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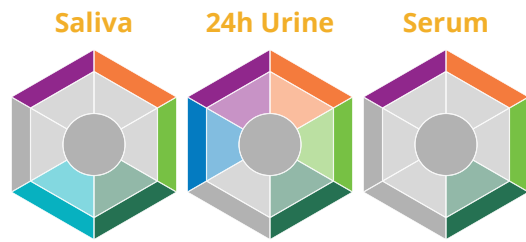
TESTING CATALOG

Second Edition

Updated April 2023

INTRODUCTION

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Finding the root cause of patient health problems can be like a puzzle.

Get more pieces to your hormone puzzle with DUTCH.

Only DUTCH gives you insight into:

- EASY PATIENT COLLECTION
- ESTROGEN METABOLITES
- ESTROGEN
- NUTRITIONAL ORGANIC ACIDS
- PROGESTERONE
- ANDROGEN METABOLITES
- TESTOSTERONE
- 8-OHDG (OXIDATIVE STRESS)
- MELATONIN
- FREE CORTISOL PATTERN
- CORTISOL AWAKENING RESPONSE (CAR)
- NEUROTRANSMITTER METABOLITES
- CORTISOL METABOLITES

WHAT IS DUTCH?

Precision Analytical created the DUTCH Test (dried urine test for comprehensive hormones) to help providers solve complex patient cases. DUTCH is a group of validated tests that provide a complete evaluation of sex and adrenal hormones, including metabolites. The simple and convenient at-home collection for patients, and clinical support on every DUTCH report, puts you in the driver's seat—allowing you to solve your patients' most complex hormone issues.

This advanced hormone testing was developed to improve on available hormone testing options. DUTCH offers the most extensive profile of sex and adrenal hormones along with their metabolites. Additionally, the daily (diurnal) pattern of free cortisol is included, along with melatonin (6-OHMS), 8-OHDG, and nine organic acids. This unique combination of clinical information is not available by any other method.

WHY USE DUTCH?

Easy Patient Collection – Patients collect just four or five dried-urine samples over a 24-hour period. Dried samples are stable for several weeks making them convenient to ship worldwide.

Analytical and Clinical Validation – Precision Analytical's testing methods go through a rigorous validation process to verify accuracy, recovery, and linearity. We pride ourselves in relentlessly pursuing the most accurate and precise techniques available for testing. See the data on the next page to support the analytical and clinical validation of this powerful new testing model.

Effective HRT Monitoring – DUTCH testing was designed to be optimally effective for most forms of hormone replacement therapy. Unique methods are used for improved monitoring of oral progesterone and vaginal hormones.

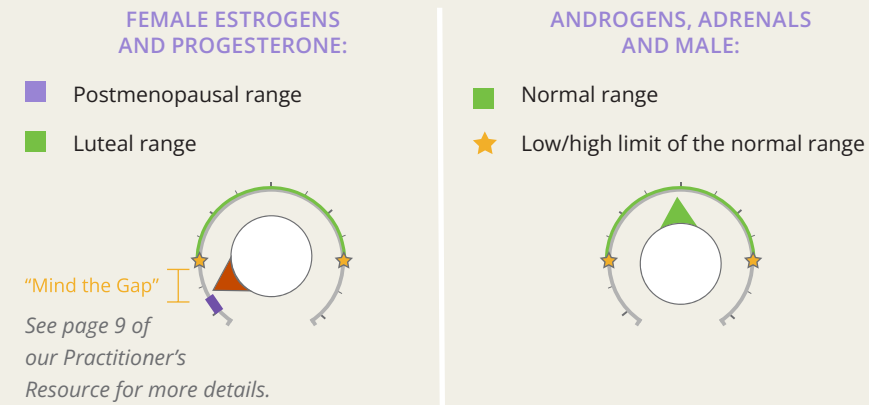
HOW DOES DUTCH COMPARE TO OTHER METHODS?

DUTCH vs. Saliva – While the free cortisol pattern in saliva has clinical value, there is a significant missing piece to surveying a patient's HPA axis function with saliva testing – measuring cortisol metabolites. To properly characterize a patient's cortisol status, free and metabolized cortisol should both be measured to avoid misleading results when cortisol clearance is abnormally high or low. Likewise with sex hormones, measuring estrogen and androgen metabolites gives a fuller picture for more precise clinical diagnosis of hormonal imbalances and HRT monitoring.

DUTCH vs. 24-Hour Urine – There are two primary drawbacks to 24-hour urine testing of hormones. First, the collection is cumbersome, and as many as 40% of those who collect, do so in error (Tanaka, 2002). Secondly, dysfunction in the diurnal pattern of cortisol cannot be ascertained from a 24-hour collection. Some providers add saliva for daily free cortisol. DUTCH eliminates the need for two tests.

DUTCH vs. Serum – While the most universally accepted testing method (due to the availability of FDA-cleared analyzers that are reliable and inexpensive), serum testing is lacking in some areas. Adrenal hormones cannot be effectively tested in serum because free cortisol cannot be tested throughout the day. There is also a lack of extensive metabolite testing (especially for cortisol and estrogens).

UNDERSTANDING DUTCH DIALS



TAKING THE TEST

Patients should always read test kit instructions prior to starting a DUTCH Test. The instructions will explain food restrictions, activity restrictions, water intake, and supplement and medication guidelines to optimize the DUTCH Test results.

To determine when to do the DUTCH Test, please see discussion on: when do I collect DUTCH Test samples? This discussion will focus on how to collect the samples.

PEER-REVIEWED PUBLISHED VALIDATION

Do values compare favorably to 24-hour collections?

The DUTCH correlation to 24-hour collections is excellent (see figure 1). Because the dried samples span about 12-14 hours of the day (6-8 hours overnight plus 2 hours per day collection), they represent the entire day's hormone production. A weighted average of the four samples is combined and measured for all hormones other than cortisol and cortisone. Values must be presented relative to creatinine (ng per mg of creatinine) to correct for hydration. This replaces the 24-hour value. The excellent correlation to 24-hour collections makes this model a very respectable alternative to 24-hour collections. With the addition of diurnal free cortisol, it becomes an improvement.

Do dried samples compromise the analysis?

Dried samples are accurate for hormone testing, and values correlate to liquid samples (see figure 2). Samples are stable once they are dried and easier to ship than liquid samples.

Learn more about DUTCH Trust

Check out page 11 in our Practitioner's Resource to see a list of all our peer-reviewed and published research that validates our testing method. We're always working on advancing the available research, for more information, visit: dutchtest.com/research

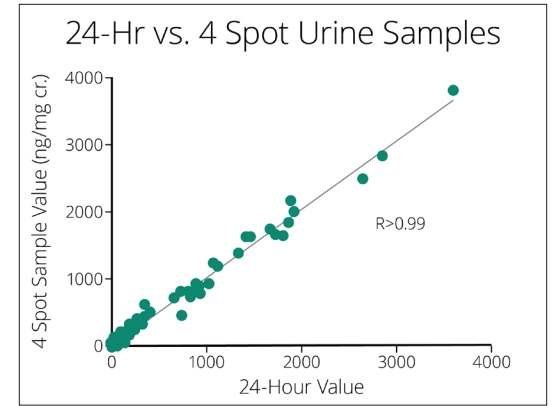


Figure 1

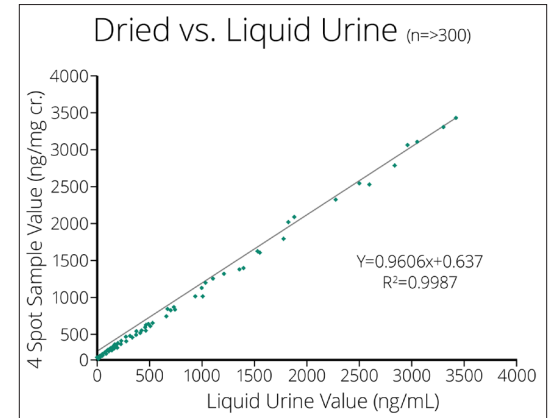
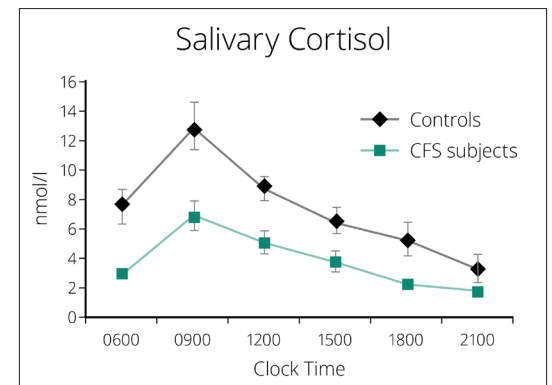
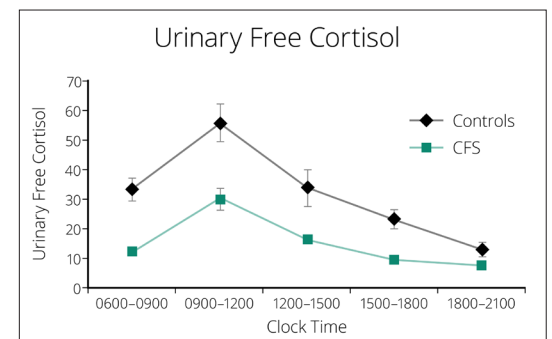


Figure 2



Figures 3 & 4 (above)

Jerjes (2005, 2006) studied the diurnal pattern of free cortisol in chronic fatigue patients (CFS) in both saliva and urine, finding very good agreement between the two lab tests.

TEST KITS



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COMPLETE

\$300	\$499
PROVIDER PRICE	MSRP

For female patients experiencing:

- Fatigue or low energy
- PMS
- Vaginal dryness
- Brain fog
- Low libido
- Weight gain
- Fertility concerns
- Hot flashes or night sweats

For male patients experiencing:

- Erectile dysfunction or low libido
- Decreased muscle mass
- Abdominal weight gain
- Fatigue or low energy
- Brain fog

The DUTCH Complete measures:

The report includes metabolites of estrogens (9, including E1, E2, E3, 2-OHE1, 4-OHE1, 16-OHE1, 2-MeOE1, 2-OHE2, 4-OHE2), androgens (8, including testosterone, DHT and DHEA-S), progesterone (2), cortisol (3), melatonin (6-OHMS), 8-OHdG, and OATs (9, including Vanilmandelate, Homovanillate, Kynurenate, Methylmalonate, Xanthurenate, Pyroglutamate, Quinolate, Indican, and b-Hydroxyisovalerate).

This test combines the DUTCH Sex Hormones, Adrenal, and OATs Panels.

WHAT IS THE DUTCH COMPLETE™?

Our flagship test, the DUTCH Complete is a comprehensive dried urine test that evaluates sex and adrenal hormone production and metabolism. The DUTCH Complete includes organic acid testing to provide insights into nutritional deficiencies, oxidative stress, gut dysbiosis, melatonin levels, and neuroinflammation. Providers can also gain insights into the overall diurnal pattern of free cortisol and the total distribution of cortisol metabolites. The DUTCH Complete evaluates sex hormones and their metabolites, cortisol (stress hormone), melatonin metabolites, and markers for oxidative stress, nutritional deficiencies, and more.

When is the DUTCH Complete recommended?

This test is recommended when you are looking for information about:

- Sex hormones (estrogens, progesterone, and testosterone) production and metabolic patterns
- Adrenal hormones (DHEA and cortisol) production and metabolic patterns
- Diurnal free cortisol and cortisone patterns
- Melatonin production through the night
- Micronutrient availability and oxidative stress (targeted organic acids panel)

Another test is better suited when:

- You want a more complete picture of HPA axis function. The cortisol awakening response (CAR) provides an additional evaluation of HPA axis function and can independently suggest HPA axis dysfunction. There are times when the diurnal cortisol curve will be within normal limits, but the CAR is not. The DUTCH Plus® provides both looks at adrenal function.
- You wish to evaluate a female's full menstrual cycle. The DUTCH Cycle Mapping Plus provides the detail of the DUTCH Plus while also measuring sex hormones at timepoints throughout the menstrual cycle.

PATIENT COLLECTION SCHEDULE

The DUTCH Complete uses four dried urine samples collected over the course of one day, from waking to bedtime. While adhering to their most common wake/sleep schedule, the patient should collect as close as possible to the below timeline.

Sample #1: Waking Sample - Urine

Collect within 10 minutes; do not lay awake in bed before collecting sample.

Sample #2: 2 Hours After Waking Sample - Urine

No alcohol or caffeine and no more than one cup of fluids between samples #1 & #2.

Sample #3: Dinnertime Sample - Urine

Approximately 5pm. Do not drink fluids for two hours before collecting. No alcohol, caffeine or large fluid intake after lunch.

Sample #4: Bedtime Sample - Urine

Approximately 10pm. Do not drink fluids for two hours before collecting.

Sample #5: Optional Extra Sample - Urine

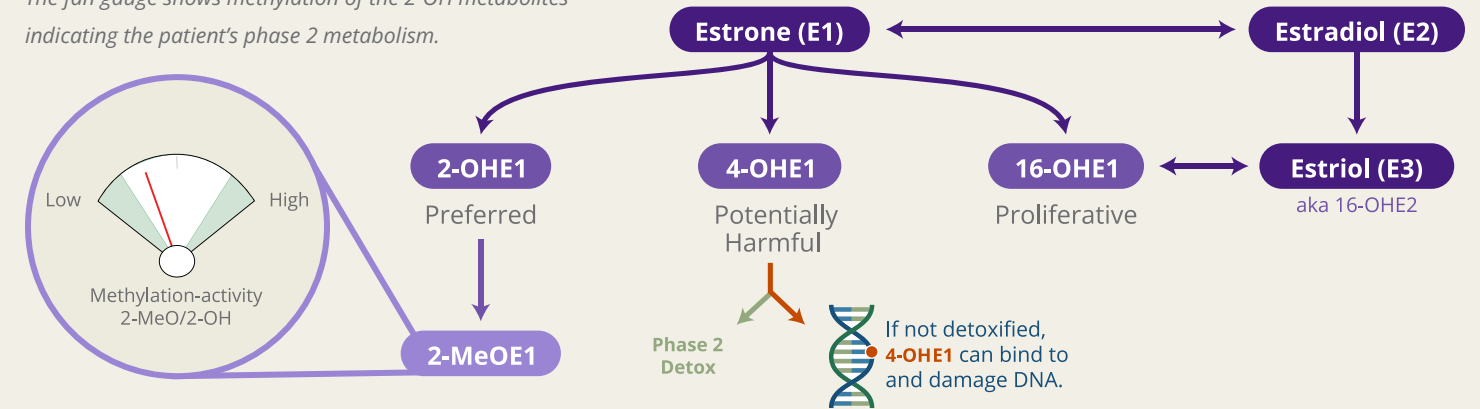
Collect at your first waking sleep disturbance with urination, if you wake and urinate a second time during the night, do not collect.

HIGHLIGHTS FROM THE REPORT

Estrogen Metabolism

It's important for providers to assess estrogen detoxification pathways. 2-OH is the most stable of the three pathways. 4-OH metabolites can become reactive quinones, causing DNA damage and an increased risk for certain cancers. 16-OHE1 is a proliferative estrogen and may contribute to heavy bleeding, breast tenderness, Estrogen Receptor (ER)+ tumor growth, and more.

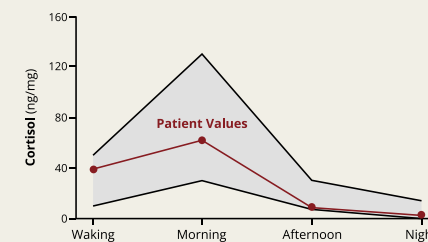
The fan gauge shows methylation of the 2-OH metabolites indicating the patient's phase 2 metabolism.



Cortisol Production and Metabolism

Daily free cortisol patterns can reveal answers to questions about HPA axis health. Cortisol should have a diurnal pattern that is highest in the morning and lowest at night before bedtime. High cortisol production can be associated with stress, anxiety, vigorous exercise, migraines, and acute inflammation. Low cortisol production can be associated with chronic stress, Traumatic Brain Injuries (TBIs), Post-traumatic Stress Disorder (PTSD), and other conditions.

DAILY FREE CORTISOL PATTERN



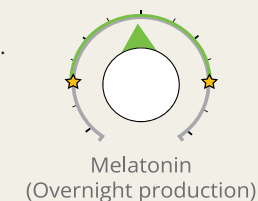
METABOLIZED CORTISOL



Comparing metabolized cortisol with total free cortisol can provide insights into a patient's cortisol metabolism rate. Abnormal cortisol clearance may be attributed to things like thyroid disorders, obesity, or chronic fatigue.

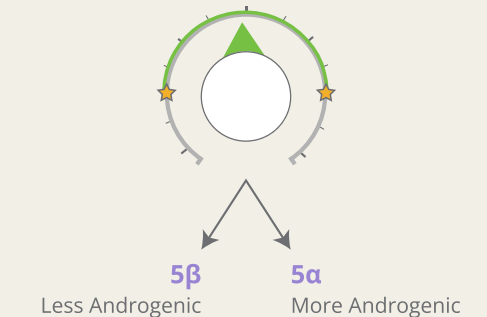
Melatonin Production

The pineal gland produces melatonin throughout the night. Melatonin is a powerful antioxidant, which helps improve mitochondrial function.



Androgen Metabolism

The enzyme 5a reductase makes more potent androgens than 5b reductase.




The fan gauge shows the relative ratio of the 5a to 5b metabolites.



Scan the QR Code


to see a full sample report for the DUTCH Complete

DUTCH COMPLETE PANELS



\$180
PROVIDER PRICE
\$399
MSRP

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SEX HORMONES




Scan the QR Code
to see a full sample report for
DUTCH Sex Hormones




\$180
PROVIDER PRICE
\$399
MSRP

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ADRENAL




Scan the QR Code
to see a full sample report for
DUTCH Adrenal



\$160*
PROVIDER PRICE
\$299*
MSRP

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ORGANIC ACIDS

*If added to a smaller panel (Adrenal or Sex Hormones), only costs an additional \$50.



Scan the QR Code
to see a full sample report for
DUTCH Organic Acids

DUTCH SEX HORMONES

The DUTCH Sex Hormones Panel is the ultimate test for HRT monitoring and great for baseline measurements, as well. It is a unique method for more accurate vaginal hormone and oral progesterone monitoring.

This panel measures:

Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9).

DUTCH ADRENAL

The DUTCH Adrenal Panel provides free cortisol patterns that parallel saliva with the addition of metabolite measurements for an improved marker for total cortisol production.

This panel measures:

Urinary Cortisol (4), Cortisone (4), and Cortisol Metabolites (3); Creatinine (4), and DHEA-S.

DUTCH ORGANIC ACID TEST (OATS)

The DUTCH OATs profile is a combination of biomarkers to compliment hormone metabolite measurements including a series of organic acids and other select tests. Organic acids related to nutrient deficiencies include biochemical intermediates that are proven to become elevated in the absence of sufficient nutrient status and other biomarkers may indicate oxidative stress, melatonin deficiency, and/or gut dysbiosis, all of which impact patient hormone stories.

Methylmalonate (MMA) is a great example as it is proven to be elevated in both serum and urine when patients show functional deficiency in vitamin B12. In this case, patients may have insufficient B12 due to diet or lifestyle or patients may have "normal" levels of B12 but carry genetic variants in the transport protein to get vitamin B12 into the cell. Whatever the cause, if a functional deficiency exists in the cell, MMA becomes elevated.

Neurotransmitter Metabolites

These organic acids are the primary metabolite of dopamine, norepinephrine and serotonin. Patients with an imbalance in these neurotransmitters may experience symptoms that are also common with an imbalance in hormones. Hormones (cortisol and estrogen are examples) included in DUTCH testing also directly alter some of these metabolites, so their inclusion provides an even more comprehensive picture of your patient's hormone health.

HOMOVANILLATE (HVA) - Primary Metabolite of Dopamine

If dopamine in circulation is low, HVA is usually low. People with low dopamine often report fatigue, low motivation, depression and addiction issues. These symptoms are similar to those with low hormones. Conversely, if there are low levels of SAM, magnesium, FAD and NAD, dopamine cannot be converted to HVA. In these cases, HVA may be low even though circulating dopamine levels may be normal or elevated.

VANILMANDELATE (VMA) - Primary Metabolite of Norepinephrine/Epinephrine

Cortisol, DHEA and norepinephrine/epinephrine are all released from the adrenal gland at different layers. A marker of the "other" major adrenal hormone gives providers more insight into adrenal and HPA axis function. If norepinephrine/epinephrine in circulation are low, VMA will usually be low. Epinephrine production (from norepinephrine) is actually a cortisol-dependent reaction and measuring VMA along with adrenal hormones enhances DUTCH adrenal testing even more.

QUINOLINATE - Neurotoxin Derived from Tryptophan

Quinolate is a neurotoxin derived from tryptophan. Elevated quinolate is seen in brain and nerve tissue damage, especially in disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, motor neuron diseases, multiple sclerosis, epilepsy, amyotrophic lateral sclerosis, and major depressive disorder. We can also see elevated quinolate due to low serotonin and need for vitamin B3 (niacin). The causes of elevated quinolate include neuroinflammation, general inflammation, infection, phthalate exposure, and/or oral tryptophan use.

Nutritional Organic Acids

These organic acids act as functional markers of nutrient deficiency. When the body has inadequate cellular levels of vitamin B12, vitamin B6 or glutathione, levels of their corresponding organic acid build up and spill into the urine. In some cases, these markers are more effective than measuring the nutrient directly.

B-HYDROXYISOVALERATE - Marker for Biotin

b-Hydroxyisovalerate is made when the body is deficient in biotin. This marker has an inverse relationship with biotin, therefore elevated levels represent deficiencies in biotin. Biotin is an important cofactor in mitochondrial function, metabolism of fatty acids, glucose, and protein, as well as ROS production. Factors that influence biotin levels include inadequate dietary intake, long-term and high-dose B5 supplementation, dysbiosis/gut health, antibiotic use, medications, and biotinidase deficiency.

INDICAN - Marker for Gut Health

Indican is a byproduct of tryptophan putrefaction by microbes in the gut. Production of indican occurs when tryptophan creates indoles in the colon. When there is concern of dysbiosis, there can also be concern for poor metabolism of sex hormones (including estrogen) along with chronic low-grade inflammation that can impact cortisol production and metabolism. This test is not diagnostic but generally warrants further testing to rule out gut dysbiosis.

KYNURENATE (KYNURENIC ACID OR KYNA) - Marker for Vitamin B6

KYNA is a product of the metabolism of tryptophan if there is a deficiency of Vitamin B6. Chronic stress, reactive oxygen species (ROS) and possibility LPS from gram negative gut bacteria/leaky gut causing inflammation can increase KYNA as well. KYNA is useful in the body - anti-inflammatory, neuroprotective, some anti-ulcerative properties and antagonizes hypermobility of the intestines.

XANTHURENATE (XANTHURENIC ACID) - Marker for Vitamin B6

If levels of estrogen or cortisol are high, it may exacerbate xanthurenate elevations and increase the need for B6. Xanthurenate complexes with insulin and decreases insulin sensitivity. Xanthurenate can also bind to iron and create a complex that increases DNA oxidative damage resulting in higher 8-OHdG levels. If both markers are elevated, there is likely an antioxidant insufficiency.

B-HYDROXYISOVALERATE

Results: High b-Hydroxyisovalerate = Low biotin

Symptoms of Biotin Deficiency: Hair loss, symptoms of other B-vitamin deficiencies.

Treatment Options: Increase supplemental biotin.

INDICAN

Results: Accumulated levels of indican in the urine may suggest gastrointestinal dysbiosis or malabsorption.

Symptoms of Excess Indican: A positive indican result may signal gut problems. Results can also be explained by the diet or medical history of a particular patient. Evaluating urinary indican results is nuanced. Low levels of indican do not necessarily correspond with a small degree of dysbiosis. The same is true of high indican levels.

Treatment Options: Evaluate gut health further (stool testing/food intolerances, SIBO, etc.)

KYNURENATE

Results: High Kynurenate = Low Vitamin B6

Symptoms of Vitamin B6 Deficiency: Fatigue, shortness of breath, irritability, anxiety and depression, and low energy.

Treatment Options: Food high in B6 include turkey breast, grass-fed beef, pinto beans, avocado, pistachios, chicken, sesame and sunflower seeds. Supplementation may be advised.

XANTHURENATE

Results: High Xanthurenate = Low Vitamin B6

Symptoms of Vitamin B6 Deficiency: Changes in mood, such as irritability, anxiety and depression, confusion, muscle pains, low energy, or fatigue.

Treatment Options: Foods high in B6 include turkey breast, grass-fed beef, pinto beans, avocado, pistachios, chicken, sesame and sunflower seeds. Supplementation may be advised.

METHYLMALONATE

Results: High MMA = Low Vitamin B12

Symptoms of Vitamin B12 Deficiency: Fatigue, brain fog, memory problems, muscle weakness, unsteady gait, numbness, tingling, depression, migraines/headaches and low blood pressure.

Treatment Options: Common foods high in B12 include beef liver, sardines, lamb, wild salmon, grass-fed beef, nutritional yeast and eggs. Supplementation may be advised.

PYROGLUTAMATE

Results: When levels of pyroglutamate are high or low, there may be insufficient glutathione.

Symptoms of Glutathione Deficiency: Glutathione is one of the most potent antioxidants in the human body. It is especially important in getting rid of toxins and can protect against cancer, aging, heart problems and brain diseases.

Treatment Options: High-quality lean protein, fresh fruits and vegetables, spices, increase alpha-lipoic acid, increase selenium, or add a multivitamin with glutathione-supporting vitamins.

8-OHDG

Results: Elevated levels of 8-OHdG may suggest oxidative stress or DNA damage is occurring.

Oxidative stress can be associated with: High Cortisol, rheumatoid arthritis, Huntington's Disease, Parkinson's Disease, Alzheimer's Disease, cystic fibrosis, breast cancer, and other various cancers.

Treatment Options: Address the cause. Reduce stress and avoid toxins. Encourage increased intake of fruits and vegetables. Support antioxidant status. (Vit. C, Melatonin, Vit. E) Assess and evaluate glutathione (N-Acetyl Cysteine).



Scan the QR Code

to view the resources referenced about 8-OHdG

METHYLMALONATE (METHYLMALONIC ACID OR MMA) - Marker for Vitamin B12

This marker is considered superior to measuring serum B12 levels directly. A 2012 publication by Miller showed that 20% of those tested had a genetic defect in the protein that transports B12 to cells. These patients may have a functional B12 deficiency, even if serum levels of B12 are normal.

PYROGLUTAMATE (PYROGLUTAMIC ACID) - Marker for Glutathione

In a DUTCH report, this marker can be low or high. Research supports that when pyroglutamate is high there is need for glutathione. When pyroglutamate is low, this suggests that glutathione levels are still not quite optimal and may need more support from precursors to help create glutathione. Glutathione is a potent antioxidant which helps cells stay healthy and clean by removing toxins.

8-OHDG (8-HYDROXY-2-DEOXYGUANOSINE) - Marker for Oxidative Stress

Oxidative stress refers to cellular damage or DNA damage. The body needs healthy and robust cells and DNA. Cell-signaling influences blood sugar, hormone production, detoxification, the creation of new cells, etc. Oxidation is like aging. If cells age too quickly, the body is unable to heal and recover well.

8-OHdG measures the effect of endogenous oxidative stress and DNA damage, it is also used to estimate the DNA damage in humans after exposure to cancer-causing agents such as tobacco smoke, asbestos fibers, heavy metals, and polycyclic aromatic hydrocarbons.

What Happens? When local antioxidant systems fail, oxidative damage permanently occurs to lipids of cellular membranes, proteins, and DNA. In nuclear and mitochondrial DNA, 8-OHdG is predominantly formed due to free radical-induced oxidative (pro-mutative) lesions.

Studies and Cancer: 60 women with malignant tumors in a breast cancer study¹ and 82 men in a prostate cancer study showed 8-OHdG levels significantly higher than controls². Levels did not decrease with prostatectomy but did decrease with androgen suppression hormone therapy.

Additional Information: Orange juice (but not pomegranate, apple, grapefruit or cranberry) reduced oxidative stress measured by 8-OHdG³. Taking micronutrient and mineral supplements with antioxidants improved 8-OHdG in people who otherwise did not eat vegetables⁴. When renoprotective effects of berberine were measured by 8-OHdG in patients with both hypertension and type 2 diabetes, berberine reduced 8-OHdG among other measures⁵. 8-OHdG increased in the kidney and liver with a copper releasing implant, and researchers supposed that this might also happen with copper IUDs in humans⁶. Smokers who have high 8-OHdG can lower it by taking moderate amounts of fish oil with combined EPA/DHA⁷. Urinary BPA increases associated with urinary 8-OHdG increase⁸. Urinary methylparaben (MP) and ethylparaben (EP) increase along with 8-OHdG in pregnant women and their infants⁹.