FLUIDS iQ®

RESULTS: SALIVA HORMONE TEST

Accession #: 100035624 • Patient: JOHN SMITH

Patient: JOHN SMITH
Sex: Male **Age:** 51 yr **Date of Birth:** 1971-01-01
Height: 5 ft 8 in **Weight:** 135 lbs **Waist size:** 32 in

Hormones: No
Health Care Professional: Jane Smith

Accession #:	**100035624**
Sample received:	2022-10-17
Report issued:	2022-10-18
Sample collection:	
2022-10-12	06:30 AM
2022-10-12	12:15 PM
2022-10-12	18:10 PM
2022-10-12	22:45 PM

STRESS AND METABOLIC PROFILE

INSULIN Fasting (Morning) µIU/ml **8.1**

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

INSULIN Non-Fasting (Noon) µIU/ml **0.7**

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

Secretory IgA (Morning) µg/ml **291.1**

Reference range 0 - 330

CORTISOL (C) ng/ml

		Reference range	Median
Morning	**6.5**	2.0 - 10.7	3.9
Noon	**2.5**	0.7 - 3.5	0.9
Afternoon	**2.1**	0.5 - 3.1	0.6
Night	**1.5**	0.3 - 3.2	0.3
TOTAL	**12.6**	3.5 - 20.5	5.6

DHEA-S (DS) ng/ml **6.2**

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

TOTAL C:DS RATIO **2:1**

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

The reference range is derived from a normal distribution of results that encompass 95% of randomly selected individuals in a population.

The median represents the number in the middle of the data set.

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

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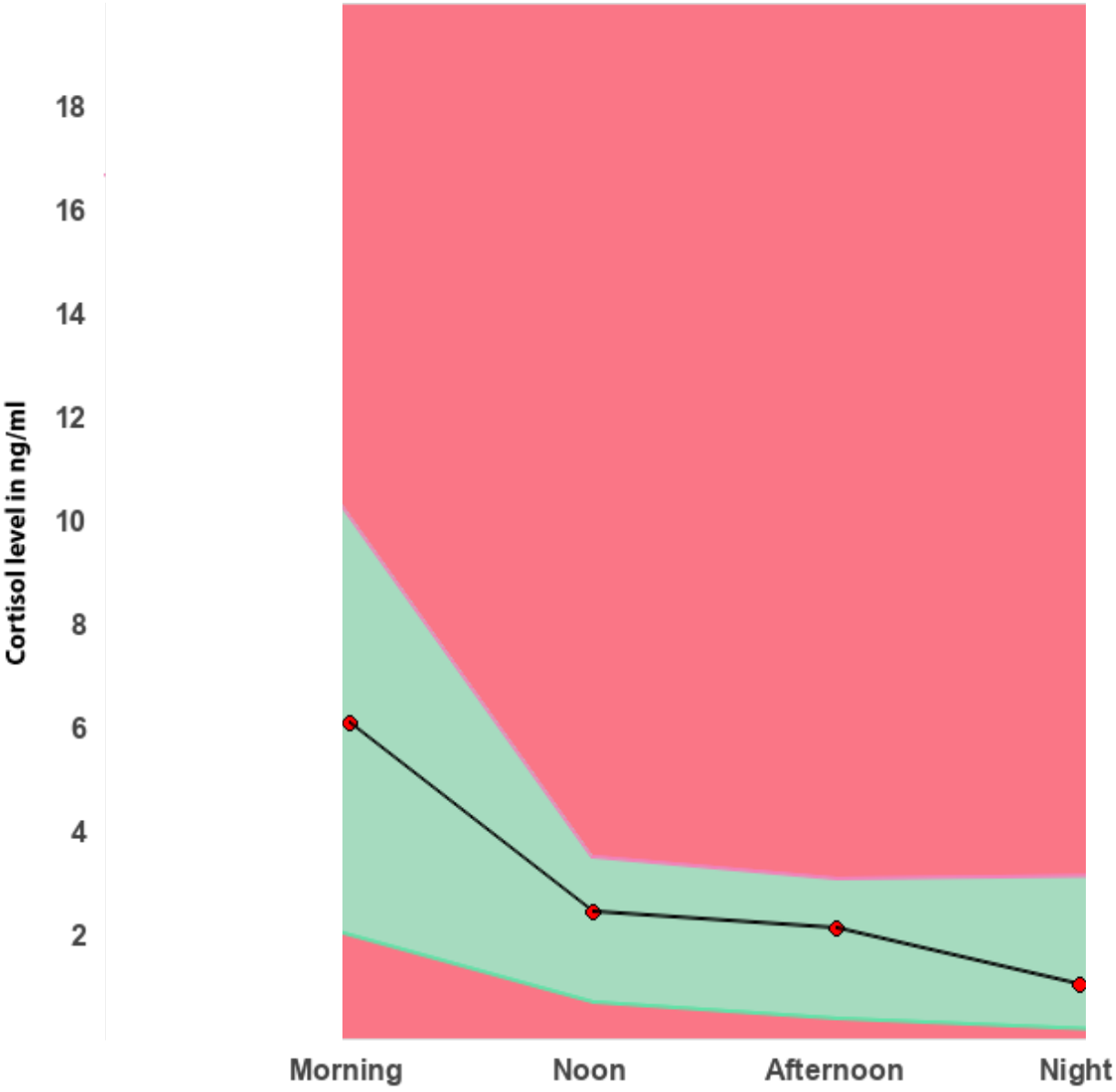

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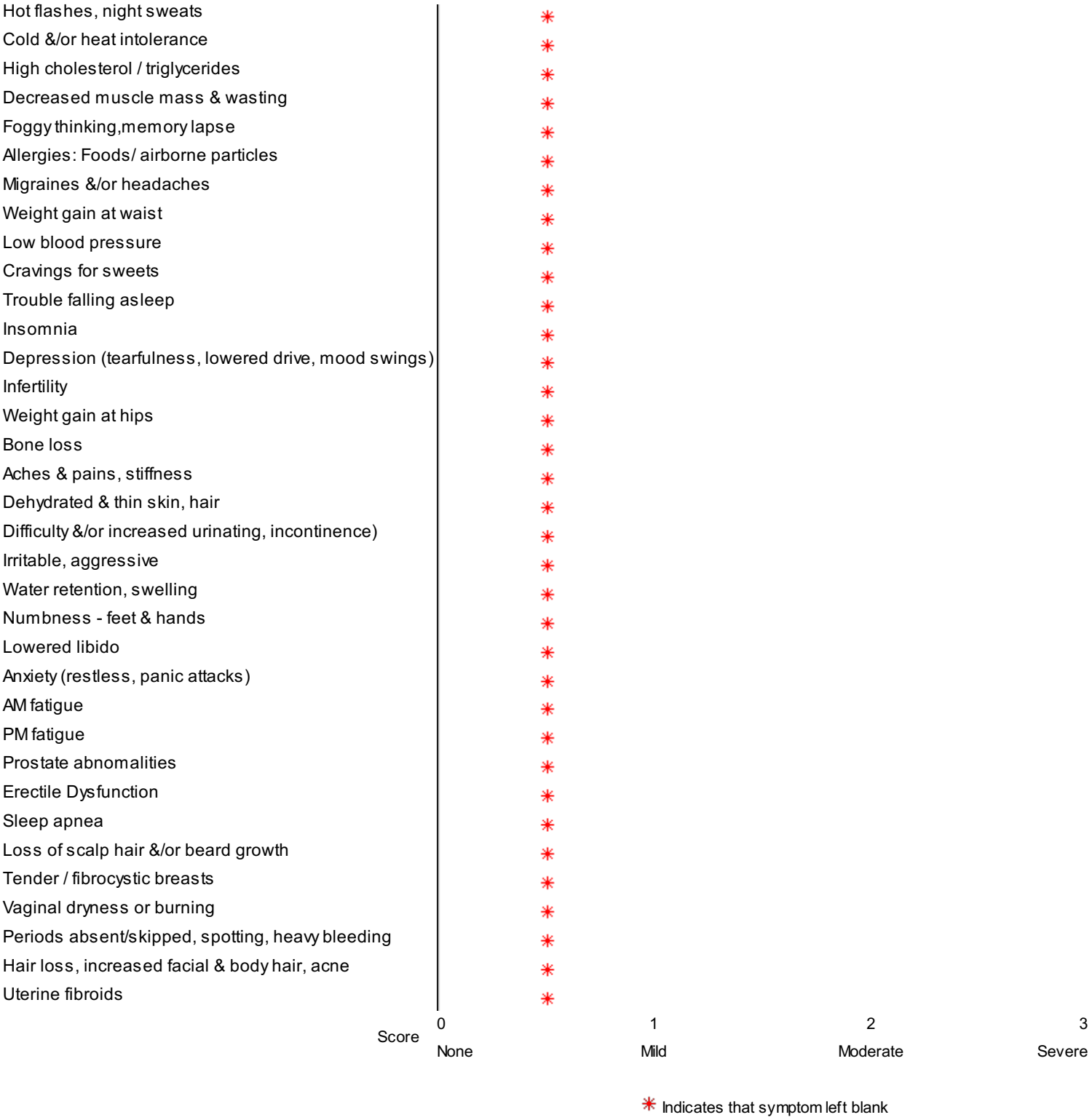
JD Clinic AN:



Understanding Hormone and Insulin 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 exceeds the reference range. DHEA is at its highest in early adulthood, but sometimes higher levels can occur regardless of age. Adrenal disease is the main cause of high DHEA levels, either due to adrenal hyperplasia or tumors - either benign or cancerous. Side effects will differ between men and women, and are usually dose dependent. Women tend to convert excess DHEA into testosterone, which can lead to acne and hirsutism. Men tend to convert the excess DHEA into estrogen, which can cause decreased libido or fatigue.

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] 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.

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).[9] 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.[10] 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.[11]

HYPOMETABOLISM

Hypometabolism is not an illness in itself, but rather can be termed a "condition", encompassing a variety of illnesses.[12] 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, cancer, and type 2 diabetes. 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.

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.

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.[13]

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.[14] 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.[15] 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.

a) Fasting Saliva Insulin: This test is chiefly used to measure insulin levels when diagnosing diabetes and insulin resistance. Elevated insulin levels are most often caused by insulin resistance - a condition in which the body doesn't respond well to the effects of insulin. Insulin resistance may eventually lead to the development of type 2 diabetes and may increase the risk of heart disease, cancer, and Alzheimer's.

b) Non-Fasting Saliva Insulin: In blood, one uses the A1C test, which measures the average blood sugar level of an individual over a period of two to three months. 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.

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.[16] 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.[17] 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.[18]

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.[19] Stress, both physical and emotional, and mediated by cortisol, can result in an inadequate production of SIgA in response to a mucosal infection.[20] 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.[21]

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.

References

1. Fukaya M et al. Topical steroid addiction in atopic dermatitis. Drug, Healthcare and Patient Safety 2014; 6: 131-138.
2. Nieman, LK. Recent Updates on the Diagnosis and Management of Cushing's Syndrome. Endocrinol Metab 2018; 33:139-146.
3. Crona J, Beuschlein F, Pacak K and Skogseid B. Advances in adrenal tumors 2018. Endocrine-Related Cancer 2018; 25: R405-R420.
4. Gill J. Low Cortisol, High DHEA, and High Levels of Stimulated TNFα, and IL-6 in Women with PTSD. J Trauma Stress. 2008; 21: 530–539.
5. Kaur J. A Comprehensive Review on Metabolic Syndrome. Cardiology Research and Practice. Volume 2014; 1-21.
6. Storey KB and Storey JM. Tribute to P. L. Lutz: putting life on 'pause' – molecular regulation of hypometabolism. The Journal of Experimental Biology 2007; 210: 1700-1714.
7. Goodyer IM, et al. Adrenal steroid secretion and major depression in 8- to 16-year-olds. III. Influence of cortisol/DHEA ratio at presentation on subsequent rates of disappointing life events and persistent major depression. Psychol Med 1998; 28: 265–273.
8. Michael A, et al. Altered salivary dehydroepiandrosterone levels in major depression in adults. Biol Psychiatry 2002; 48: 989–995.
9. Kaur J. A Comprehensive Review on Metabolic Syndrome. Cardiology Research and Practice 2019; 2014: 1-21.
10. Johnson RJ, et al. Sugar, Uric Acid, and the Etiology of Diabetes and Obesity. Diabetes 2013: 62: 3307–3315.
11. Perlmutter D. Drop Acid: The Surprising New Science of Uric Acid. Little Brown Spark. 2022. ISBN 9780316315395.
12. Storey KB and Storey JM. Tribute to P. L. Lutz: putting life on 'pause' – molecular regulation of hypometabolism. The Journal of Experimental Biology 2007; 210: 1700-1714.
13. Hayashi T, et al. Patterns of Insulin Concentration During the OGTT Predict the Risk of Type 2 Diabetes in Japanese Americans. Diabetes 2013; 36; 1229-1235.
14. Fabre B, et al. Measurement of fasting salivary insulin and its relationship with serum insulin in children. Endocr Connect 2012; 1: 58–61.
15. Fekete Z, et al. Salivary and plasma insulin levels in man. Biochem Mol Biol Int. 1993; 30: 623–629.
16. Kan C, et al. A systematic review and meta-analysis of the association between depression and insulin resistance. Diabetes Care 2013; 36: 480–489.
17. Webb M, Davies M, Ashra N, et al: The association between depressive symptoms and insulin resistance, inflammation and adiposity in men and women. PLoS One 2017; 12: 1-15.
18. Watson KT et al. Incident Major Depressive Disorder Predicted by Three Measures of Insulin Resistance: A Dutch Cohort Study. Am J Psychiatry 2021; 178: 914–920.
19. Tsujita S and Morimoto K. Secretory IgA in Saliva can be a Useful Stress Marker. Environ Health Prev Med 1999; 4: 1-8 17.
20. Laurent, HK, et al. Secretory IgA Reactivity to Social Threat in Youth: Relations with HPA, ANS, and Behavior. Psychoneuroendocrinology 2015; 59: 81-90.
21. Stone AA, et al. Evidence that secretory IgA antibody is associated with daily mood. Journal of Personality and Social Psychology 1987; 52: 988–993.