

Functional Medicine University's Functional Diagnostic Medicine Training Program

INSIDER'S GUIDE

Interpretation and treatment: male hormone profile

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Clinical Reasons for Male Hormone Evaluation

As men age, they may experience any of the following as a result of declining levels of testosterone and other androgens (DHEA, androstenedione):

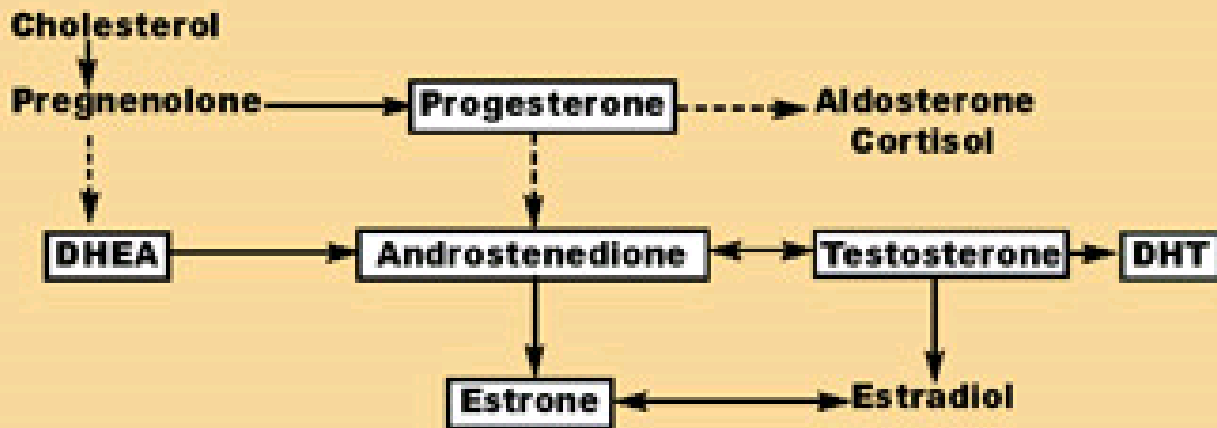
- Diminished libido
- Erectile dysfunction
- Increased body fat
- Decreased bone mass
- Muscle mass and strength
- Loss of hair on the head
- Prostate problems
- Insomnia
- Depression
- Irritability
- Loss of zest for life

Snap Shot of Male Sex Hormones

The male hormone profile available from **Diagnostechs Laboratory and BioHealth Diagnostics** provides a snap shot of male sex hormone levels from a single saliva collection. In addition to testosterone, the following androgens are tested:

- Cortisol
- DHEA-S
- Dihydrotestosterone (DHT)
- Androstenedione
- Progesterone
- Estrone

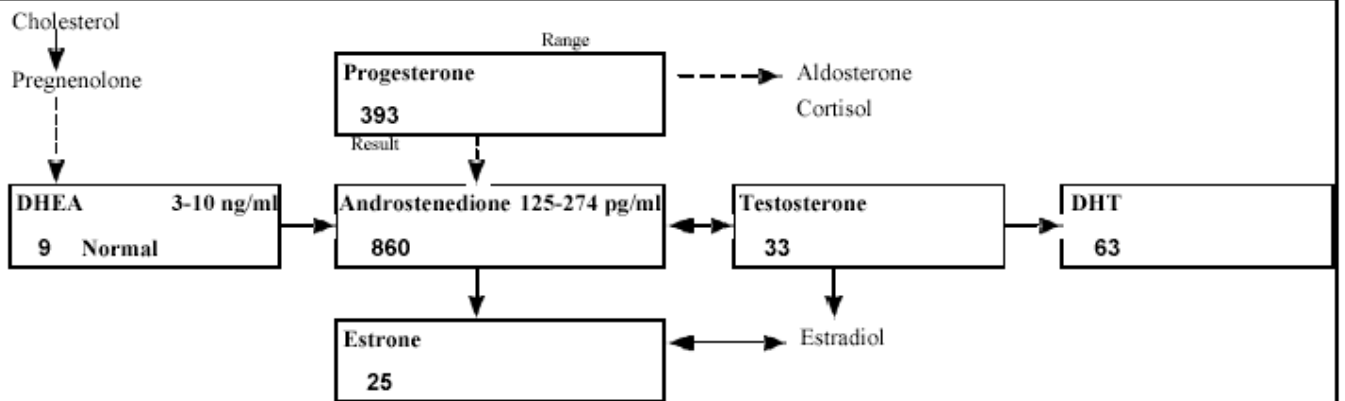
Diagram 1. Androgen Production Pathway



The pathway above, shows the relation of cholesterol & pregnenolone, which are the precursors to steroid hormones. DHEA is the main precursor to male & female hormones.

MHP Male Hormone Panel

ANDROGEN PATHWAY

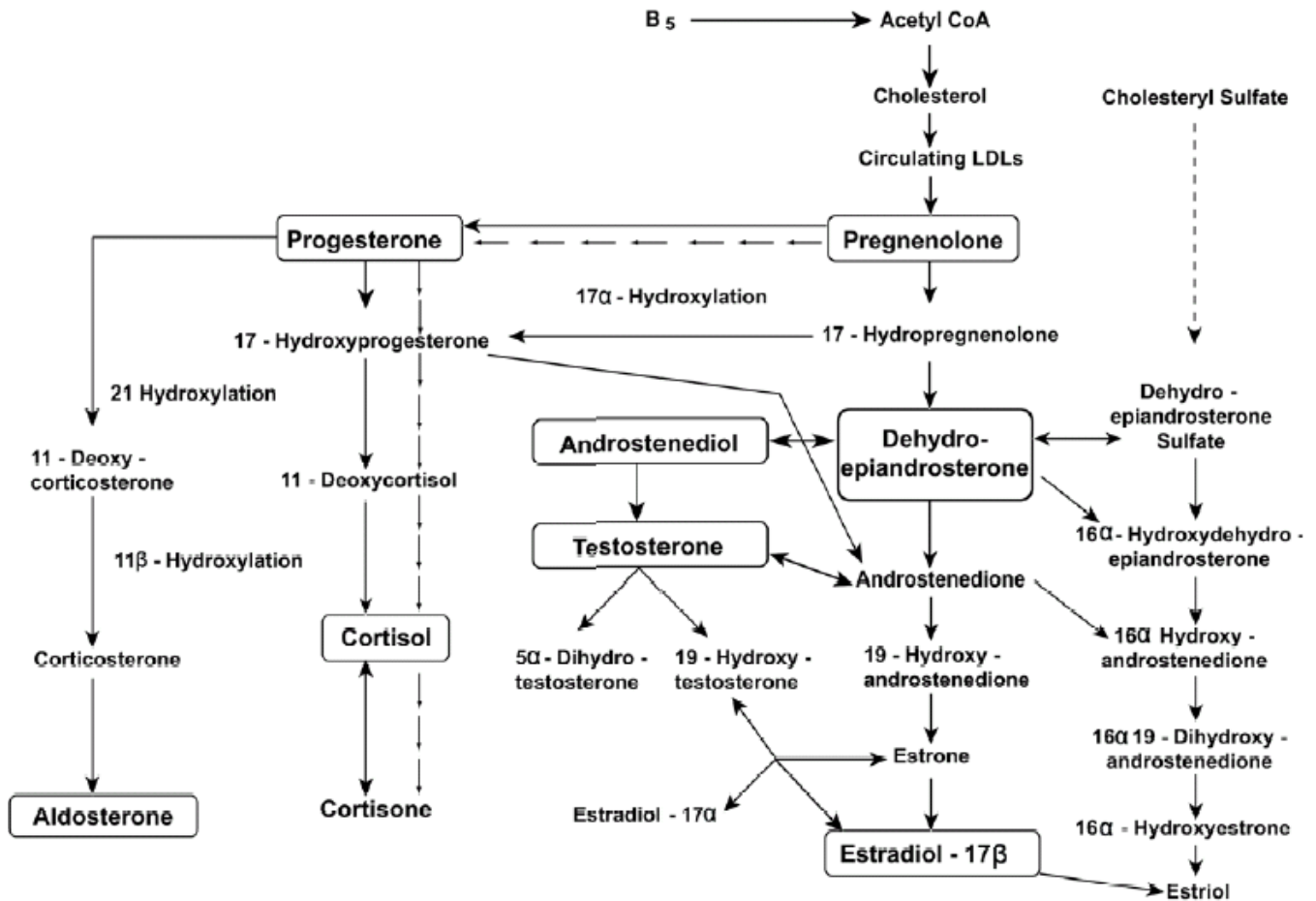


Hormone	Range	Age
Testosterone (Male)	70 - 135	< 20 yrs
	60 - 110	20 - 30 yrs
	50 - 80	31 - 40 yrs
	40 - 70	41 - 50 yrs
	35 - 65	51 - 60 yrs
	20 - 55	61 - 70 yrs
	15 - 45	> 70 yrs
Dihydrotestosterone (Male)	22 - 72	30 - 39 yrs
	52 - 123	40 - 49 yrs
	51 - 107	50 - 59 yrs
	39 - 89	> 60 yrs
Androstenedione (Male > 15 years)	100 - 150	Borderline Low
	151 - 350	Normal
	351 - 450	Borderline High
Androstenedione (Female > 15 years)	75 - 124	Borderline Low
	125 - 274	Normal
	275 - 400	Borderline High
Estrone (Female)	38 - 68	40 - 49 yrs
	26 - 64	50 - 59 yrs
	35 - 65	> 60 yrs

Biochemical Hormonal Markers

Gaining an appreciation of the Steroidal Hormone Principle Pathways and its metabolites will aid you in your clinical decision-making as it relates to male hormone dysfunctions.

The following is a snapshot of the Steroidal Hormone Principle Pathways, however, to help in your understanding of male hormone dysfunctions, key pathways have been separated from the below diagram. This will help you focus on the clinical therapeutics necessary to restore your male patient to a level of optimal hormonal functionality.

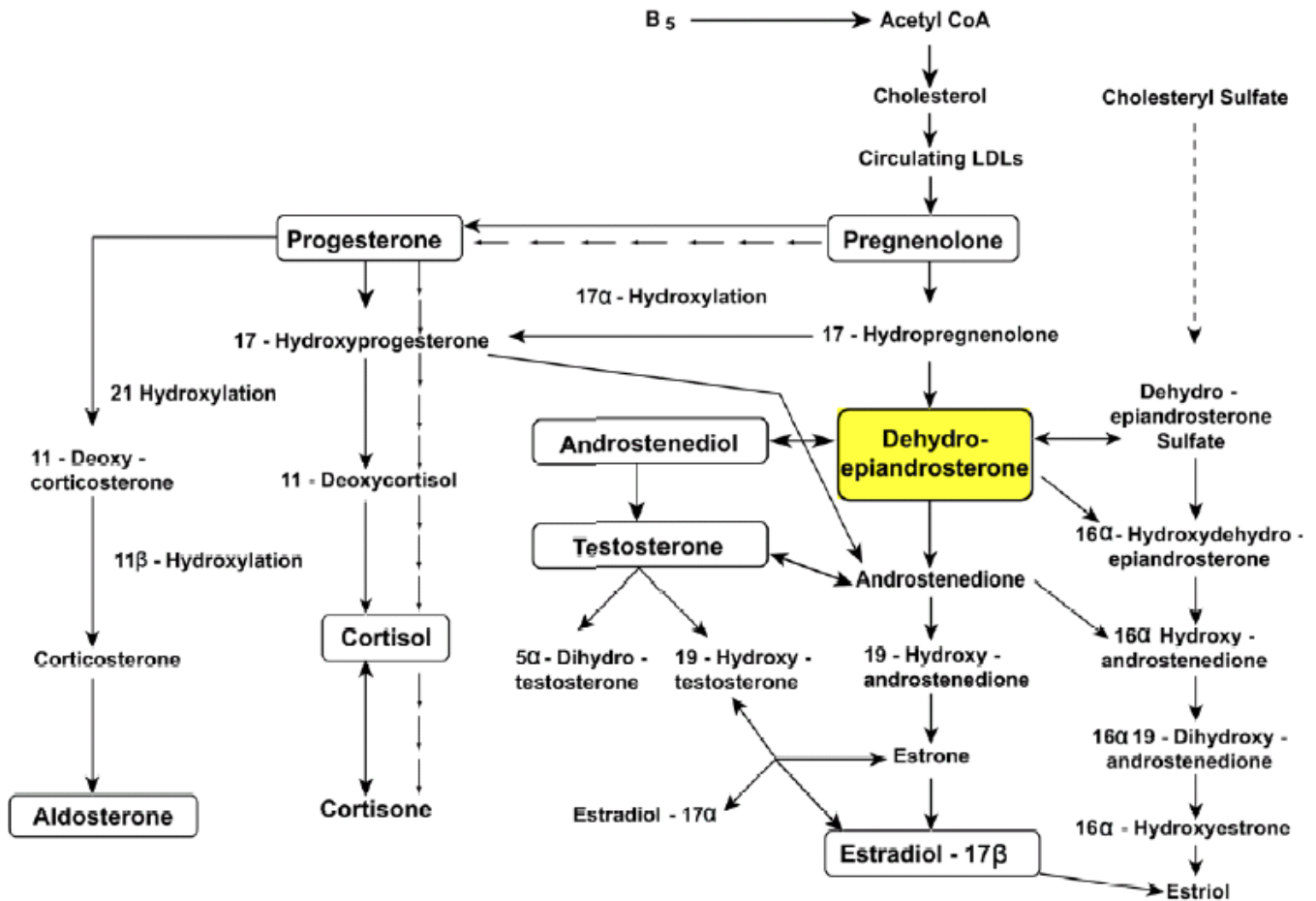


Cortisol

It is a major marker of the complex control loops regulating the sex hormones. The general effect of excess cortisol is usually stimulatory and catabolic; a deficiency of cortisol usually results in a slowing of physiology. If morning cortisol is elevated, it could indicate an infection in the body, nocturnal hypoglycemia and/or increased risk for a cardiovascular event. It also means that pregnenolone is being diverted to cortisol production (pregnenolone steal), perhaps at the expense of producing male hormones.

DHEA

DHEA is the major precursor of androstenedione, testosterone and the estrogens (including estrone). Chronically depressed DHEA output results in an imbalance in sex hormones.



Testosterone

Testosterone is an anabolic steroid that is synthesized from cholesterol. Cholesterol is metabolized into pregnenolone, which is converted to either androstenediol or androstenedione, both of which are then converted to testosterone.

Testosterone is primarily produced by the action of LH on the Leydig cells of the testis, although small amounts of testosterone are secreted by the adrenal glands. Testosterone can then be converted to estradiol or dihydrotestosterone, an extremely powerful androgen.

Testosterone is the direct precursor of dihydrotestosterone.

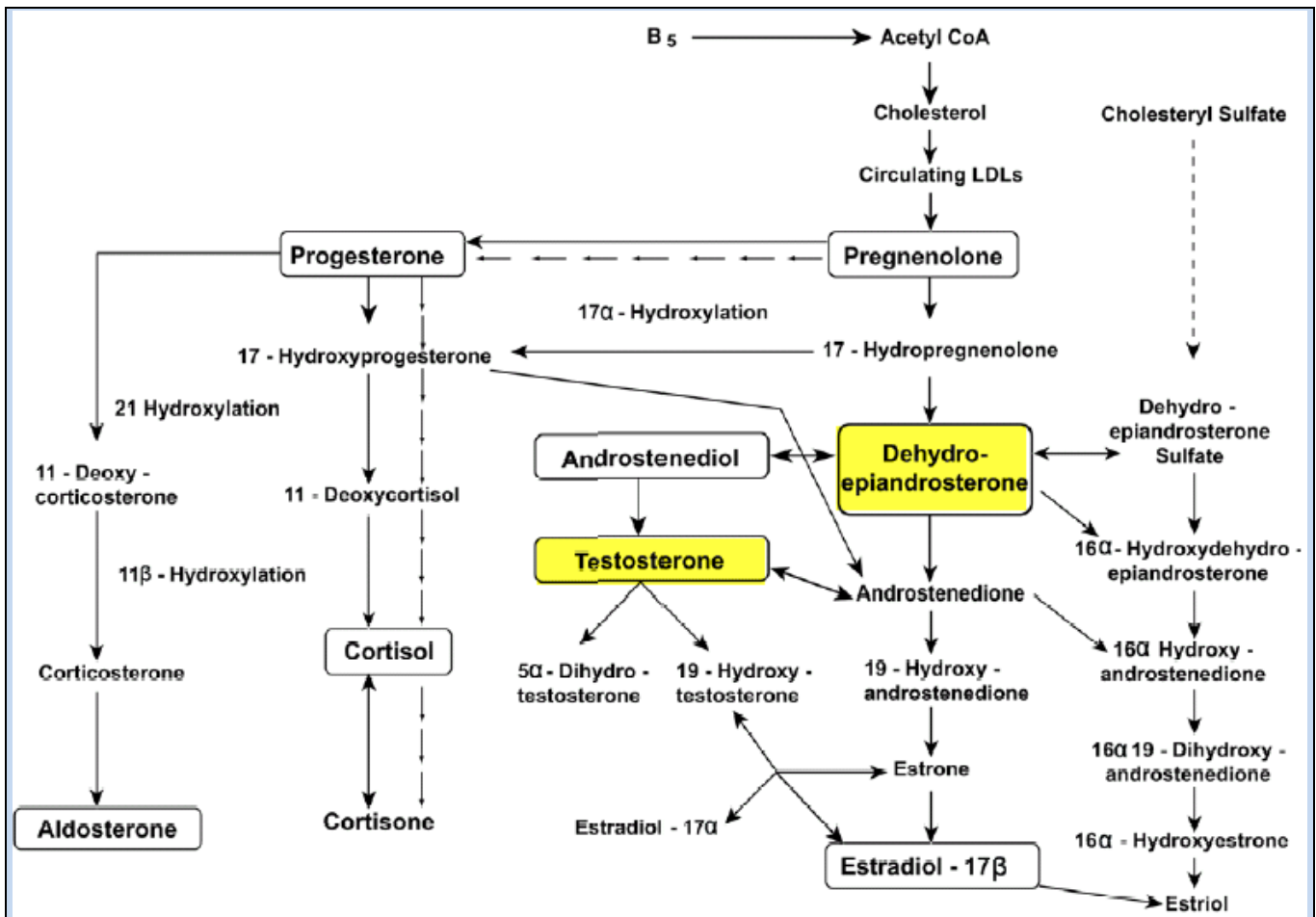
5-Alpha-reductase is the enzyme that drives the conversion to DHT, and **aromatase** is the enzyme that drives the conversion to estradiol

Excessive levels of testosterone have been associated with **high cholesterol, prostate problems, atherosclerosis and aggression.**

Benefits of Salivary Testosterone vs. Serum Testosterone

Approximately 97 to 98% of plasma testosterone is bound to sex hormone-binding globulin (SHBG) or albumin with only 2 to 3% is available as free testosterone

While total serum testosterone is useful to determine whether there is normal response of the Leydig cells to FSH and LH, the salivary testosterone provides valuable data on the true level of the bioavailability of testosterone.



Treating Hormonal Dysfunction

Low Testosterone

If **low testosterone** is reported than the following should be ruled out:

Conversion problem of Androstenedione to Testosterone

Clinical Recommendations

- Vitamin E, Lipoic Acid, Co-Enzyme Q10 and Zinc

Look up stream in the androgen pathway for depressed DHEA, pregnenolone steal, etc.

Clinical Recommendations

- Treat accordingly based on what you find.

Depressed levels of androstenedione will contribute to a depressed testosterone

Clinical Recommendations

- Androstenedione:** 10 to 50 mg/day

Depressed Testosterone pending all other potential biochemical androgen markers are within optimal limits:

Clinical Recommendations

- Testosterone:
- 50 to 100 mg/day; as oral capsule, percutaneous gel, intramuscular injection or patch
- Stinging nettle
- Damiana (*Turnera diffusa*)
- Sarsaparilla

High Testosterone

Herbal Medicine

The following herbs all have been found to have **antiandrogenic like activity** and may be of value to **decrease testosterone** levels.

- ❑ **Saw palmetto berries:** (Is anti-androgenic by inhibiting formation of dihydrotestosterone (DHT))
- ❑ **Chaste tree berries**
- ❑ **Pygeum (Pygeum africanum):** decreases DHT synthesis & testosterone uptake by prostate

Basic Nutritional Therapeutics

Diindolylmethane (DIM)

Diindolylmethane (DIM) is a natural compound formed during the autolytic breakdown of glucobrassicin present in food plants of the *Brassica* genus, including broccoli, cabbage, Brussels sprouts, cauliflower and kale. Constituents such as Diindolylmethane help with estrogen metabolism and detoxification of steroids.

Clinical Pearls

Mean testosterone concentration has been noted to drop as much as 50% from morning to evening. Testing should be done at the same time of day to provide accurate baseline and follow-up information.

Hypothyroidism can impact testosterone levels as well. An underfunctioning thyroid results in a low metabolic rate and can lead to a lower testosterone level. Nutrients such as boron and zinc, and an adequate supply of arginine and branched-chain amino acids are associated with adequate testosterone levels.

Medical conditions commonly responsible for lowering testosterone levels

- ❑ Diabetes mellitus
- ❑ Liver disease
- ❑ Hemochromatosis
- ❑ Obesity, especially with increased abdominal fat.

Medications found to lower testosterone levels include

- ❑ Ketoconazole
- ❑ Cimetidine
- ❑ Glucocorticoids.

Smoking and chronic alcohol use lower T levels.

Excessive alcohol effects testicular production of testosterone.

Restoring T levels without addressing alcoholism would fail to address the fundamental cause of the imbalance.

Dihydrotestosterone (DHT)

Dihydrotestosterone (DHT) is made from testosterone by the **enzyme 5-alpha reductase**. Increased production of DHT in has been found to be a cause of prostate growth (hyperplasia) and male pattern baldness.

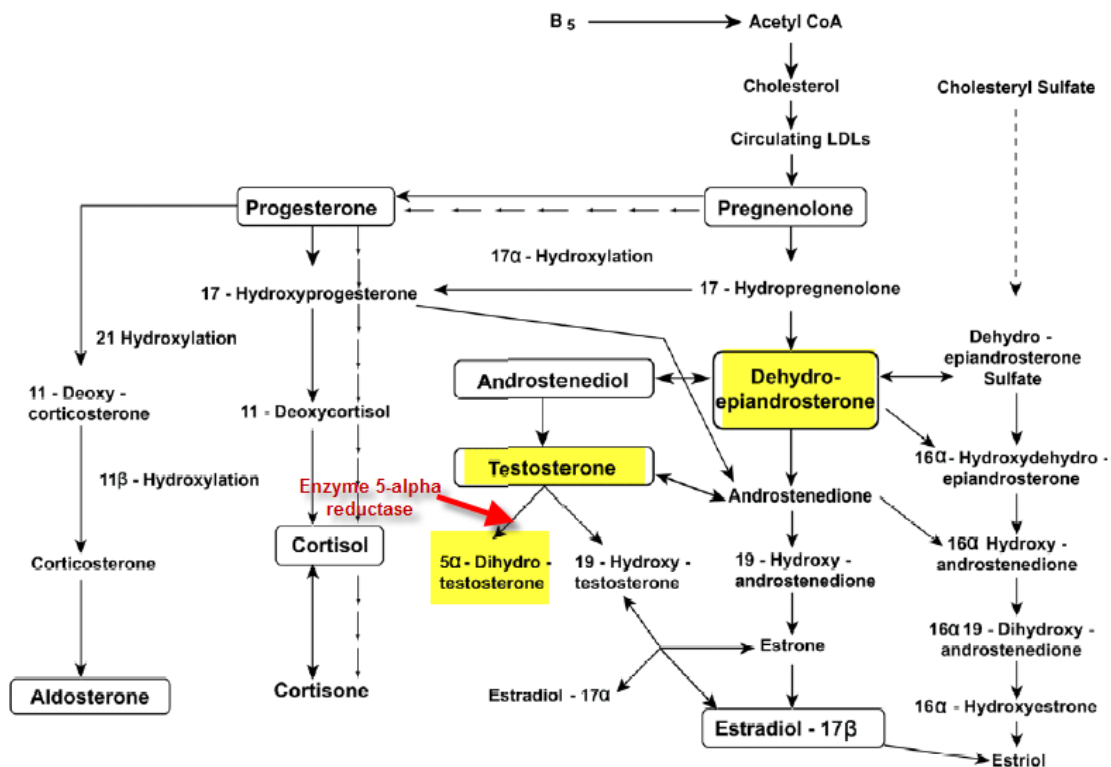
DHT is required for prostate differentiation and function. Inhibitors of this enzyme are used therapeutically to diminish the development of benign prostate hypertrophy

In males, **progesterone** acts to limit the conversion of testosterone to DHT. In cases of benign prostate hyperplasia (BPH), drugs like Propecia and Proscar are used to **inhibit 5-alpha reductase**, while not interfering with the beneficial effects of testosterone.

Saw palmetto is popular herb available without a prescription. It has proved effective in treating symptoms of BPH. Its primary function appears to be inhibiting the 5 alpha-reductase enzyme.

Licorice (Glycyrrhiza glabra) has also been found to inhibit conversion of testosterone to dihydrotestosterone

DHT definitely contributes to libido and sexual arousal. Aggressive lowering of DHT, even without decreasing T has the potential adverse effect of decreasing libido and sexual arousal.



Androstenedione

Androstenedione is a weak androgen which is a metabolite of DHEA and a direct precursor of testosterone. Androstenedione can also be converted to estrone by the enzyme aromatase. In men, excessive androstenedione results in excessive estrone production.

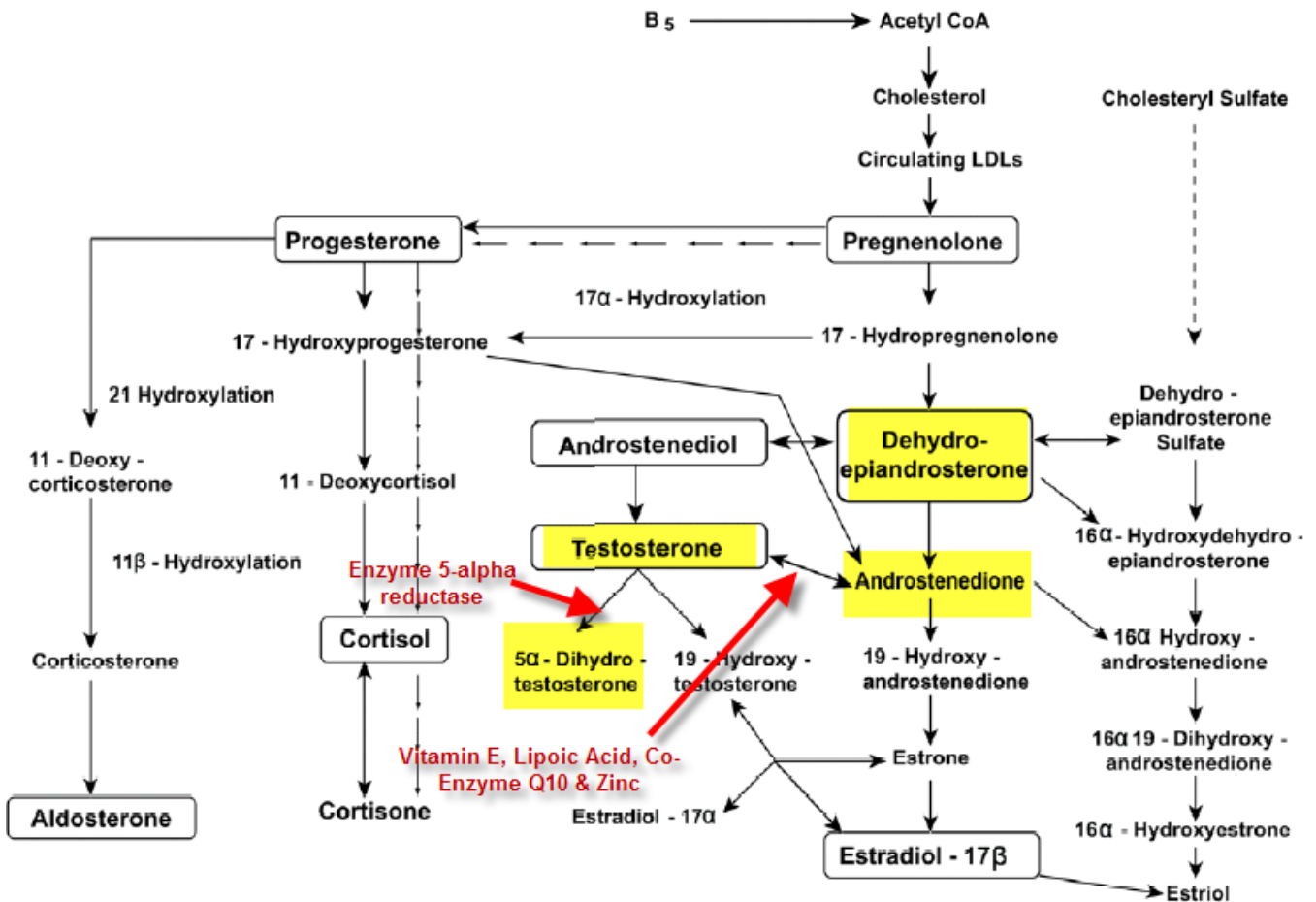
Androstenedione (also known as 4-androstenedione) is a 19-carbon steroid hormone produced in the adrenal glands and the gonads as an intermediate step in the biochemical pathway that produces the androgen testosterone and the estrogens estrone and estradiol.

Testosterone is primarily secreted in the testes of males and the ovaries of females, although small amounts are also secreted by the **adrenal glands**.

From the age of 30, there is commonly a **1 to 2% decrease in production of testosterone from the testes**. As testes begin to lose its ability to produce testosterone, the adrenals begin to assist in making more **androstenedione in hopes of being converted to testosterone**.

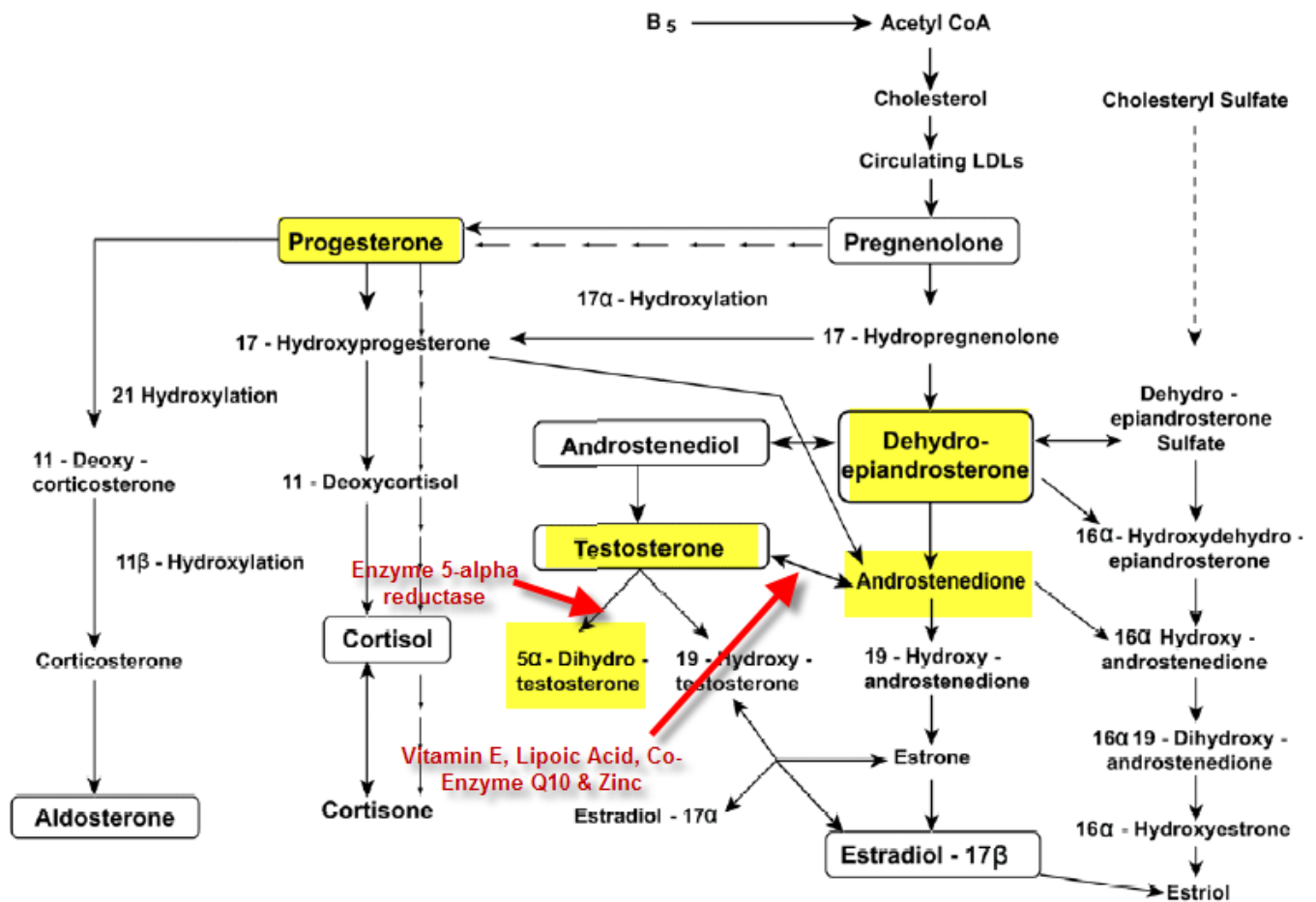
When there is an increase of androstenedione without increasing levels of testosterone, this represents a **biochemical glitch** indicating a need for one or more the following natural agents:

Vitamin E, Lipoic acid, Co-Enzyme Q10 and zinc



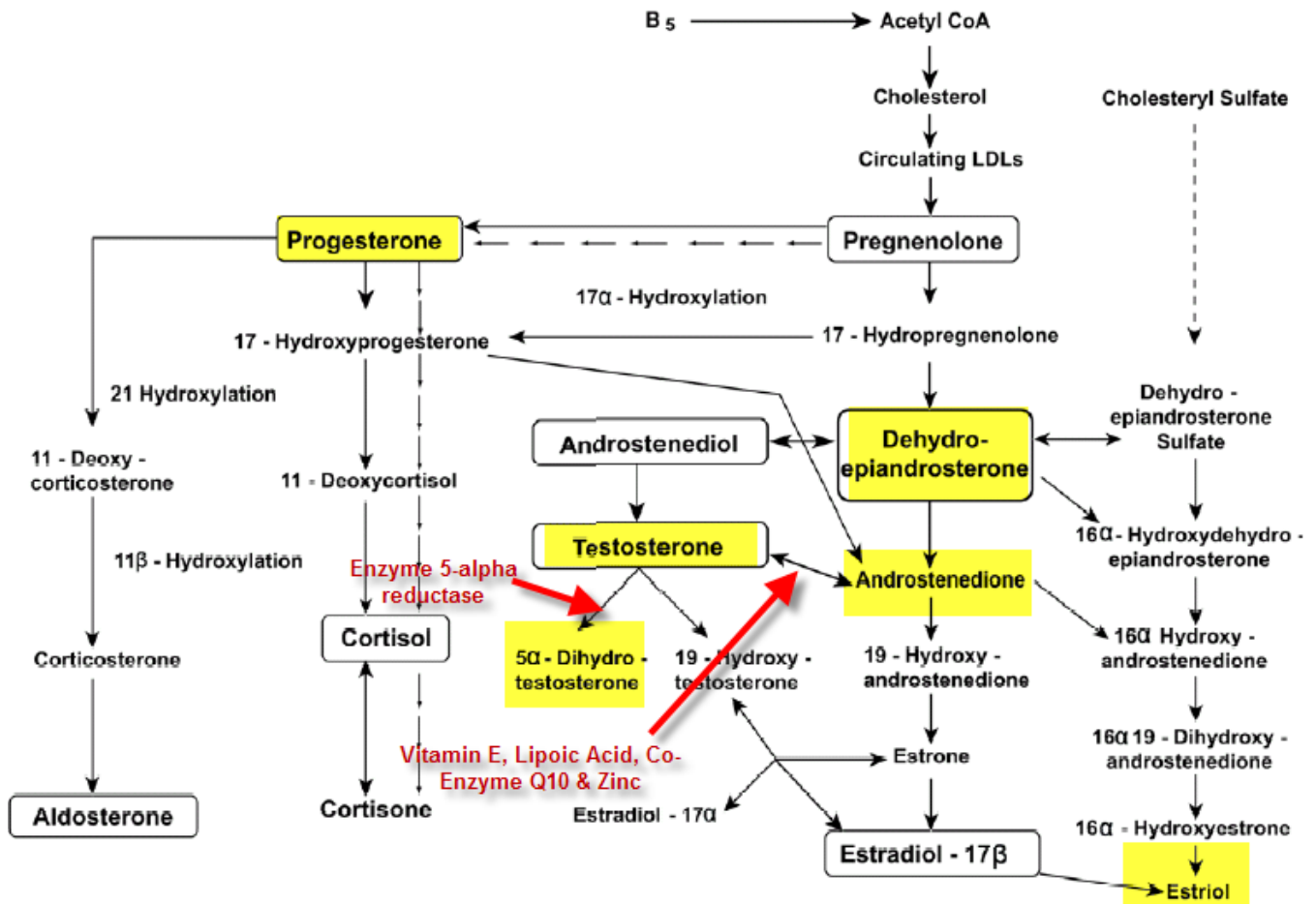
Progesterone

Progesterone is largely made from pregnenolone in the adrenal glands of males. It is calming to the nervous system and activates the GABA chloride channel to help the body shut down both physically and mentally for sleep, rest and recovery. It acts to **limit the conversion of testosterone to DHT** and is an antagonist to the effects of estrogens in the bodies of males and females.



Estrone

Estrone is an estrogen produced in the fat cells, muscle cells and skin of men and women. In men, almost all estrone is converted from androstenedione, which is produced in the testes and adrenal glands. **Estrone is stored in adipose tissue: the more body fat the higher the level of estrone.** This becomes a vicious circle as estrone promotes the storage of more fat. While a necessary antagonist to androgens in males, excess estrone can lead to weight gain and prostate enlargement.



Summary of the Thinking Process

The primary objective of ordering a comprehensive male hormone panel which would include testosterone and the listed androgens above vs. only ordering a testosterone is to identify biochemical dysfunctions along the androgen pathway.

Case in point: If testosterone is depressed due to a conversion problem of androstenedione to testosterone, then any attempt to increase testosterone without improving the conversion of androstenedione to testosterone would ultimately lead to a poor outcome.

The point to take away is to be very observant of the possible biochemical glitches which would lead to a dysfunctional male hormone profile and of course to increased risk of male hormone disease entities.

Credit is contributed to the following labs for their advancement in the field of functional medicine:

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