FLUIDS iQ®

RESULTS: SALIVA HORMONE TEST

Accession #: 100035645 • Patient: JOHN SMITH

Patient: JOHN SMITH
Tel: (814) 873-2625 **Email:** test@test.com
Sex: Male **Age:** 42 yr **Date of Birth:** 1981-02-19
Height: 6 ft 1 in **Weight:** 142 lbs **Waist size:** 26 in

Hormones: No
Health Care Professional: Jane Smith

Accession #: **100035645**
Sample received: 2023-04-11
Report issued: 2023-04-11

Sample collection:
2023-04-04 06:30 AM
2023-04-04 12:45 PM
2023-04-04 18:15 PM
2023-04-04 22:30 PM

ADVANCED STRESS AND HORMONE PROFILE

17-β ESTRADIOL (E2) pg/ml **2.8**

		Reference range
Female		
21-50 years	Follicular phase	1.3 - 7.8
	Mid cycle	3.8 - 16.0
	Luteal phase	1.2 - 8.4
51-75 years	Post Menopausal	0.6 - 4.4
Male		1.0 - 4.7

PROGESTERONE (Pg) pg/ml **28.4**

		Reference range
Female		
	Follicular phase	19.6 - 86.5
	Luteal phase	99.1 - 332.6
	Post Menopausal	6.0 - 56.4
Male		12.7 - 65.1

Pg:E2 RATIO **10.1:1**

Optimal (Luteal): 100 - 300:1 when E2 1.2-3.3 pg/ml

Melatonin (Daytime\Noon) pg/ml **4.2**

Reference range 0 - 5

Secretory IgA (Morning) µg/ml **185.7**

Reference range 0 - 330

CORTISOL (C) ng/ml

		Reference range	Median
Morning	**8.1**	2.0 - 10.7	3.9
Noon	**3.2**	0.7 - 3.5	0.9
Afternoon	**2.8**	0.5 - 3.1	0.6
Night	**2.3**	0.3 - 3.2	0.3
TOTAL	**16.4**	3.5 - 20.5	5.6

DHEA-S (DS) ng/ml **2.6**

	Reference range	Median
Female	0.2 - 2.5	2.0
Male	0.2 - 3.7	2.0

TOTAL C:DS RATIO **6:1**

Reference range	Median
4:1 to 5:1	3:1

TESTOSTERONE (T) pg/ml **90**

	Reference ranges	
Age (years)	Male	Female
Less than 20	Range not applicable	
20 - 29	41.4 - 142.5	5.5 - 49.0
30 - 39	31.8 - 100.4	5.2 - 49.0
40 - 49	30.1 - 97.8	4.5 - 49.0
50 - 59	30.0 - 92.0	3.6 - 49.0
60 - 69	23.2 - 86.9	2.9 - 38.8
Greater than 69	Range not applicable	

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INSULIN Fasting (Morning) µIU/ml	**3.6**

Reference ranges	
Normal (non-elevated)	< 5.0 *
Borderline	5.0 - 18.0
Elevated	> 18.0

INSULIN Non-Fasting (Noon) µIU/ml	**19.3**

Reference ranges	
Low	< 10.0 *
Normal (non-elevated)	10.0 - 30.0
Elevated	> 30.0

6-8 hr fast prior to morning sample:	**YES**

Carbohydrate Stimulation Test done	**YES**

The reference range is derived from a normal distribution of results that encompass 95% of randomly selected individuals in a population. Median represents the middle number in a data set.

Dr. Aron Gonshor PhD, DDS, FRCD(C), FAO • Laboratory Director

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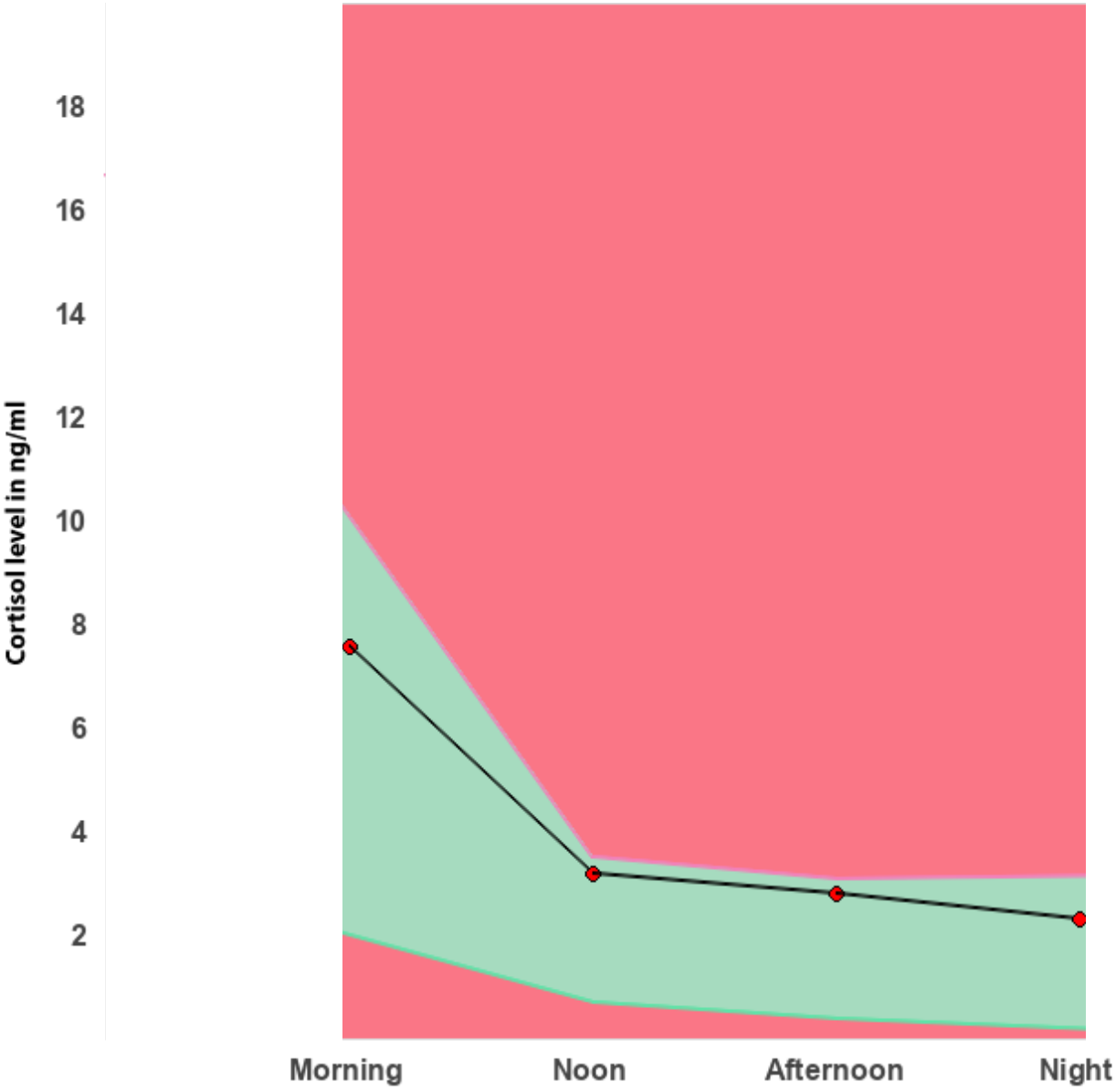

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JD Clinic AN:

	Score
Hot flashes, night sweats	*
Cold &/or heat intolerance	*
High cholesterol / triglycerides	*
Decreased muscle mass & wasting	*
Foggy thinking,memory lapse	*
Allergies: Foods/ airborne particles	*
Migraines &/or headaches	*
Weight gain at waist	*
Low blood pressure	*
Cravings for sweets	*
Trouble falling asleep	*
Insomnia	*
Depression (tearfulness, lowered drive, mood swings)	*
Infertility	*
Weight gain at hips	*
Bone loss	*
Aches & pains, stiffness	*
Dehydrated & thin skin, hair	*
Difficulty &/or increased urinating, incontinence)	*
Irritable, aggressive	*
Water retention, swelling	*
Numbness - feet & hands	*
Lowered libido	*
Anxiety (restless, panic attacks)	*
AM fatigue	*
PM fatigue	*
Prostate abnomalities	*
Erectile Dysfunction	*
Sleep apnea	*
Loss of scalp hair &/or beard growth	*
Tender / fibrocystic breasts	*
Vaginal dryness or burning	*
Periods absent/skipped, spotting, heavy bleeding	*
Hair loss, increased facial & body hair, acne	*
Uterine fibroids	*

0	1	2	3
None	Mild	Moderate	Severe

* Indicates that symptom left blank

Understanding Hormone Excess and Deficiency

The comments provided here are for educational purposes only. They should not be interpreted as being diagnostic or treatment recommendations. Those decisions are the responsibility of the health care professional. Moreover, the reference range shown in this report is derived from a normal distribution of results that encompass 95% of randomly selected individuals in a population.

IN THE PRESENT TEST

CORTISOL

The Morning cortisol level lies inside the reference range. Cortisol levels are normally highest shortly after waking and indicate normal adrenal function at its circadian peak.

The Noon cortisol level lies inside the reference range and indicate that the adrenal glands are responding well to the needs of the day, especially in glycemic control. This highlights the importance of the adrenal glands in the regulation of blood glucose levels.

The Afternoon cortisol level lies inside the reference range and indicate that the adrenal glands are responding well to the needs of the day, especially in glycemic control.

The Nightime cortisol level lies inside the reference range, and indicates that adrenal glands are functioning normally within the circadian cycle. It is a good indicator of a normal baseline level of adrenal activity.

DHEA-S (Dehydroepiandosterone Sulphate)

DHEA-S lies within the reference range. DHEA, together with cortisol, plays an important role in maintaining normal blood glucose levels (glycemic control). Normal levels are important in proper metabolism of carbohydrates, fats and proteins.

General Discussion

CORTISOL

About Cortisol: Cortisol is a hormone produced by the adrenal glands, a part of the HPA axis, a cascade of endocrine pathways that respond to specific negative feedback loops involving the hypothalamus, anterior pituitary gland, and adrenal gland. Cortisol plays an important role in breaking down glycogen to glucose in liver and muscle tissue. It mobilizes glucose, so as to maintain normal blood sugar levels, the primary energy source for the brain. Cortisol levels are highest in the early morning (approximately 8 am) and reach the lowest level about midnight to 4 am, or three to five hours after the onset of sleep. Diurnal cycles of cortisol levels are found in human saliva. Cortisol production comes in response to daily stress, as well as emotional upset, infections and surgery. It prevents the release of substances in the body that cause inflammation, and is used to treat conditions resulting from over activity of the B-cell-mediated antibody response. Examples include inflammatory and rheumatoid diseases, as well as allergies. Low-potency hydrocortisone, available as a non-prescription medicine in some countries, is used to treat skin problems such as rashes, and eczema [1, 2, 3].

Low Cortisol, especially if it remains so throughout the day, may indicate advanced adrenal insufficiency, sometimes called adrenal exhaustion. It is caused by stress, such as sleep deprivation, emotional stress, poor diet, nutrient deficiencies, and/or synthetic glucocorticoid medications that suppress cortisol production. Chronic stress depletes cortisol and is associated with symptoms of morning and evening fatigue, aches and pains, fibromyalgia, cold body temperature, decreased stamina, slow pulse rate, low blood sugar (sugar craving) and low blood pressure. In addition, one often encounters increased allergies (immune dysfunction), and sensitivity to chemicals. Symptoms of thyroid deficiency can also be due to low cortisol levels. Exercise, more adequate sleep, a diet with adequate protein, 'bio-identical' progesterone, adrenal extracts and nutritional supplements are often helpful in correcting low cortisol.

High Cortisol. Although normal cortisol levels are essential for life, chronically elevated levels can be very detrimental. Increased cortisol production by the adrenals is a normal response to routine stress. However, when stress is chronic and cortisol output remains high over a prolonged period of months and years, breakdown of normal tissues (muscle wasting, thinning of skin, bone loss) and immune suppression can result. Common symptoms of chronically high cortisol include sleep disturbances, fatigue, anxiety, depression and weight gain in the waist. Stress and the resulting persistently elevated cortisol levels can contribute to premature aging and chronic illness.

DHEA-S (Dehydroepiandrosterone Sulphate)

About DHEA: DHEA, a testosterone precursor, is the most abundant circulating steroid hormone. DHEA is produced predominately by the adrenal glands, the gonads, and the brain, where it functions predominantly as a metabolic intermediate in the biosynthesis of the androgen and estrogen sex steroids. DHEA-S is the sulphated form, and in blood it approaches levels 300 times that of free DHEA. Whereas DHEA levels are at a peak in the early morning, DHEA-S levels show no diurnal variation. From a practical point of view, measurement of DHEA-S is preferable to DHEA, as its levels are more stable. In the young the levels approach the high end of the range. They decrease with age and get to the lower end of normal in middle age.

Low DHEA-S can be caused by highly depressed adrenal function and is commonly seen in accelerated aging and diseases such as cancer.

High DHEA-S can be associated with insulin resistance/PCOS (polycystic ovaries)[4] or DHEA supplementation.

TOTAL CORTISOL : DHEA-S RATIO

Ratios often use the 'mean' value for the analytes being considered. The 'mean' represents the sum of all values, divided by the total number of values. It is also referred to as the 'average', and is a way of deriving the central tendencies of a group of values, because it takes into account every value in the data set. However, one can also use the 'median' value to show the ratio. The median is the 'middle' value, for which half of the observations are larger and half are smaller. The advantage of the median is that it removes extreme measurements from a data set and is not distorted by outliers or skewed data. It therefore often provides a better representation of a 'typical' value.

In the present report, when using the 'median' values for total cortisol and DHEA-S, the median ratio is 3:1 (4:1 to 5:1 if one uses the 'average' values), and is an indicator of the adrenal output of cortisol and the androgens. It is age dependent, since there is a decline in DHEA-S with age, while the levels of morning cortisol remain relatively stable or increase slightly. If the ratio is higher than normal it is due to adrenal dysfunction. When the body experiences chronic stress, pregnenolone, the precursor to all other steroidal hormones, begins to overproduce cortisol. This is at the expense of all the other steroidal hormones (DHEA and its metabolites, including progesterone, testosterone, and the estrogens). As pregnenolone is diverted to cortisol, DHEA-S depletion begins. This creates an elevated cortisol to DHEA-S ratio. If the ratio is lower than normal for that age, and the DHEA-S level is within the normal range, it is probably due to the maintenance of DHEA-S output with advancing age. However, if the ratio for that age is lower than expected, it is probably due to high DHEA-S levels, low cortisol, or both of these.

Total Cortisol : DHEA-S Ratio and Metabolic Syndrome

Various studies have shown that both cortisol and DHEAS are related to metabolic syndrome[5] , discussed in detail below, and type 2 diabetes[6] . While high cortisol concentrations are associated with an increased risk of metabolic syndrome, high DHEA-S levels appear to be protective. By far, the strongest associations of these disease states is with the Total Cortisol : DHEA-S ratio. The higher the coefficient, the greater the risk of metabolic syndrome.

Total Cortisol : DHEA-S Ratio and Depression

A high salivary Cortisol : DHEA ratio, when seen in conjunction with stressful life events, has been shown to be predictive of major depression and its persistence[7]. More recent studies[8] present data in which the salivary cortisol : DHEA ratio clearly differentiates depressed patients from controls, 82.5% of depressed subjects having ratios above the 85th percentile of the control group. Therefore, decreased levels of DHEA and a consequent elevation of the Cortisol : DHEA ratio appears to reflect an additional state of abnormality in adult depression.

ESTROGENS

(Estrone-E1, 17-β Estradiol-E2, Estriol-E3) Estrogens are the primary female sex hormones. They play important roles in stimulating growth of the reproductive tissues, maintaining healthy bones, increasing the levels of neurotransmitters in the brain and helping keep the cardiovascular system healthy. During menopause estrone is the predominant circulating estrogen and during pregnancy it is estriol. Though estriol is the most plentiful of the three estrogens it is also the weakest, whereas estradiol is the strongest, with a potency of approximately 80 times that of estriol. Thus, estradiol is the most important estrogen in non-pregnant females who are between the first menstruation (menarche) and menopause stages of life. However, during pregnancy this role shifts to estriol, and in postmenopausal women estrone becomes the primary form of estrogen in the body. All of the different forms of estrogen are synthesized from androgens, specifically testosterone and androstenedione.

Low Estradiol is unusual in premenopausal women, unless they have no ovulation, or are taking birth control pills, since the latter can suppress ovarian estrogen production. It is much more common in post-menopausal women whose ovaries were removed, or those who have not had hormone replacement. Symptoms and signs of low estrogen levels include sleep disturbances, foggy thinking, hot flashes, night sweats, vaginal dryness, thinning skin, incontinence, and heart palpitations.

High Estradiol in premenopausal women is usually due to over production of androgens by the adrenal glands and ovaries (DHEA and testosterone), or by estrogen replacement therapy (ERT). In postmenopausal women high estradiol levels are usually due to estrogen supplements. Excess estrogen levels, such as estradiol, even at normal premenopausal levels, when not balanced by adequate progesterone, may create what is referred to as "**Estrogen Dominance**". Symptoms may include irritability, anxiety, mood swings, weight gain at the hips, water retention, bleeding problems (due to uterine lining overgrowth and fibroids) and thyroid deficiency.

Estrogen in Females and Males:

Estrogen is considered to be the female hormone, whereas testosterone is considered the male hormone. However, both hormones are present in both sexes. The sexual distinctions are not qualitative differences, but rather result from quantitative divergence in hormone concentrations and differential expressions of steroid hormone receptors. In males, estrogen is present in low concentrations in blood, but can be extraordinarily high in semen; as high as 250 pg/ml in testicular fluids, which is higher than serum estradiol in the female. It is well known that male reproductive tissues have estrogen receptors, but the role of estrogen in male reproduction remains unclear.

Estrogen regulates the reabsorption of luminal fluid in the head of the epididymis. Disruption of this essential function causes sperm to enter the epididymis diluted, rather than concentrated, resulting in infertility. This finding raises further concern over the potential direct effects of environmental estrogens on male reproduction and reported declines in human sperm counts.

In males, the main biologically active estrogen is estradiol. The primary source of estradiol in men is from the conversion (aromatization) of testosterone by estrogen synthase. As men age, the production of androgens from the adrenals and gonads is decreased. The aromatization of testosterone to estradiol is often maintained, but due to a variety of factors, more testosterone is aromatized in fatty tissues, causing a further imbalance of the ratio of testosterone to estrogen; i.e. too much estradiol and not enough testosterone. The result is a deficiency of beneficial testosterone and an excess amount of estradiol.

As men age, the amount of testosterone produced in the testes diminishes greatly. Yet estradiol levels remain persistently high. The reason for this is increasing aromatase (estrogen synthase) activity along with age-associated fat mass, especially in the belly. Estradiol levels correlate significantly to body fat mass and more specifically to subcutaneous abdominal fat. The epidemic of abdominal obesity observed in aging men is associated with a constellation of degenerative disorders, including heart disease, diabetes, and cancer.

Subcutaneous abdominal fat acts as a secretory gland, often producing and emitting excessive levels of estradiol into an aging man's blood. One's waist circumference is a highly accurate prognostic measurement of future disease risk, with excess estradiol secretion being at least one of the deadly mechanisms associated with the difficult to resolve problem of having too much abdominal fat.

Symptoms of excess estrogen in aging men include the development of breasts, having too much abdominal weight, feeling tired, suffering loss of muscle mass, and having emotional disturbances. Many of these symptoms correspond to testosterone deficiency as well.

PROGESTERONE

Progesterone is produced in the ovaries at about 10- 30 mg/day and is important for normal reproductive and menstrual function, especially during the latter half (luteal phase) of the menstrual cycle. It plays a role in the health of the heart, skin, bone, blood vessels and other body tissues. It is also important in breast development, maintaining pregnancy and the control of neurotransmitters in the brain. Although Progesterone is found in both females and males, its role in male physiology is not well understood.

Low Progesterone plays a role in abnormal uterine bleeding in females. It may also have an association with lowered neurological function and osteoporosis. Low progesterone is more common in postmenopausal women who are no longer ovulating, have had their ovaries removed, or are using contraceptives or hormone replacement therapy. Low Progesterone levels in males may play a role in male infertility.

High Progesterone is found in states of stress and anxiety in men and women. Symptoms can include excessive sleepiness, dizziness, bloating and susceptibility to yeast infections. In women it can also result in abnormalities in blood glucose levels (dysglycemia), hair loss or baldness (alopecia), acne and breast tenderness.

PROGESTERONE:ESTRADIOL RATIO (Pg:E2)

This ratio describes the relationship between progesterone and estradiol levels. It is used clinically to determine the dominance of one hormone over the other.

The ideal Pg:E2 ratio is in the 100:1 to 300:1 range in premenopausal women and in postmenopausal women who have progesterone supplementation. This ratio is not useful when considering postmenopausal women who have low estrogen levels, or women on hormone replacement therapy (HRT) or oral contraceptives.

A low Pg:E2 ratio indicates an estrogen dominance, and women may experience many severe symptoms, such as anxiety, breast tenderness, headaches or migraines, depression, digestive problems, fuzzy thinking, palpitations, irregular bleeding, water retention, weight gain and more. If estrogen levels stay unopposed, women may go on to develop infertility, skipped periods (amenorrhea), heavy bleeding (hypermenorrhea), fibroids, uterine cancer, heart disease and stroke, and decreased cognitive ability, among other conditions.

An elevated Pg:E2 ratio may indicate progesterone dominance and the symptoms will be those seen with high progesterone levels (see above).

ANDROGENS

The endocrine glands secrete 5 androgens through a similar pathway: Testosterone, dehydroepiandrosterone (DHEA) and its sulphated form (DHEA-S), androstenedione, and androstenediol. Testosterone, and its biologically active metabolite dihydrotestosterone (DHT), are the only androgens with direct androgenic activity. DHEA-S, DHEA, and androstenedione are all precursors of testosterone.

a) TESTOSTERONE

Testosterone is considered the “male hormone”. In men it is produced by the testes and in much smaller amounts by the ovaries in women. It is responsible for many of the secondary sex characteristics seen in men such as a deeper voice and hair on the chest, in addition to contributing to a healthy libido, regulating the immune system, maintaining optimal memory, building muscle mass, and maintaining energy levels. In both men and women testosterone levels are highest in the teens and then decline gradually with age, playing a role in the loss of bone density. In women, premenopausal testosterone levels are usually within the high-normal range and postmenopausal levels at low-normal range.

Low Testosterone is most often a result of aging, testes or ovary removal, suppression of ovarian and testicular production by stress hormones (cortisol), the use of synthetic HRT and contraceptives, and/or damage to the testes, ovaries, and adrenal glands by medications, radiation therapies, or trauma. Chronically low testosterone, in both sexes, may cause fatigue or decreased energy as well as reduced sex drive or desire (libido). In addition, it may cause reduced stamina and the loss of bone and/or muscle mass, loss of body hair, incontinence, aches and pains, memory lapse, cognitive decline and depression. In women, testosterone imbalance has been associated with coronary heart disease and heart attacks (myocardial infarcts), especially in post-menopausal women. In men, testosterone levels decrease with age. While this decrease may not be noticeable in some men, others may experience significant changes starting in middle age, or more commonly at age 60 and above. This drop in testosterone levels is sometimes termed "male menopause", hypogonadism, or andropause.

Low testosterone levels may result in a decline in physical energy, strength, stamina, and diminished mental aggressiveness. These men may experience more aches and pains in the bones and joints and they may also have a decline in libido and a greater incidence of erectile dysfunction.

High Testosterone is the result of excess production by the ovaries, testes and adrenal glands, or androgen supplementation (testosterone, DHEA). In men high levels will manifest in increased scalp hair loss. The higher the levels the more likely these men will exhibit risky and aggressive behavior, whether sexual, injury risk, or criminal. Symptoms of high testosterone levels in premenopausal women include loss of scalp hair, increased body and facial hair, acne, and oily skin. Supplementation with topical testosterone at doses in excess of levels produced by the ovaries (0.3-1 mg) or testes (5-10 mg) can raise testosterone to levels beyond physiological range.

MELATONIN

Melatonin is a hormone produced during the dark phase of the day by the pineal gland, a small endocrine gland in the brain that regulates the sleep-wake cycle.

Melatonin is also synthesized in the enterochromaffin (EC) cells throughout the intestine and to a lesser extent in lymphocytes, mast cells, epithelial cells and the bone marrow. In the gut, L-tryptophan is a crucial precursor of melatonin synthesis and the EC cells, as well as bacteria within the microbiome, have been reported to be the major sources of L-tryptophan-induced increase of circulating melatonin. Interestingly, at any time of the day or night, the gut contains at least 400 times more melatonin than the pineal gland, but does not contribute to the circulating rhythm of Melatonin[9]. This non-pineal melatonin seems to act locally. These local effects are involved in a myriad of actions, including metabolism, immune function, gut function, inflammation, mitochondrial function, free radical scavenging, direct anti-oxidant activity, redox status and influence on anti-oxidant enzymes[10].

In a 24-hour circadian cycle, melatonin reaches its highest levels during sleep, the middle of the night, often spiking to levels above 50 pg/ml. It then falls to very low levels by the time of waking (~5 pg/ml). The pineal gland begins producing melatonin in the evening, so that some individuals may have rising levels that reach to between 10-15 pg/ml at bedtime[11]. Melatonin has numerous functions in body hemostasis, of which three major ones are noted here.

a. It has major physiological importance in the control of sleep time and duration. It is central to the modulation of both circadian and annual biorhythms and has a remarkably tight association with sleep propensity[12].

b. It is involved in the regulation of GI motility & local anti--inflammation[13].

c. It acts as a strong lipophilic antioxidant, specifically offering mitochondrial protection. Melatonin scavenges free radicals (OH-) and upregulates glutathione, acting to promote antioxidant enzymes such as glutathione peroxidase (GPx), glutathione reductase (GR), superoxide dismutase (SOD) and catalase (CAT)[14].

These melatonin functions interact. As an example, good circadian rhythm helps to decrease oxidative stress, whereas chrono (sleep) disruption causes an increase in reactive oxygen and nitrogen species[15].

Low levels of melatonin can cause imbalances that may have far reaching effects, including menstrual difficulties, sleep disorders, depression and Seasonal Affective Disorder. The synthesis and physiological use of melatonin is strongly affected by the length of day, seasonal changes, aging and artificial illumination - especially prolonged exposure to blue light emanating from computers and other similar devices. A deficient production of melatonin can also result in lowered basal body temperature, insomnia, and sleep/wake disorders.

The disturbance in the circadian rhythm of melatonin may influence other hormones, such as thyroid and testosterone. It may lead to an elevated estrogen/progesterone ratio, decreased cardiovascular and antioxidant protection, as well as immune suppression[16]. Therefore, accurate measurement of melatonin levels is essential for the development of therapeutic regimes, such as timing of artificial light and melatonin administration.

Excess melatonin is associated with anxiety, stress and depression. These elevated levels are also present in those diagnosed with Seasonal Affective Disorder, a form of depression. It has been observed that this form of bipolar disorder might have elevated sensitivity to light; i.e., a greater decrease in melatonin secretion in response to light exposure at night. This should be contrasted with drug-free, recovered bipolar patients, who show normal light Sensitivity[17]. Elevated melatonin is also associated with a lowered estrogen/progesterone ratio, inhibition of ovulation, low thyroid and adrenal function, and hypotension.

METABOLIC SYNDROME

Metabolic syndrome is a disorder of energy utilization and storage, diagnosed by a co-occurrence of three out of five of the following medical conditions: Elevated blood pressure, elevated fasting plasma glucose, high fasting serum triglycerides (VLDL triglyceride), low levels of fasting serum high-density lipoprotein (HDL) cholesterol and central-waist abdominal obesity, also known as visceral overweight (male- pattern or apple-shaped adiposity), manifested by fat (adipose) tissue accumulation mainly around the waist and trunk. Metabolic syndrome increases the risk of developing diabetes and cardiovascular disease, particularly heart failure. Some studies have shown the prevalence in the USA to be an estimated 34% of the adult population, and increasing with age.

Recent research indicates prolonged **chronic stress** can contribute to metabolic syndrome by disrupting the hormonal balance of the hypothalamic-pituitary-adrenal axis (HPA-axis)[18]. The principal signs and symptoms of metabolic syndrome, as noted above, are often accompanied by impaired fasting glucose and insulin resistance, or pre-diabetes, which can manifest by numbness in the feet or hands.

Extensive literature in recent years has the shown the strong relationship of metabolic syndrome to the intake of high levels of fructose, from both exogenous and endogenous sources, leading to the creation of uric acid[19]. This has highlighted the critical importance of proper nutrition, and how a poor, or suboptimal diet, can result in uric acid dysregulation & the development of metabolic dysfunction[20].

HYPOMETABOLISM

Hypometabolism is not an illness in itself, but rather can be termed a "condition", encompassing a variety of illnesses[21]. The characteristic of hypometabolism is that the biochemical processes of the body are not functioning as fast, or as well as they should. Since the biochemical reactions of the body give off heat (exothermic), hypometabolism results in hypothermia, a lowered body temperature. While the enzymatic reactions of the body give off heat, the enzymes themselves are also dependent on body heat to have their most efficient action. When body temperature is below 98.2 degrees Fahrenheit, enzymes are not functioning at their best efficiency.

This enzymatic dysfunction produces a variety of signs and symptoms, which are common to all hypometabolic conditions. These include fatigue (AM and PM), cold and heat intolerance, migraines (headaches), depression and weight gain. Other symptoms include irritability, sleep disturbance such as insomnia, anxiety (panic attacks), as well as poor memory and concentration (foggy thinking). Many individuals experience irregular periods, low sex drive, low ambition and motivation. This may be accompanied by fluid retention, irritable bowel, hair loss, dry skin and hair and generalized muscle aches and joint pain.

INSULIN

Regulation of Blood Sugar

Obesity is a major risk factor for a large number of conditions, including cardiovascular diseases, hypertension, type 2 diabetes and cancer. A key factor in minimizing the impact of obesity involves reducing the prevalence of childhood obesity and monitoring overweight and at-risk individuals early on in the disease progression. Measuring salivary insulin, as a pre-screening method for type 2 diabetes, is an effective adjunct to preventative treatment, that can start before permanent damage or obesity related comorbidities occur.

Insulin is a hormone created by the Langerhans β-cells of the pancreas, that controls the amount of glucose in the bloodstream. Insulin also helps store glucose in the liver, fat, and muscles. Finally, it regulates the body's metabolism of carbohydrates, fats, and proteins.

Cortisol is a potent insulin-antagonistic hormone, inhibiting insulin secretion, stimulating glucagon secretion and disrupting insulin signaling. Cortisol inhibits insulin release and reduces GLP-1 (glucagon-like peptide-1) production, and its positive effects on insulin secretion, thereby also reducing insulin secretion. This is all part of the physiological stress response, which causes the release of cortisol, a glucocorticoid, from the adrenal glands. Designed to increase energy availability in the short term, cortisol acutely impairs insulin secretion and increases hepatic glucose output.

a) Cortisol, Hypoglycemia and Adrenal Insufficiency

During acute stress the adrenal glands respond by releasing cortisol, the primary stress hormone. As cortisol rises, both fat and muscle become less sensitive to insulin, making more glucose available in the bloodstream. Cortisol helps the body to manage stress, converting protein into glucose to boost decreasing blood glucose levels. In this regard it works in tandem with insulin to maintain constant blood sugar levels and reduce inflammation.

With chronic stress, a problem arises for both the adrenals and blood glucose levels. Because the body is forced to generate more energy, at a certain point it can no longer meet the high demand for glucose. The body then enters a stage of hypoglycemia (low blood sugar), manifesting low cortisol levels, despite the continued high levels of stress. This is often seen in individuals suffering from adrenal insufficiency.

With increased insulin and decreased cortisol levels, blood sugar may drop at an alarming rate, because cortisol, amongst other hormones, is not facilitating the conversion of carbohydrates and fats into glucose.

In addition, stress itself can trigger large blood glucose swings, which can hamper the body's ability to maintain a blood sugar balance, further worsening the symptoms of hypoglycemia.

Finally, elevated fasting insulin levels - a hallmark of insulin resistance - can precede the onset of type 2 diabetes by several years and may be used to monitor and assess changes in lifestyle to reduce disease risk[22].

b) Cortisol and Stress-Induced Hyperglycemia

During periods of stress, the adrenals release stress hormones like cortisol and adrenaline. This creates an energy boost for a 'fight or flight' response. But the increased levels of these hormones actually make it harder for insulin to work properly, creating a state known as insulin resistance.

In addition, glycemic dysregulation, often referred to as "stress-induced hyperglycemia", may lead to high cortisol levels, insulin resistance and decreased insulin secretion. The pathophysiology of this hyperglycemic state is multifactorial. During chronic illness, complex interactions between counterregulatory hormones and cytokines may cause excessive production of glucose, which is also coupled with insulin resistance.

Stress increases glycogenolysis (glycogen breakdown into glucose in the liver) and gluconeogenesis (synthesis of new glucose from non-carbohydrate precursors). Glycogenolysis is triggered by increased catecholamines, whereas gluconeogenesis is triggered by an increase in stress response glucagon. Additionally, insulin resistance exacerbates hyperglycemia and is described as the inability of muscle and adipocyte tissue to take up glucose, which is caused by an alteration of insulin signaling and the decrease in type 4 glucose transporters (GLUT-4) during chronic stress.

Measuring Insulin in Blood and Saliva

Fasting salivary insulin has a near-linear correlation to fasting serum levels (0.92) and is a reliable option to the serum measurements[23]. Earlier research has shown that there is a ~30 minute delay in the rise of salivary insulin and the spike in serum insulin levels during an oral glucose tolerance test[24]. Therefore, saliva presents a non-invasive way of assessing and monitoring insulin levels in overweight or obese pre-symptomatic individuals. It has also shown usefulness in clinical situations such as imbalanced blood lipids and early stage diabetes.

Fasting Saliva Insulin: This test is chiefly used to measure insulin levels when diagnosing diabetes and insulin resistance. The latter is a condition in which the cells in muscles, fat, and liver don't respond well to insulin, leading to greater difficulty for those cells to take up glucose from the blood. Insulin resistance may eventually lead to the development of type 2 diabetes and may increase the risk of heart disease, cancer, and Alzheimer's.

Non-Fasting Saliva Insulin: In blood, non-fasting insulin is used to determine the cause of hypoglycemia (low blood sugar), as well as to diagnose or monitor insulin resistance. With saliva insulin the levels vary with type of meal and time of sample collection. Non-fasting insulin levels may be elevated in cases of insulin resistance and have been found to be an accurate screening tool for identifying those at risk for type 2 diabetes and heart disease later in life.

Insulin Resistance and Depressive Disorders

There is accumulating biological evidence linking insulin resistance with the development of depressive disorders, a leading cause of disability worldwide[25]. Both men and women show metabolic derangements associated with the depressive disorders, with women tending to show elevations in biomarkers related to an increased risk of type 2 diabetes, while men also exhibited marked increases in CRP, a biomarker of cardiovascular disease risk[26]. In a very recent study from Holland, three surrogate measures of insulin resistance positively predicted 'incident major depressive disorder', defined as the occurrence of a participant's first depressive episode, in a 9-year follow-up period among adults with no history of depression or anxiety disorder. The findings highlight that these measurements may have utility for evaluating the risk for the development of major depression among patients with insulin resistance or metabolic pathology[27].

SECRETORY IgA (SIgA)

Secretory IgA (SIgA) reflects the resilience of the immune response and the effect of stress on the immune system. SIgA is a product of activated B cells lying in intimate contact with mucosal membranes in the nasal passages, oral cavity, lacrimal glands, the gastrointestinal and respiratory tracts, as well as the genitourinary tract. All these mucosal surfaces are exposed to the external environment, and SIgA is an important part of the first line of immune defense against pathogens that cause infection. It binds to these infectious pathogens and prevents their adhesion and penetration into the body.

SIgA is analyzed from an AM saliva collection sample. The reference ranges for SIgA in this report are derived from published literature and laboratory data:

Low levels of SIgA (<75.0 µg/ml) may be an indication of an impaired intestinal barrier function, chronic GI infections, bacterial overgrowth of the small intestine (SIBO), parasitic infections, gliadin intolerance, inflammatory bowel disease, as well as food allergies and sensitivities. Decreased levels also occur with the use of anti-inflammatory drugs and in cases of autonomic nervous system imbalance. Chronic stress, both physical and mental, is generally associated with low levels of SIgA[28]. Stress, both physical and emotional, and mediated by cortisol, can result in an inadequate production of SIgA in response to a mucosal infection[29]. In particular, when cortisol levels are chronically elevated, SIgA production decreases, which increases the risk of infection.

There is also evidence that SIgA levels are associated with daily mood: Antibody response has been shown to be lower on days with high negative mood relative to days with lower negative mood. Conversely, SIgA antibody response is higher on days with high positive mood relative to days with lower positive mood, suggesting that minor life events' role in health may be mediated by the secretory immune system[30].

Equivocal levels of SIgA (75.0-145.0 µg/ml) need to be considered in the context of the patient's overall presentation and available diagnostic data. Certain individuals may have SIgA deficiency which isn't genetic, but rather is caused by environmental or lifestyle factors such as poor diets, nutrient deficiencies, certain drugs (including anti-inflammatories), viruses, impaired immune function and excessive stress.

High levels of SIgA (145.0-330.0 µg/ml) may reflect an activated immune response to chronic infections including viral infections such as EBV (Epstein–Barr virus), CMV (Cytomegalovirus) and HIV. It may also be an indication of acute stress, intestinal barrier dysfunction, and/or acute active infection of the digestive system, or acute exacerbations of inflammatory conditions such as Crohn's disease or ulcerative colitis. In addition, it may indicate heavy smoking, alcoholism, as well as acute oral infections, such as periodontitis. In general, high levels of SIgA point to possible acute active infections and inflammatory reactions, which heighten the activation of the immune system.

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