ENDOCRINE, STEROIDS, and AGING

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Purpose

As everyone matures past the age of the twenties, the body begins to change. There has been a drive for the fountain of youth as long as we have had a recorded history. Since there is no such magic bullet, it is prudent to look at the functioning of the body to determine what are the controlling factors relating to deterioration with age. The same factors that are influenced by age are, not surprisingly, the factors involved in young adulthood and strength development.

The endocrine system is the control mechanism. Specifically the steroids or sex related hormones are the control vehicles. Therefore, their actions must necessarily be investigated, if we expect to make any progress in dealing with specific aging issues and promoting body health.

After the necessary discussion of hormone development, the stimulating actions of steroids are identified. Then the effects of the body and corrective action are available. There is something you can do to slow the aging process, improve health, and develop strength. It is your choice.

Endocrine

The endocrine system is a group of glands that produce secretions to control the body metabolism. Metabolism is the process of converting one substance into another for a specific purpose. The components before metabolism are called precursors while the resulting products are called metabolites. Hormones are endocrine chemicals that are transmitted by the blood to the receptor tissue on which it has a stimulating effect.

Hormones are grouped in three categories – steroids, peptides, and amines.

Amines (-NH2) are composed of a single amino acid. They are strongly basic substances derived from ammonia (NH3) by replacing a hydrogen with a univalent hydrocarbon. An amino is the radical NH2 derived from ammonia. Amine hormones.

Peptides are an amide (-CONH2) from the combination of the amino (NH2) group of one amino acid with the carboxyl (COOH) group of another. They are composed of three of more amino acids. The chain may vary from a small peptide to large polymer proteins.

Steroids are fat-soluble organic compounds having 17 carbon atoms in 4 rings. They affect the development and growth of the reproductive organs. Steroids are grouped into three categories - progesterone, estrogens, and androgens. All three are present in both males and females. However, the ratio is different.

The discussions are indicative of the major pathways for the hormone control. The body provides multiple sources and conduits for development. Therefore, a stimulus or antagonist to one area may not always produce results at the levels expected. This is a critical issue to any attempt at modifying particular hormone effects.

Initial - hypothalmus

The origin of the hormone process is in the hypothalamus area of the brain. The hypothalamus receives feedback from organ hormones and activates the control hormones that signal the pituitary. Although the hypothalamus is the primary source, the body always has back-up systems for hormone production. All these are peptides, with the exception of the amino dopamine.

Thyrotropin releasing hormone (TRH) directs the thyroid amines T3, T4, and calcitronin.

Growth hormone inhibiting factor (GIH, somatostatin) inhibits growth hormone release.

Prolactin inhibiting factor (PIF, dopamine) inhibits prolactin production. It acts as a brake to stop other stimuli.

Prolactin releasing factor (PRF) stimulates prolactin if dopamine is turned off.

Corticotrophin releasing factor (CRF) is a steroid stimulator.

Follicle stimulating hormone releasing factor (FSHRF) is a steroid stimulator.

Luteinizing hormone releasing factor (LHRF) is a steroid stimulator.

LHRH with FSHRF is gonadotropin releasing hormone (GnRH). Gonadotropins influence the gonads of both male (testes) and female (ovaries).

Amine hormones – thyroid & pineal

The amine hormones have the simplest structure. There are three categories – melatonin, thyronines, and catecholamines. All are produced from the amino acid tyrosine, with the exception of melatonin, which is derived from typtophan.

Catecholamines include dopamine, epinepherine, and nor-epinepehrine, which are discussed in other sections.

Melatonin is secreted by the pineal gland during the night in the absence of light. There are no target glands. It is a control hormone that manages biorhythms, synchronizes hormone

secretion, modulates immune response, and is a regulator of stress.

Tetraiodothyronine (T4, thyroxine) is a thyronine formed by combining the amino acid with iodine. It responds to temperature, increases the rate of carbohydrate metabolism, and raises the rate of protein synthesis and breakdown. The hormone excites the nervous system and leads to increased activity of the endocrine system. It provides negative feedback to thyrotropin.

Triiodothyronine (T3) is less prevalent than T4 but is more active. The ratio of T4 to T3 is crucial.

Calcitonin is the third thyroid hormone. However, it is a polypeptide rather than an amine. It is also secreted in the parathyroid and thymus. The target is bones and kidneys. It is not stimulated from the hypothalmus, but is under control of the blood calcium level. A rise in level stimulates the release. Bones respond by absorbing more calcium from the blood. Kidney cells respond by excreting more calcium. Since it is a peptide, it cannot be taken orally because it would be digested. It opposes the action of parathyroid hormone, which increases blood calcium taken from the bones.

Independent – parathyroid and pancreas

Parathyroid hormone (PTH) is not stimulated by the hypothalamus It is under direct negative feedback control of the blood calcium level. The hormone is released when calcium falls and is reduced when calcium rises. When calcium in the blood falls, the hormone causes release of calcium from the bones, reabsorption of calcium from fluid in the kidneys and absorption of calcium from the intestine. PTH reduces reclaiming of phosphate from the kidneys so it causes a drop of phosphate in the blood. The parathyroid is four glands that lie on top of the thyroid.

The pancreas has two sections. The exocrine section makes many of the enzymes necessary for digestion. The endocrine portion is discrete islands of cells called the islets of Langerhans.

Insulin is under direct negative feedback of glucose in the blood. As glucose rises, the insulin hormone is secreted. It causes target cells to take up glucose, stimulates the storage of glucose, and inhibits the making of glucose. Diabetes describes disorders that are marked by elevated blood levels of glucose and there is excess urine excretion.

Glucagon is also under negative feedback of the glucose level in the blood. As glucose levels fall, glucagon is released. It targets cells to release stored glucose and to synthesize glucose. This is in iddrect opposition to insulin and causes very tight control of glucose levels in the blood.

Control - anterior pituitary

The pituitary, which is the master endocrine gland, is located at the base of the brain. The anterior pituitary uses hypothalamus hormones to create new hormones that control other glands and tissues. The anterior pituitary secretes six peptide hormones. The seventh, a special case, is secreted in placenta. The first three are broad spectrum, while the last three are involved in steroid synthesis.

Thyroid-stimulating hormone (TSH, thyrotropin) targets the thyroid. It is a glycoprotein motivated by TRH. TSH activates the synthesis and secretion of thyroid hormones. It is controlled by feedback from thyroid hormones.

Growth hormone (GH, somatotropin) has no specific target gland. It is stimulated by somatostatin. The hormone affects all cells of the body. GH has effects on the growth of bone and cartilage, protein metabolism, RNA formation, electrolyte balance, fat and glucose metabolism. Although it is critical to a growing child, it remains important throughout life. Since there is no specific target, it does not have direct feedback control.

Prolactin (PRL, lactogen) has no specific target gland. It is inhibited by dopamine. If the brake is released, prolactin is stimulated by PIF, TRH, GnRH, mammary stimulus, and stress. Increase in estrogen causes the production of more prolactin, hence it can be an estrogen indicator. Prolactin is involved in breast development and then causes the synthesis of milk. PRL stimulates the enzyme that converts testosterone to DHT in males. Since it does not have a specific gland, there is no direct feedback to control prolactin. It is open loop from the pituitary.

Adrenocorticotrophic hormone (ACTH, corticotropin) is stimulated by CRF. ACTH regulates steroid synthesis in the adrenal gland. There it stimulates the production of cortisol, which has a negative feedback to the hypothalamus and pituitary to control ACTH levels. ACTH is also stimulated by individual biorhythms and stress.

Follicle stimulating hormone (FSH, follitropin) targets the gonads of male (testes) and female (ovaries) where it regulates steroid synthesis. It causes the making of sperm in males through the Sertoli cells. FSH causes the making of ovarian follicles in females. It then stimulates estrogen synthesis and secretion. Inhibin is a polypeptide that provides a negative feedback to the pituitary. It is created in the Sertoli cells for males while it is from the follicles and corpus luteum for females.

Luteinizing hormone (LH, leutropin) targets the gonads where it regulates steroid synthesis. It causes the making of testosterone in the Leydig cells of males. In women, LH works with FSH to stimulate the ovaries to produce progesterone and estrogen. Estradiol causes a negative feedback during the first half cycle of menstruation and a positive feedback during the second half cycle. Progesterone is the master control to modulate the hypothalamus and pituitary.

Chorionic gonadotropin (CG) is the third hormone to target the gonads. Unlike the others, it is secreted by the chorion, the outermost extraembryonic membrane which gives rise to the placenta, seven days after ovulation if the ova has been fertilized (i.e. in pregnancy). CG stimulates the ovarian corpus luteum to secrete high levels of estrogen and progesterone. It is not detectable in females who are not pregnant or males.

Control - posterior pituitary

The posterior portion of the pituitary is adjacent to the hypothalamus. Neurons with their cell bodies in the hypothalamus and their terminal portions in the pituitary release two hormones. These peptide hormones are stored within the posterior pituitary area until the signal to release them is received.

Antidiuretic hormone (ADH, vasopressin) causes the kidneys to reabsorb more water from the forming urine within the renal tubules. Without ADH, the kidney tubules are almost completely impermeable to water and a very dilute urine is excreted. ADH has a direct effect on vascular smooth muscle causing vasoconstriction and an increase in blood pressure when present in large doses. There is a feedback to the hypothalamus to release more ADH causing the kidneys to absorb more water and the blood pressure to decrease. Alcohol inhibits ADH secretion.

Oxytocin stimulates smooth muscle cells around milk producing cells, in the pregnant uterus, and associated with orgasm. It is stimulated by a reflex action in response to sucking or contractions. Oxytocin is released to cause more forceful contractions of the smooth muscles. In a preliminary study, oxytocin was shown to be associated with the ability to maintain healthy interpersonal relationships. Emotion, anxiety, and pain can inhibit oxytocin release.

Control - intermediate pituitary

Melanocyte stimulating hormone (MSH) may be generated in the intermediate lobe of the pituitary. MSH stimulates the activity of the pigment melanin in the epidermis. This also provides ultraviolet protection for the skin.

Stress – adrenal medulla

The adrenal is located on top of the kidney (renal). The cortex or outer portion produces steroids. The medulla, which is an extension of the nervous system, produces stress hormones released in response to stress or fright. The fright causes fight or flight. The resting rate production is sufficient to maintain blood pressure without cardiovascular stimulation from the central nervous system. Unlike other hormones, these amino hormones are stored until needed for a quick response. Both hormones are produced together.

Epinepherine (adrenaline) causes heightened general activation of body systems in conjunction with the sympathetic nervous system. It is stimulated by fear, competition, and sexual attraction.

Nor-epinephrine (nor-adrenaline) increase blood pressure and acts as a neurotransmitter.

Steroids

Now that we have covered the background operation of the hormone system, let us look at the stimulating topic of sex hormones. These are closely related to age problems and strength development.

Steroids are derived from cholesterol. There are two paths for the synthesis of the steroids. One of these is the adrenal route under the control of ACTH. The other is the reproductive organ route under the influence of LH and FSH.

In the adrenals, pregnenolone is made from cholesterol by the stimulus of ACTH. The activating enzyme is cholesterol side-chain cleavage (SCC, cytochrome, P450). Pregnenolone is called the grandparent steroid, since it is the precursor molecule of all steroids.

The adrenal steroids are in three groups: glucocorticoids, mineralocorticoids, and androgens. The glucocorticoids, cortisol and corticosterone, regulate carbohydrate metabolism. The mineralocorticoids, like aldosterone, regulate sodium and potassium. The androgens - dehydroepiandrosterone (DHEA), androstenedione, and androstenediol - regulate gonadal steroids.

The gonadal steroids are separated into male and female. Although all the steroids are present in both, they are in different ratios. The three male steroids are androstenedione, testosterone, and their metabolite dihydrotestosterone (DHT). The three female steroids (estrogens) are estrone (E1), estradiol (E2), and their metabolite estriol (E3).

The three adrenal stress hormones are cortisol, DHEA and adrenaline. Adrenaline is the only non-steroid and is short lived. Cortisol is a stress hormone stimulated by physical stress and is long lived. It affects the breakdown of glucose, protein, and fat, and has anti-inflammatory and anti-allergy effects. Cortisol like other steroids, is rhythmic. If the levels are too high during the night and morning, bones do not develop well, skin is not regenerated, immune system is compromised, and the thyroid is negatively influenced.

Relationships

The relationships between the steroids, precursors, and metabolites are discussed. The following chart also gives the enzyme that promotes the production of the metabolite.

Anabolic steroids stimulate the synthesis of protein and building muscle mass. They are often associated with the androgen hormones. They are simply a different molecular form of the androgens.

Androstenediol is a metabolite of DHEA in the adrenals. The enzyme is 17-ketosteroid reductase.

Androstenedione is a metabolite of DHEA in the adrenals by the enzyme 3-ß hydroxysteroid dehydrogenase. The majority (over 60%) is secreted in the testes and ovary. It is also a metabolite of 17-OH progesterone by the enzyme 17, 20 desmolase. It is a precursor and metabolite of testosterone by the enzyme 17-ketosteroid reductase.

Androsterone (ADT) is a metabolite of progesterone, androstenedione, and testosterone in the testes and is excreted in the urine.

Dihydrotestosterone (DHT) is a metabolite of DHEA, androstenedione, and testosterone through the adrenal route by the enzyme 5α - reductase.

Dehydroepiandrosterone (DHEA, androstenolone) is a metabolite of 17-OH pregnenolone in the adrenal cortex by the enzyme 17, 20 desmolase. It is also produced in the testes. Obese and older people have reduced levels.

Estradiol (E2) is a potent estrogen formed in the ovary and testes. The predominant conversion in men is in peripheral tissue. E2 is a metabolite of androstenediol and testosterone by the enzyme aromatase. It is also a precursor and metabolite of estrone by the enzyme 17-ketosteroid reductase.

Estriol (E3) is the weakest estrogen and is a metabolite of estrone and estradiol. It is excreted in the urine.

Estrone (E1) is a potent estrogen formed in the ovary, testes, and peripheral tissue. It is a metabolite of androstenedione by the enzyme aromatase. It is also a precursor and metabolite of estradiol by the enzyme 17-ketosteroid reductase.

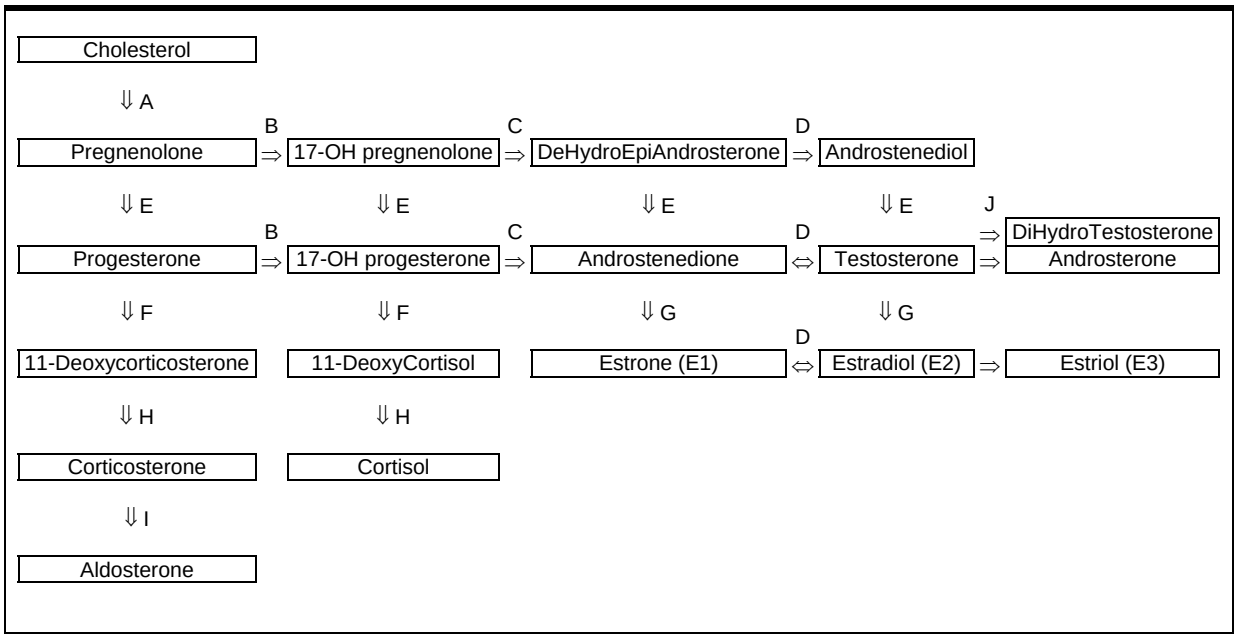
Testosterone is the prevalent male hormone. It is a metabolite of androstenediol by the enzyme 3-ß hydroxysteroid dehydrogenase. It is also a precursor and metabolite of androstenedione by the enzyme 17-ketosteroid reductase.

Steroid biosynthesis

The precursor and metabolite relationships of the steroids are shown in the matrix. Enzymes promote the metabolism of hormones. The enzymes are identified by letters, which are noted below the table.

Aging

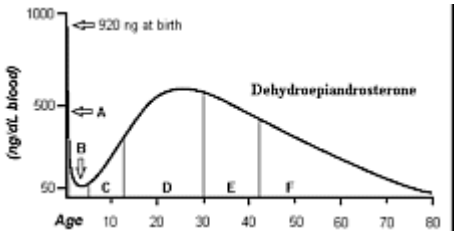
The quantity and ratios of hormones obviously change with age. While a youth, the hormones begin to increase. Then in young adulthood, the rate of growth changes. Most decrease, but a few increase in quantity. The ratios to other hormones also change. Often a ratio is more important than an actual value.



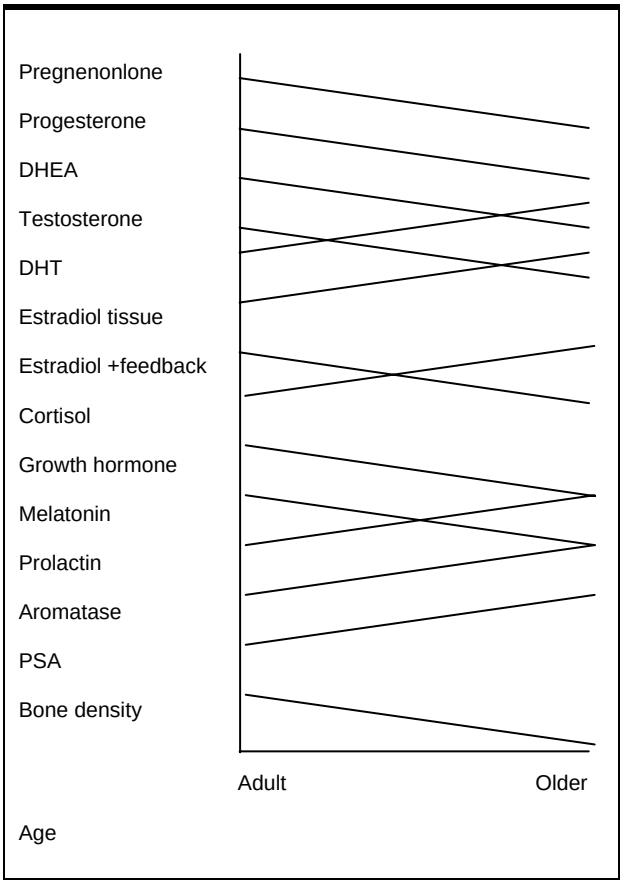
A	SCC enzyme	F	21-hydroxylase
B	17-hydroxylase	G	Aromatase
C	17, 20 desmolase	H	11-hydroxylase
D	17-ketosteroid Reductase	I	18-hydroxylase & 18-hydroxysteroid dehydrogenase
E	3-ß hydroxysteroid dehydrogenase	J	5-α reductase

The glands associated with the hormones tend to shrink with age. This causes less production of the directly affected hormones. However, those that are indirectly affected tend to rise.

The actual change of hormone levels tends to follow the impulse response and exponential decay curve similar to that shown for DHEA.



The following curves are to show trends and do not reflect actual values or the shape of the curve. Nevertheless, the trends in adulthood do indicate the interrelationship between the steroids and other indicators of health.



It is clear there is a corresponding relationship between many hormones and body functions. It is important that the proper measures be used in correcting any health condition or improving strength.

Tests

Before analysis of a condition can exist, it is imperative to have data. That is obtained by tests. For steroid related conditions, the following tests are required: cortisol, DHEA, estradiol, progesterone, testosterone, melatonin, LH, FSH, (GnRh), Prolactin, thyroid stimulating hormone (TSH) and prostate specific antigen (PSA) for men. Although the suite is extensive, it provides the data to locate the source of the problems. Often the firsts tests are symptom related to determine what will be the next suite. Then other tests may be indicated.

Blood tests have been used traditionally. However, they are becoming under scrutiny for several reasons. These require an invasive puncture, are expensive, and sometimes are unrepresentative of free components. Since blood is the transport system, it does not always indicate the hormone state after conversion to the free state.

Urine analysis is used for some tests. However, it is skewed since it contains the excreted byproducts of hormone metabolism in addition to other hormones.

An additional technology that has been approved by the World Health Organization is saliva testing. It too is less than perfect, but it has the benefit of ease of administration, which lowers cost. In addition, it indicates actual response of the cells, since it is measured after hormone conversion.

Aging factors

The leading challenges as people age are heart, prostate, weight, bone conditions, sexual function, and cancer. Interestingly, at the steroid level, all these are related. Excessive estrogen ratio to other hormones appears to be the culprit.

In women, the estrogen produced by the positive feedback during the second half of the cycle is shut off. Therefore the total estrogen is lower. However, the tissue-generated estrogen continues to increase just like men. In both men and women, the estrogen increase seems to be a response to compensate for the decrease in activity by other hormones.

Additional estrogen promotes prolactin production. In men, that in turn stimulates the enzyme that converts testosterone to DHT. DHT is a much stronger androgen than testosterone. It is created in the body's attempt to maintain testosterone strength. That causes prostate growth and increasing PSA. In women, it drives breast growth and increase risk of cancer.

If estrogen production is controlled in men, then more testosterone is available, since it is not converted to estrogen or DHT. If estrogen production is controlled in women, then the progesterone balance is improved and women are less susceptible to breast cancer and heart problems. The control of estrogen maintains a more youthful health.

Fat cells synthesize aromatase, which promotes estrogen production. Estrogen, diet, and lack of exercise promote fat cell production. The cycle increases until there is an external change.

Estrogen does not build bones, but it can slow their weakening. Testosterone and progesterone actually promote building of more bone density.

Excessive testosterone is often blamed for many ailments. However, much of conventional wisdom is flawed based on data. Testosterone levels are higher in youth and there are few of the problems associated with aging and decreasing strength. Increase in testosterone balances the systems to normal. Therefore, it is not necessary for the body to produce DHT and additional estrogen to compensate for low androgens.

Cortisol increases with stress. This creates a strain on the body systems. In an effort to combat inflammation and deterioration, cortisol increases with age. As a result, it is called the death hormone. Growth hormone decreases with age. The simultaneous effect is deterioration of the body.

Progesterone is the balancing hormone. Because of its location as a major precursor in the steroid matrix, it can convert to other hormones by the corticosterone - aldosterone path or by the androstenedione - testosterone path.

Pregnenolone is a precursor to progesterone. Therefore, it contributes to the same effects as progesterone. In addition, it generates the DHEA string with the associated benefits.

The stimulation of progesterone and pregnenolone appear to be key to combating problems associated with enhancing performance and slowing aging. Hormones are only a signaling and control system. The body still requires other minerals, vitamins, and enzymes to perform any of the tasks.

External changes

Hormone supplements and adjustments should be used with care, since hormone balance is crucial to body functions. Oral hormone ingestion is less effective and requires large doses to overcome the small conversion to usable hormones. The process in the intestinal tract is less than effective. Then conversion in the liver places an excessive load, which can result in hepatic damage. The more effective technique is to use transdermal cream containing the appropriate compounds.

Because fresh, unprocessed foods are rich in enzymes, they can have significant impact on hormone production. In addition, some foods contain significant quantities of phytoestrogens, which can influence the feedback system.

Petroleum chemicals and their hydrocarbon derivatives include plastics, pesticides, herbicides, and many medicines and food additives. These chemicals have an estrogen effect on the body although different compounds operate to various extents. Therefore, they upset the ratio balance, can attach to receptors, and can influence hormone production through the feedback mechanism.

Since synthetic hormones and nutraceuticals are petroleum derivatives, they should be avoided because of side effects. In addition, any change from the natural structure will have a different effect on the body. The body is very sensitive to variations in each molecule and will react differently to the subtle variations of synthetics.

The preferred procedure for hormone change is to influence the production of the enzyme that influences metabolism of the hormone.

Compensation

If tests reveal a discrepancy in some area, the matrix is used to determine where the problem exists, what interactions are involved, and what compensation is required.

Nutrition can be used to improve maintenance and reduce deterioration, but seldom is the level of nutrients adequate to heal a condition. Nevertheless, nutrition is an on-going process to healing and maintenance.

Food extracts are concentrated nutrition supplements and they can have improved effects and may assist recovery from an acute condition.

Specific nutraceuticals are molecular compounds that can be formed in therapeutic amounts. These may assist chronic conditions. Generally therapeutic quantities are used for a short time only. The lower levels, nutrition supplements, and diet are used for maintenance.

Action

To enhance performance and mitigate the effect of many health challenges, steroid maintenance is critical. Pregnenolone and progesterone using transdermal creams are cornerstones of any overall program. Oral ingestion is not effective.

Next include aromatase inhibitors to help control the estrogen production and reduce the prolactin production. If necessary, dopamine supplement will further reduce prolactin. Then 5-alpha reductase inhibitors will control DHT production. Be careful. If 5-alpha reductase inhibitors are used without aromatase inhibitors, then more testosterone is available to convert to estrogen. This actually makes the age related problems worse and reduces muscle mass production..

The next section will identify foods, food derivatives, and supplements that can be used to promote these areas of good health.

This information is not intended to diagnose or treat any disease or condition. It is strictly for educational purposes.

About the author: Dr. Durham is a researcher, scientist, author, lecturer, forensic engineer, and university professor who is recognized in numerous *Who's Who*.

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