost 6,000 women that were premenopausal.
- Women with the highest levels of progesterone who had regular cycles had a 88% reduction in the risk of developing breast cancer.
In another study over 1,000 women were studied for over 30 years who had treatment for infertility. The trial was done to look at subsequent breast cancer risk.

Women who were deficient in progesterone had 5.4x increased risk of developing premenopausal breast cancer and were 10x as likely to die from any cancer.

Testosterone

- Increases sexual interest
- Increases sense of emotional well-being
- Increases muscle mass and strength
- Helps maintain memory
- Helps skin from sagging
- Decreases excess body fat
- Helps maintain bone strength
- Elevates norepinephrine in the brain (tricyclic affect)
Symptoms of Testosterone Loss

- Muscle wasting
- Weight gain
- Fatigue
- Low self-esteem
- Decreased HDL
- Dry, thin skin, with poor elasticity
- Thinning and dry hair
- Droopy eyelids
- Sagging cheeks
- Thin lips
- Anxiety
- Memory is not as sharp
Causes of Low Testosterone

► Menopause
► Childbirth
► Chemotherapy
► Adrenal stress or burnout
► Endometriosis
► Depression
► Psychological trauma
► Birth control pills
► HMG–CoA–reductase inhibitors
Treatment

► Testosterone replacement should be transdermal.
► Use the bio–identical form. Methyltestosterone has been associated with an increase in liver cancer.
► If used transdermally must rotate sites.
► In order for testosterone to work well, estradiol must also be optimized.
► Without enough estrogen, testosterone cannot attach to brain receptors.
► If testosterone is given alone it can increase plaque formation.
How Else Can Testosterone Levels Be Raised?

- Decrease calorie intake
- Increase protein in the diet
- Take the amino acids arginine, leucine, glutamine
- Exercise
- Get enough sleep
- Lose weight
- Reduce stress
- Take zinc if deficient (Zinc is needed for the metabolism of testosterone.)
Symptoms of Elevated Testosterone

- Anxiety
- Depression
- Fatigue
- Hypoglycemia
- Salt and sugar cravings
- Agitation and anger
- Facial hair
- Acne
- Insulin resistance
- Weight gain
- Hair loss or unwanted hair growth
- Increased risk of heart disease
Treatment of Elevated Testosterone

► Saw palmetto
► Metformin
► Spironolactone
SHBG

- SHBG is a carrier protein for testosterone and DHT and somewhat for E2 estrogen.
- If SHBG is high then there is less E2 and testosterone available for use by the body.
- If SHBG is low, more estrogen and testosterone are available for usage.
- Low SHBG may be a marker for low thyroid function.
High insulin levels are a negative modifier for SHBG as are high prolactin levels.

Estrogen by mouth increases SHBG by 50%.

Equine estrogens increase SHBG by 100%.

Transdermally applied estrogen minimally increases SHBG unless there is an overdose.
DHEA

- Is a hormone made by the adrenal glands.
- A small amount is also made in the brain and skin.
- DHEA production declines with age starting in the late twenties.
- By the age of 70 the body may only make $\frac{1}{4}$ of the amount of DHEA it made earlier.
- DHEA makes estrogen and testosterone in both women and men.
- DHEA levels may also change when the patient has stress at any age.
Functions of DHEA

- Decreases cholesterol
- Decreases formation of fatty deposits
- Prevents blood clots
- Increases bone growth
- Promotes weight loss
- Increases brain function
- Increases lean body mass
Functions of DHEA (Cont.)

► Increases sense of well-being
► Helps one deal with stress
► Supports the immune system
► Helps the body repair itself and maintain tissues
► Decreases allergic reactions
► Lowers triglycerides
Etiologies of Low DHEA

- Menopause
- Decreased production
- Stress
- Aging
- Smoking (nicotine inhibits the production of 11-β-hydroxylase which is needed to make DHEA)
Replacement of DHEA

- Increase muscle strength and lean body mass
- Activate immune function
- Increase quality of life
- Improve sleep
- Increase feeling of wellness
- Decrease joint soreness
- Increase sensitivity of insulin
- Decrease triglycerides
- Stop the damaging effects of stress
- Elevate growth hormone levels
Dosage

- Women are more sensitive to the effects of DHEA and need less DHEA than men.
Symptoms of DHEA Excess

- Fatigue
- Anger
- Depression
- Deepening of voice
- Insomnia
- Mood changes
- Weight gain
- Facial hair
- Acne
- Sugar cravings
- Restless sleep
- Irritability
Don’t microanalyze every nice breeze that comes your way.
Cortisol

- Is the only hormone in the body that increases with age.
- Is made by the adrenal glands.
- When one is stressed cortisol elevates and then it is supposed to come right back down. This does not always happen in today’s world of 365–24–7.
- Overbooking is an issue with everyone. Know how much work and responsibility to take on.
Time is the coin of your life.
It is the only coin you have,
And only you can determine how it will be spent
Be careful lest you let other people spend it for you.
Remember \textit{life} isn’t a \textbf{busy} contest.
Functions of Cortisol

- Balances blood sugar
- Weight control
- Immune system response
- Bone turnover rate
- Stress reaction
- Sleep
- Protein synthesis
Functions of Cortisol (Cont.)

- Mood and thoughts
- Influences testosterone/estrogen ratio
- Influences DHEA/insulin ratio
- Affects pituitary/thyroid/adrenal system
- Participates with aldosterone in sodium reabsorption
- Is an anti-inflammatory
What Elevates Cortisol

- Stress
- Depression
- High progestin intake
Levin and Montaquila, *Dogplay*: (2010)
Consider **fresh air**
God’s **prozac**.
Consequences of Elevated Cortisol

- Decreased immune system
- Increased osteoporosis risk
- Fatigue
- Irritability
- Sugar cravings
- Shakiness between meals
- Confusion
- Memory is not as sharp
Consequences of Elevated Cortisol (Cont.)

- Low energy
- Night sweats
- Binge eating
- Increased blood pressure
- Increased cholesterol
- Increased triglycerides
- Increased blood sugar
Consequences of Elevated Cortisol (Cont.)

- Increased insulin/insulin resistance
- Increased infections
- Thin skin
- Easy bruising
- Muscle weakness
- Weight gain around the middle
- Sleep disturbances
- Impaired hepatic conversion of T4 to T3
Abnormal Cortisol Levels Are Associated With

- Menopause
- CFS
- Fibromyalgia
- Depression
- Impotence
- Anorexia nervosa
- Insulin resistance/diabetes
- Generalized memory loss
- IBS
- Exacerbations of multiple sclerosis
Abnormal Cortisol Levels Are Associated With (Cont.)

- Panic disorders
- PMS
- Infertility
- Sleep disorders
- Osteoporosis
- Heart disease
- Rheumatoid arthritis
- Breast cancer
- Alzheimer’s disease
Adrenal Burnout (Hypoadrenalism)

- Cortisol and DHEA levels decline
Symptoms of Hypoadrenalism

- Fatigue
- Low blood pressure
- Sensitivity to light
- Insomnia
- Digestive problems
- Emotional imbalances/lack of motivation
- Hypoglycemia
- Decreased sexual interest
Symptoms of Hypoadrenalism (Cont.)

- Decreased immunity
- Lack of stamina
- Emotional paralysis
- Poor wound healing
- Alcoholism and drug addiction
- Allergies
- Unresponsive hypothyroidism (does not respond to treatment)
- Feeling of being overwhelmed
Causes of Hypoadrenalism

- Nutritional deficiencies
- Long-term stress
- Dysbiosis
- Chronic inflammation
- Chronic pain
- Toxic exposure
- Overly aggressive exercise
- Hypoglycemia
- Poor sleep hygiene
- Depression
- Severe allergies
Hormones Are A Web

- If cortisol is increased, it decreases the making of progesterone and its activity.
- Cortisol competes with progesterone for common receptors.
- When cortisol is elevated, thyroid hormone is more bound and less active.
- Decreased estradiol in a woman is a stressor to her body (causes decline in function of NE, serotonin, dopamine, and acetylcholine).
Treatment of Hyperadrenalism

- Replacement of DHEA if it is low with adrenal support
- Adaptogenic herbs
- Calming herbs
- Stress reduction techniques
- If cortisol is high in the evening then add phosphatidylserine 300 mg which may be taken any time of the day.
Nutrients
- Vitamin C
- B vitamins
- Calcium
- Magnesium
- Zinc
- Selenium
- Copper
- Sodium
- Manganese
Treatment of Hypoadrenalism

- Stress reduction techniques
- Adaptogenic herbs
- Adrenal extracts (if adaptogenic herbs do not work)
- Calming herbs
- Licorice (cannot use if the patient has hypertension)
- Cortef
Levin and Montaquila, *Dogplay* (2010)
Become a pathological optimist.
Estrogen, progesterone, DHEA, and thyroid hormones are all important for the regulation of glucose in the body.

- Estrogen lowers blood sugar in a women.
- Testosterone decreases blood glucose in a male.
- Progesterone raises blood sugar if not balanced with estrogen.
Functions Of Insulin In The Body

- Counters the actions of adrenaline and cortisol in the body
- Helps the body repair
- Helps convert blood sugar into triglycerides
- Keeps blood glucose levels from elevating
- Plays a major role in the production of serotonin
- At normal levels increases development of muscle
Levels of Insulin

It is important that the levels of insulin in the body not be too high or too low.
Low Insulin Levels

- Insulin is not working effectively in the body
- This is a pre-diabetes state
Symptoms of Insulin Deficiency

- Bone loss
- Depression
- Fatigue
- Insomnia
Causes of Insulin Deficiency

► Eliminating carbohydrates from the diet
► Not eating enough
► Over-exercising
Excess Insulin Is Associated With

► Acne
► Aging process accelerates
► Asthma
► Breast cancer
► Colon cancer
► Depression and mood swings
► Diabetes/insulin resistance
► Estrogen levels that are too low
► Irritable bowel syndrome
► Migraine headaches
Excess Insulin Is Associated With (Cont.)

- Heart disease
- Heartburn
- Hypercholesterolemia
- Hypertension
- Hypertriglyceridemia
- Infertility
- Insomnia
- Osteopenia/osteoporosis
- Weight gain
Causes of Excess Insulin Production

- High carbohydrate diet
- Soft drinks
- Diet pills
- Eating a low-fat diet
- Intake of trans-fats
- Elevated DHEA levels
- Excess caffeine intake
- Intake of thyroid medication that is excessive or not needed
Causes of Excess Insulin Production (Cont.)

- Excessive progesterone replacement
- Increased testosterone levels
- Insomnia
- Lack of exercise
- Low estrogen levels
- Skipping meals
- Smoking
Causes of Excess Insulin Production (Cont.)

- Hypothyroidism
- OTC meds that contain caffeine
- Stress
- Use of natural stimulants
- Use of recreational stimulants
- Using artificial sweeteners
- Yo-yo dieting
Causes of Excess Insulin Production (Cont.)

- **Medications**
  - Beta blockers
  - Birth control pills
  - Steroids
  - Thiazide diuretics
  - Some antidepressants and antipsychotics
Pregnenolone

- Precursor to DHEA, estrogen, progesterone, and testosterone
- Is made from cholesterol
  - If the patients cholesterol is below 140 they may not make pregnenolone effectively
- Decreases with age
  - At age 75, most people have a 65% decline compared to age 35.
Functions of Pregnenolone

- Regulates the balance between excitation and inhibition in the nervous system
- Increases resistance to stress
- Improves energy both physically and mentally
- Enhances nerve transmission and memory
- Reduces pain and inflammation
- Blocks the production of acid-forming compounds
Functions of Pregnenolone (Cont.)

- Modulates the neurotransmitter GABA
- Helps to repair nerve damage
- Promotes mood elevation
- Improves sleep
- Enhances acetylcholine transmission
- Modulates NMDA receptors
  - Regulates pain control, learning, memory, and alertness
Causes of Low Pregnenolone Levels

- Aging process
- Eating too much saturated fat and trans-fats
- Low cholesterol levels
- Hypothyroidism
- Pituitary tumor
- Having a severe illness
  - Pregnenolone will make more cortisol and less of the other hormones to help the body deal with stress.
Symptoms of Pregnenolone Deficiency

► Arthritis
► Depression
► Fatigue
► Inability to deal with stress
► Insomnia
► Lack of focus
► Memory decline
Pregnenolone Used in Treatment

- Arthritis
- Depression
- Memory loss
- Fatigue
- Moodiness
- Improves delta-wave sleep
- Prevention of memory loss
- Endometriosis
- Seizure disorders
Pregnenolone Used in Treatment (Cont.)

- Autoimmune diseases
  - Rheumatoid arthritis
  - Ankylosing spondylitis
  - Multiple sclerosis
  - Lupus
  - Psoriasis
  - Scleroderma
Pregnenolone may protect the brain from cannabis intoxication.

Pregnenolone

- Use pregnenolone with caution in patients with seizures since it may lower the seizure threshold.
Elevated Pregnenolone Levels Can Cause the Following Symptoms

- Acne
- Drowsiness
- Muscle aches
- Fluid retention
- Headache
- Heart racing
- Insomnia due to overstimulation
- Irritability, anger, anxiety
Measurement of Hormones

- Blood
- Saliva
- Urine
# A Guide to Steroid Hormone Testing in Different Body Fluids with Different Routes of Hormone Administration

<table>
<thead>
<tr>
<th>Type of Body Fluid</th>
<th>None Endogenous Steroids</th>
<th>Oral Steroids</th>
<th>Topical Gels/Creams Steroids</th>
<th>Vaginal Steroids</th>
<th>Troche/Sublingual Steroids</th>
<th>Transdermal Patch Occluded</th>
<th>Pellet/IM Steroids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Yes</td>
<td>Yes (1)</td>
<td>No (2)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Saliva</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (3)</td>
<td>Yes</td>
<td>No (4)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Urine</td>
<td>Yes</td>
<td>Yes (1)</td>
<td>No (2)</td>
<td>No (4)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (1)</td>
</tr>
<tr>
<td>DBS</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes (3)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1) Overestimation: Metabolites likely to interfere with immunoassays
2) Underestimation: Hormone levels not reflective of tissue uptake
3) Overestimation: Requires range adjustment
4) Overestimation: Direct contamination
5) Overestimation: Direct contamination of capillary blood if ungloved hands used to apply topical hormones < 2 days prior to collection
Reference

Potential Problem with Testing Testosterone Levels in Individuals of Asian Origin

Due to deletion polymorphisms in glucuronidation pathways for testosterone, some ethnic groups (prevalence > 80% in Asians) will have “apparent” low testosterone levels in urine, but normal levels in serum, saliva, and capillary blood. This could lead to a misdiagnosis of androgen deficiency and consequent inappropriate androgen supplementation.

Epi-Testosterone, the epimer of testosterone, is normal in Asians due to a different enzyme that glucuronidates Epi-Testosterone.

When testing urine for testosterone, Epi-testosterone should always be run in concert to avoid “false-low” testosterone results.
Reference

Normal: \[ T = \text{Epi-T} \]

T-Therapy: \[ T > \text{Epi-T} \]

UGT2B17 del/del: \[ T < \text{Epi-T} \]
Summary

► All of the hormones in the body are designed to work together.
► If one is altered, or deficient, it will affect the actions of all of the other hormones.
► Consequently, bio-identical, compounded, customized hormone replacement is the only way to achieve this balance.
► One size does not fit all.