

RESULTS: SALIVA HORMONE TEST

Accession #: 100035547 • Patient: April Smith

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Patient: April Smith
Tel: (123) 456-789 **Email:** test@test.com
Sex: Female **Age:** 36 yr **Date of Birth:** 1989-02-02
Height: 5 ft 5 in **Weight:** 135 lbs **Waist size:** 28 in
1st day of last menses: Day 25, Month 10
Menstrual status: Irregular
Hormones: No
Health Care Professional: John Smith
Address: 400 March Road #420, Ottawa, Ontario K2K 3H4

Accession #: 100035547
Sample received: 2026-01-30
Report issued: 2026-10-30
Sample collection:
 2025-11-16 06:30 AM
 2025-11-16 12:30 PM
 2025-11-16 17:45 PM
 2025-11-16 22:15 PM

STRESS & HORMONE PROFILE

17-β ESTRADIOL (E2) pg/ml		11
Female	Ref. ranges	
21-50 years	Follicular phase	2.1 - 7.8
	Mid cycle	3.8 - 16
	Luteal phase	2.1 - 8.4
51-75 years	Post Menopausal	2.1 - 4.4
Male		2.1 - 4.7

PROGESTERONE (Pg) pg/ml		96.7
Female	Ref. ranges	
	Follicular phase	19.6 - 86.5
	Luteal phase	99.1 - 333
	Post Menopausal	6.00 - 56.4
Male		12.7 - 65.1

Pg:E2 RATIO*		8.8 : 1
Optimal Luteal: 10 to 150:1		

Melatonin (Bedtime\Night) pg/ml		7
Ref. range 3 - 50		

Secretory IgA (Morning) µg/ml		458
	Ref. ranges	
Very Low	< 24.0	
Low	24.0 - 200	
Mid-Range	200 - 2000	
High	2000 - 3000	
Very High	> 3000	

CORTISOL (C) ng/ml		
	Ref. ranges	Median
AM	6.1	2.2 - 9.8 3.6
Noon	0.6	0.9 - 3.5 1.1
PM	0.4	0.3 - 3.0 0.8
Night	1	0.1 - 2.8 0.5
TOTAL*	8.1	3.5 - 19.1 6.0

DHEA-S (DS) ng/ml		1
	Ref. ranges	Median
Female	0.2 - 3.6	1.7
Male	0.3 - 3.7	1.8

TOTAL C:DS RATIO*		8:1
Median 3:1		

TESTOSTERONE (T) pg/ml		48
	Ref. ranges	
Age (years)	Male	Female
Less than 20	Range not applicable	
20 - 29	41.4 - 143	9.0 - 49
30 - 39	31.8 - 100	9.0 - 49
40 - 49	30.1 - 97.8	9.0 - 49
50 - 59	30.0 - 92.0	9.0 - 49
60 - 69	23.2 - 86.9	9.0 - 39
Greater than 69	Range not applicable	

T : E2 RATIO*		4.4 : 1
P-M Female: 4 to 10:1		Male: 15 to 20:1

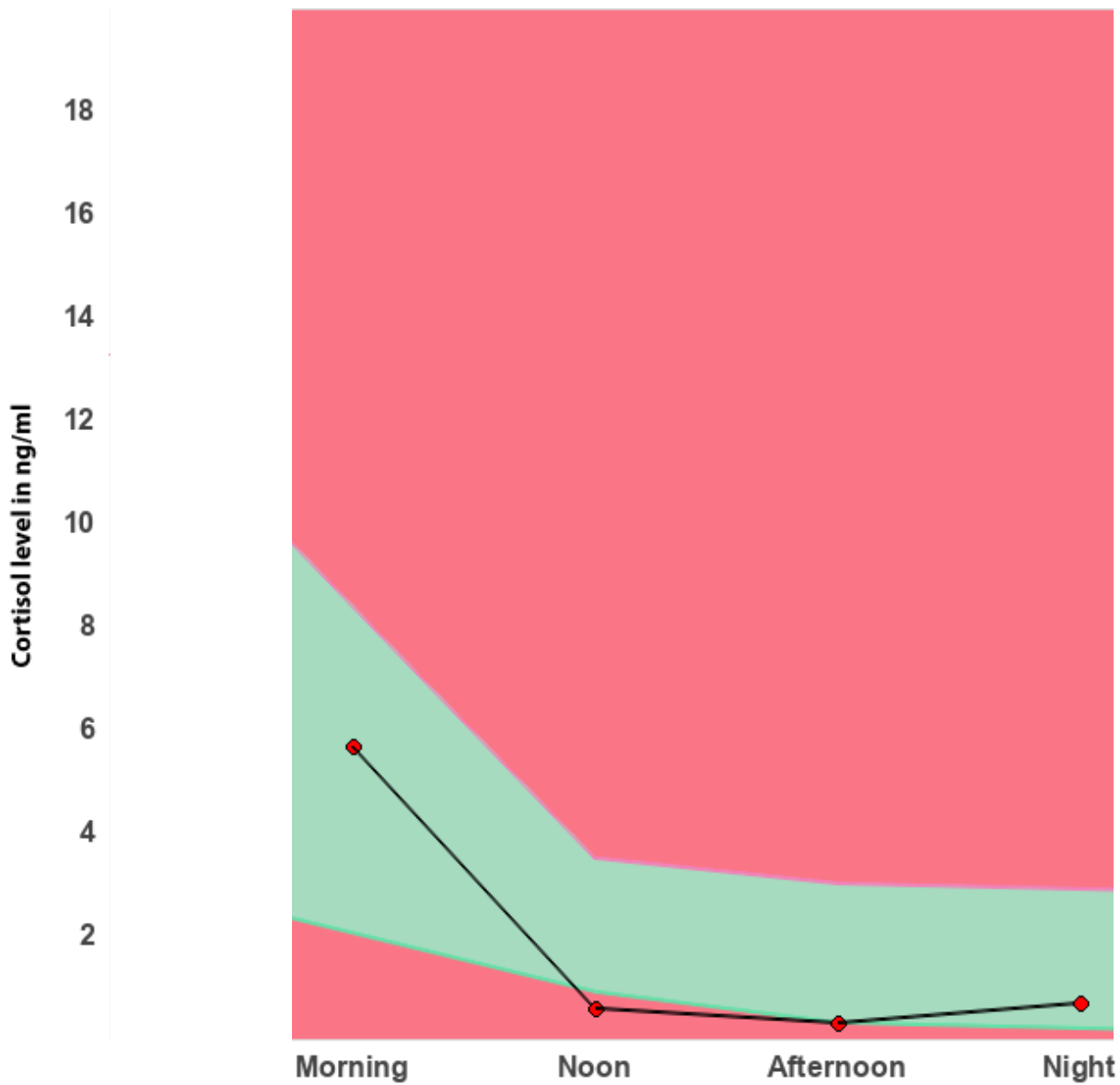
NA = Not Applicable

* Ratios displayed when values lie within lower and upper limits of Quantitation.

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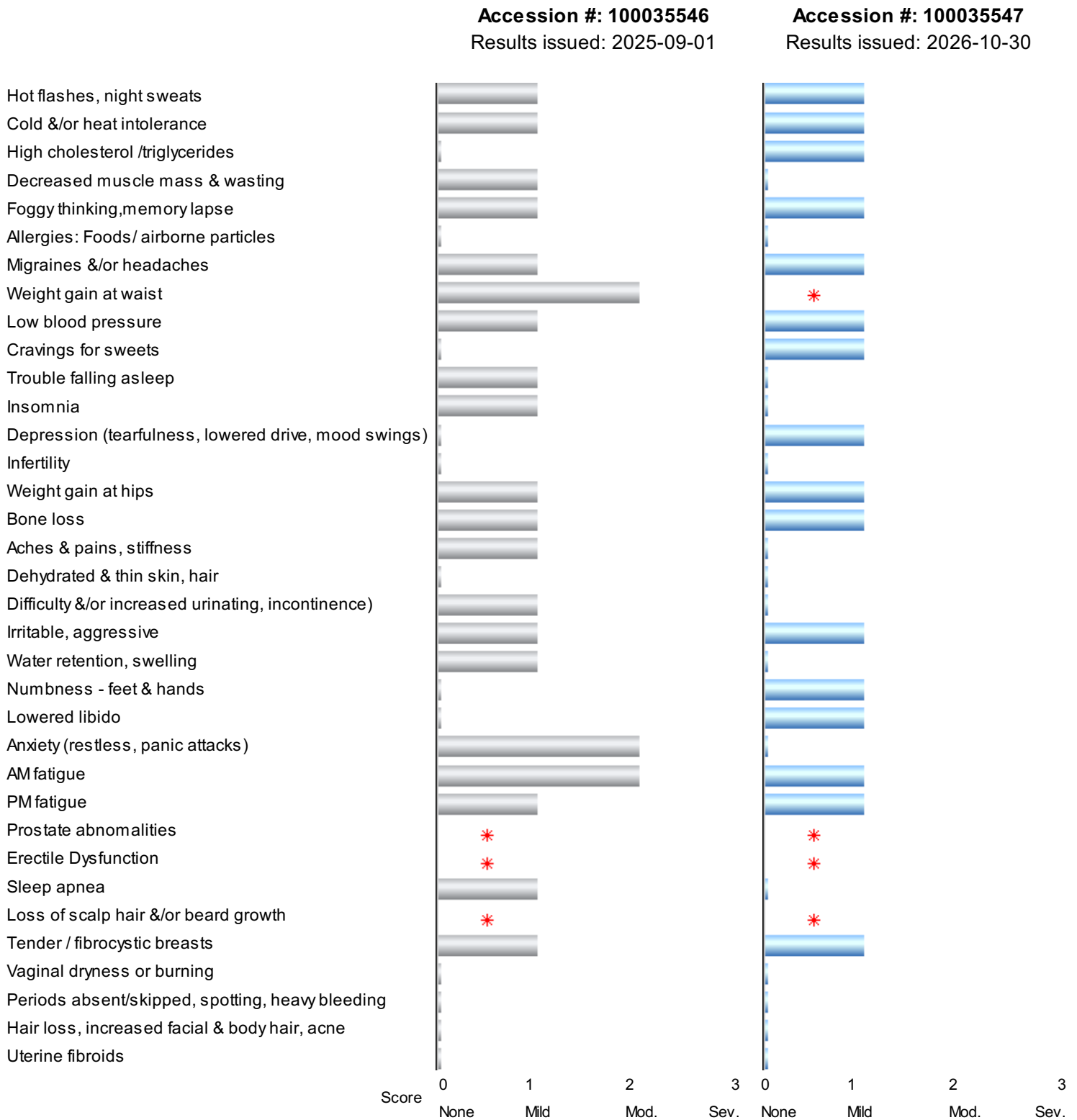
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* Indicates that symptom left blank

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[Convert to pdf, Save or PRINT >>](#)**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 falls below the reference range. As the ability of the adrenals to produce adequate cortisol diminishes, the following symptoms are common during the day: A slow down in activity as the morning progresses, afternoon fatigue and headaches.

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 Nighttime 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 (Dehydroepiandrosterone 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.

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[Convert to pdf, Save or PRINT >>](#)**General Discussion****CORTISOL**

About Cortisol: Cortisol is produced by the adrenal glands, which are controlled by parts of the brain called the hypothalamus and pituitary. 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. It 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 **Adrenal Exhaustion**, which 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, but when stress is chronic and cortisol output remains high over a prolonged period (months/years), break- down of normal tissues (muscle wasting, thinning of skin, bone loss) and immune suppression can result. Common symptoms of chronic high cortisol include sleep disturbances, fatigue, depression and weight gain in the waist and anxiety. Stress and persistently elevated cortisol levels can contribute to premature aging and chronic illness.

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[Convert to pdf, Save or PRINT >>](#)**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.

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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.

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[Convert to pdf, Save or PRINT >>](#)**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.

Low Pg:E2 Ratio: In the natural postmenopausal (P-M) state, where hormone therapy is not being used, women inherently exhibit a low Pg:E2 ratio. This occurs because the ovaries stop producing progesterone, while trace amounts of estrogen continue to be produced via peripheral conversion in fat tissue. The resulting 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 and water retention.

Obesity can also lead to a low ratio, since adipose (fat) tissue contains the aromatase enzyme, which actively converts other hormones into estrone and estradiol, thereby skewing the balance, and leading to a low ratio.

Chronic elevated stress can cause the body to prioritize making cortisol. This removes the hormonal precursors needed to manufacture progesterone, driving down the ratio.

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.

High Pg:E2 Ratio: An elevated ratio may indicate progesterone dominance, and the symptoms will be those seen with high progesterone levels. These include breast tenderness, bloating, fatigue and headaches. Some women will also complain of mood swings, including heightened anxiety and feelings of depression. The most common cause is the use of progesterone topical creams or oral supplements. The resulting high progesterone levels from exogenous (topical) creams is most reliably picked up in salivary analysis, because saliva measures the "free," unbound, and tissue-bound hormone, whereas conventional serum (blood) testing only measures hormones circulating in the aqueous portions of the bloodstream. Because the salivary glands receive the progesterone carried by red blood cells, salivary analysis will accurately reflect a sharp rise or accumulation of the hormone, often showing levels **orders of magnitude** higher than a concurrent serum test.

An increased ratio can also frequently occur when progesterone is being used to manage perimenopause symptoms, and its use is not stopped when menopause is reached, and when natural estrogen levels are decreasing significantly. This results in much more progesterone relative to estrogen, creating a very high Pg:E2 ratio.

It should also be noted that a high ratio can occur with extreme weight loss, or over-exercising. This occurs because there is a decrease the brain's signaling to the ovaries, which may result in dramatic decreases in estradiol levels, while at the same time baseline adrenal progesterone remains steady.

TESTOSTERONE:ESTRADIOL-2 RATIO (T:E2) in Males and Post-Menopausal (P-M) Females

There is no established or universally accepted optimal range for the T:E2 ratio in salivary testing, but clinical literature and laboratory findings point to estimated ranges of 15 to 25:1 in adult males, and 4 to 10:1 in post-menopausal (P-M) females. Research has also shown links between the ratio and metabolic, bone, and cardiovascular risks.

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In Males: The ratio can function to shine a light on aromatase enzymatic activity. It reflects the extent to which testosterone is converted to estrogen via the aromatase pathway. That is important because this conversion often increases with higher body fat.

A *low ratio* (<15:1), may suggest high levels of estrogen activity, or aromatase over-activity. This is often linked with signs and symptoms that include increases in central body fat, breast tissue (gynecomastia) and water retention. Often there are mood changes, including fatigue, low drive, emotional lability, and low libido.

A *high ratio* (>20:1) may indicate relatively low estrogen, which can have significant impact on bone mineral density, joint health, as well as sexual function.

Note that values for T and E2 change as a double-movement. Since one hormone is consumed to make the other, the ratio shifts, while both numbers are often still inside their reference ranges.

In Females: The T:E2 ratio is not a single fixed number, but rather a dynamic balance that changes constantly, across the menstrual cycle and life stages.

A *low ratio* indicates that estradiol levels are high relative to testosterone, or that testosterone levels are abnormally low while estrogen remains stable. One major reason is an increased aromatase activity. The aromatase enzyme converts testosterone into estradiol. In cases of excess body fat, alcohol intake, and with certain drugs, there is an increase this conversion rate, which leads to relative estrogen dominance.

More infrequently, one can encounter a low ratio when a woman is taking exogenous estrogen, or birth control pills containing estrogen, which raises the sex hormone-binding globulin (SHBG). The effect depends heavily on the route of administration, with orally administered estrogen causing a large increase in SHBG levels, while transdermal estrogen (patches, gels and sprays) having a much more limited effect. The SHBG subsequently binds free testosterone and lowers the relative active testosterone-to-estradiol balance.

A *high ratio* is mostly encountered in P-M females. This occurs because ovarian estrogen levels drop precipitously, with levels of E2 < 2 pg/ml not being unusual. At the same time, both ovarian and adrenal testosterone production decline very gradually, or remain stable. This creates a relative androgen excess, which increases the T:E2 ratio. Despite its prevalence and association with risks of cardiovascular disease and metabolic syndrome, this imbalance is frequently missed because routine evaluations often rely on absolute hormone values, rather than ratios, and standard laboratory testing lacks the sensitivity to detect the low P-M hormone ranges.

In some P-M women diminished aromatase enzyme activity fails to sufficiently clear the remaining androgen (T) pool, further shifting the T:E2 balance upward.

Clinically, one can fall into the "normal absolute value" trap, where one evaluates individual, absolute hormone values, rather than their relative balance and ratio. In such a case, the testosterone value may fall squarely within a "normal" P-M reference range, hiding the fact that it is disproportionately high compared to the near-absent estrogen levels.

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.

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[Convert to pdf, Save or PRINT >>](#)**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.

b) 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.

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

High DHEA-S can be associated with insulin resistance/PCOS⁴ (polycystic ovaries) 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 syndrome⁵ 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 studies⁸ 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.

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[Convert to pdf, Save or PRINT >>](#)**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: abdominal (central-waist) obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, and low high-density cholesterol (HDL) levels. 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 the prevalence increases 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)⁵.

The principal signs and symptoms of metabolic syndrome are central obesity, also known as visceral overweight (male-pattern or apple-shaped adiposity), with fat (adipose) tissue accumulation mainly around the waist and trunk. Other signs of metabolic syndrome include high blood pressure, with decreased fasting serum HDL cholesterol and elevated fasting serum triglyceride level (VLDL triglyceride). It is often accompanied by impaired fasting glucose and insulin resistance, or pre-diabetes, which can manifest by numbness in the feet or hands.

HYPOMETABOLISM

Hypometabolism is not an illness in itself. It would better be termed a "condition", encompassing a variety of illnesses⁶. The characteristic of hypometabolism is that the biochemical processes of the body are functioning as fast 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.

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 melatonin⁷. This non-pineal melatonin seems to act locally.

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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 enzymes⁸.

In a 24-hour circadian cycle, melatonin reaches its highest levels during sleep, in the middle of the night, often spiking to levels well 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 have rising levels that may reach up to 50 pg/ml at bedtime⁹.

This concentration of melatonin is generally considered to be in the upper range of normal, healthy endogenous production during early night/bedtime. These levels can be significantly disturbed by a host of factors including: Blue light exposure from smart phones and televisions, bright indoor lighting, shift work and the aging process. Suppression can also occur with the overuse of coffee, alcohol and smoking.

Certain medication, especially Beta-blockers, anti-inflammatory drugs (NSAIDs like ibuprofen), and certain antidepressants can reduce melatonin levels. High doses of vitamin B12 or vitamin D, taken in the evening, may inhibit melatonin release. Finally, health conditions, such as Alzheimer's disease, fibromyalgia, mood disorders, and diabetes type 2 are associated with lower melatonin levels.⁹.

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 propensity¹⁰.
- b. It is involved in the regulation of GI motility & local anti-inflammation¹¹.
- 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)¹².

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 species¹³.

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 suppression¹⁴.

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.

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This should be contrasted with drug-free, recovered bipolar patients, who show normal light sensitivity¹⁵. Elevated melatonin is also associated with a lowered estrogen/progesterone ratio, inhibition of ovulation, low thyroid and adrenal function, and hypotension.

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, the 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.

The SIgA value is shown in a box to the right. The reference ranges are shown below, in quintiles. When the value in the box lies in the very low or very high quintiles, the box is shown in red, to signify that it is outside the normal range.

Very Low levels (< 24 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 SIgA levels¹⁶.

Stress, both physical and emotional, and mediated by cortisol, can result in an inadequate production of SIgA in response to a mucosal infection¹⁷. In particular, when cortisol levels are chronically elevated, SIgA production decreases, which increases the risk of infection.

Low (24 - 200 µg/ml), **Mid-Range** (200 - 2000 µg/ml) and **High** (2000 - 3000 µg/ml) **levels** need to be considered in the context of the patient's overall presentation and available diagnostic data.

Certain individuals may have a 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. The largest number of individuals lie in the Mid-Range, which also has the largest range. This is to be expected, since the values follow a 'Normal, or Gaussian Distribution', which is often referred to as a bell curve.

Very High levels (> 3000 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 be due to heavy smoking, alcoholism, as well as acute oral infections, such as periodontitis. In general, very high levels of SIgA point to possible acute active infections and inflammatory reactions, which heighten the activation of the immune system.

FLUIDS iQ analyzes SIgA from an AM saliva collection sample. The reference ranges for SIgA in this report are derived from published literature¹⁸ and laboratory data:

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