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# What is DUTCH Cycle Mapping<sup>™</sup>?

When is DUTCH Cycle Mapping recommended? Why is Cycle Mapping Important? Reading the Report Patient Collection Schedule

### What is DUTCH Cycle Mapping + Complete™?

When is Cycle Mapping + Complete recommended? Patient Collection Schedule

# What is DUTCH Cycle Mapping + Plus<sup>™</sup>?

When is Cycle Mapping + Plus recommended? Patient Collection Schedule

# **PRICING GRID**

The DUTCH Complete™ Test Kit The DUTCH Sex Hormones Panel The DUTCH Adrenal Panel The DUTCH Organic Acids (OATs) Panel The DUTCH CAR™ Test Kit The DUTCH Plus® Test Kit DUTCH Cycle Mapping™ Test Kit DUTCH Cycle Mapping + Sex Hormones Panel DUTCH Cycle Mapping + Adrenal Panel DUTCH Cycle Mapping + Complete™ Test Kit DUTCH Cycle Mapping + Plus™ Test Kit

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### Please Note:

The information in this handout is provided for informational and educational purposes only and is not medical or treatment advice. Any information and statements regarding dietary or herbal supplements have not been evaluated by the Food and Drug Administration and are not intended to diagnose, treat, cure, or prevent any disease. The use of any information provided in this handout is solely at your own risk.

# **INTRODUCTION**



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:



# 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.

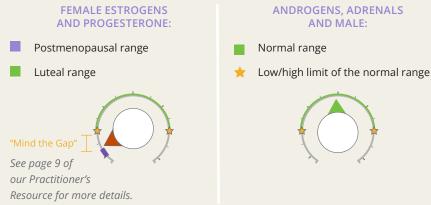
# HOW DOES DUTCH COMPARE TO OTHER METHODS?

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

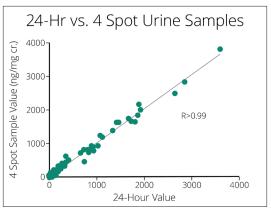


Figure 1

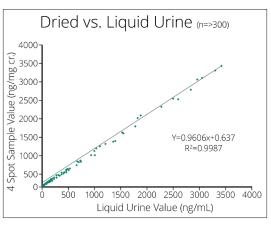
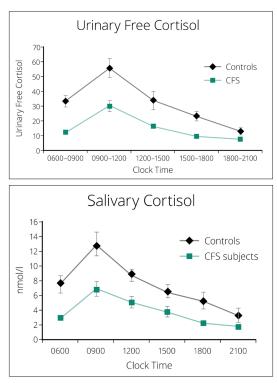


Figure 2



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.



### 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, Quinolinate, 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

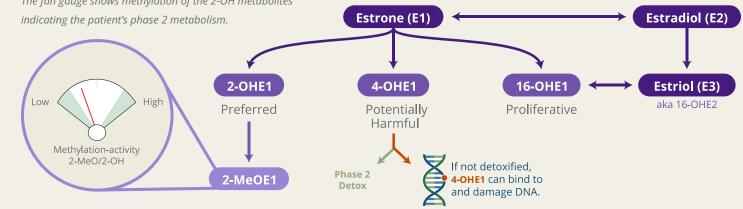
Collect at your first waking sleep disturbance with urination, if you wake and urinate a second time during the night, do not collect.

# **HIGHLIGHTS FROM THE REPORT**

## Estrogen Metabolism

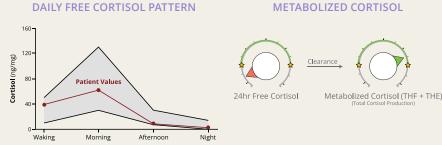
It's important for providers to assess estrogen detoxification pathways. 2-OH is the most stable of the three pathways. 4-OH metabolites can become reactive quinones, causing DNA damage and an increased risk for certain cancers. 16-OHE1 is a proliferative estrogen and may contribute to heavy bleeding,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



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

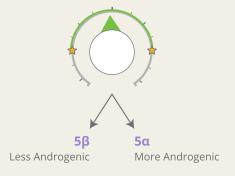
The pineal gland produces melatonin throughout the night. Melatonin is a powerful antioxidant, which helps improve mitochondrial function.



Melatonin (Overnight production)

# 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**

Health4life

ONCIERGE MEDICINE

\$399





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





MSRP



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



\*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

Quinolinate is a neurotoxin derived from tryptophan. Elevated quinolinate 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 quinolinate due to low serotonin and need for vitamin B3 (niacin). The causes of elevated quinolinate 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 OR 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 guickly, 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 study<sup>1</sup> and 82 men in a prostate cancer study showed 8-OHdG levels significantly higher than controls<sup>2</sup>. 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-OHdG<sup>3</sup>. Taking micronutrient and mineral supplements with antioxidants improved 8-OHdG in people who otherwise did not eat vegetables<sup>4</sup>. 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 measures<sup>5</sup>. 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 humans<sup>6</sup>. Smokers who have high 8-OHdG can lower it by taking moderate amounts of fish oil with combined EPA/DHA<sup>7</sup>. Urinary BPA increases associated with urinary 8-OHdG increase<sup>8</sup>. Urinary methylparaben (MP) and ethylparaben (EP) increase along with 8-OHdG in pregnant women and their infants9.

# WHAT IS THE DUTCH CAR™?

The DUTCH CAR is a saliva test that provides insight into adrenal function with details about a patient's cortisol awakening response (CAR). The CAR acts as a mini-stress test by showing the rise and fall of cortisol immediately after waking. Cortisol's rise in response to the stress of waking provides insights into hypothalamic-pituitaryadrenal (HPA) axis function and its ability to respond appropriately to daily stressors. Along with the CAR, this test also shows the patient's daily free cortisol and cortisone patterns. Cortisol should have a diurnal pattern that is highest in the morning and lowest at night before bedtime.

# When is the DUTCH CAR recommended?

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

- HPA Axis function
- Cortisol awakening response

### Another test is better suited when:

- You want a more complete picture of HPA axis function. The CAR can independently suggest HPA axis dysfunction, but comparing metabolized cortisol with total free cortisol can provide insights into a patient's cortisol metabolism rate which attributes to things like thyroid disorders, obesity, or chronic fatigue. The DUTCH Plus® provides both looks at adrenal function.
- HPA Axis dysfunction is not suspected. The DUTCH Complete<sup>™</sup> provides insights into the overall diurnal pattern of free cortisol and the total distribution of cortisol metabolites. Providers also gain further insight into sex hormones and their metabolites, melatonin metabolites, and markers for oxidative stress, nutritional deficiencies, and more.

# PATIENT COLLECTION SCHEDULE

Both men and women may collect any day, but it is recommended to collect on a typical day, while adhering to their most common wake/sleep schedule.

### Sample #1: Waking Sample - Saliva

Collect saliva immediately upon waking, complete within 5 minutes, and set a timer for 30 minutes for Sample #2.

### Sample #2: +30 Minute Sample - Saliva

Collect saliva 30 minutes after waking, complete within 5 minutes, then set the timer for 30 minutes for Sample #3.

### Sample #3: +60 Minute Sample - Saliva

Collect saliva 60 minutes after waking, complete within 5 minutes. Avoid morning food, drink, and brushing your teeth until after this collection.

### Sample #4: 4–5pm Sample - Saliva

Rinse your mouth with water 10 minutes prior to collecting. Collect between 4-5pm (before your evening meal).

### Sample #5: Bedtime Sample - Saliva

Rinse your mouth with water 10 minutes prior to collecting. Collect at bedtime, but no later than midnight.

### Sample #6: Optional Extra Sample - Saliva

If you struggle with staying asleep during the night, keep the collection tube close to your bed and collect at the time of your sleep disturbance.

# **TEST KITS** (CONT.)



# For all patients experiencing:

- Fatigue, especially on waking
- Insomnia
- Chronic fatigue
- Depression or anxiety, especially on waking
- High-stress lifestyle
- Loss of resiliency

A low or blunted CAR - can be the result of an underactive HPA axis, excessive psychological burnout, seasonal affective disorder (SAD), sleep apnea, PTSD, chronic fatigue, and/or chronic pain. A decreased CAR has also been associated with systemic hypertension, functional GI diseases, postpartum depression, and autoimmune diseases.

**An elevated CAR –** can be the result of an overactive HPA axis, ongoing job-related stress (anticipatory stress for the day), glycemic dysregulation, pain (i.e., waking with painful joints, migraine), and general depression (not SAD). A recent study showed that neither the waking nor post-waking cortisol results correlated to major depressive disorder, but the CAR calculation did. This measurement of the response to waking has independent clinical value showing dysfunction that may be hidden by other testing options.

# The DUTCH CAR measures:

Salivary cortisol awakening response (CAR), Cortisol (5), Cortisone (5), and optional insomnia cortisol measurement.



# Scan the QR Code

to see a full sample report for the DUTCH CAR



# For all patients experiencing:

- Fatigue, especially on waking
- Insomnia
- Chronic fatigue
- Depression or anxiety, especially on waking
- High-stress lifestyle
- Loss of resiliency

# 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 Plus measures:

Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9); Cortisol Metabolites (3), Creatinine (4), DHEA-S, OATs (9), Melatonin (6-OHMS), and 8-OHdG. Plus salivary cortisol awakening response (CAR), Cortisol (5), Cortisone (5), and optional insomnia cortisol measurement.

This test combines the DUTCH Complete and DUTCH CAR.

# WHAT IS THE DUTCH PLUS®?

The DUTCH Plus is a comprehensive dried urine and saliva test that maximizes the available information from sex and adrenal hormone production and metabolism. With easy, at-home sample collection over the course of one day, providers can gain insights into the overall diurnal pattern of free cortisol and cortisone, along with the total distribution of cortisol metabolites. This test offers further insight by including organic acid testing, which evaluates potential nutritional deficiencies, oxidative stress, gut dysbiosis, melatonin levels, and neuroinflammation.

With the DUTCH Plus, providers also gain additional insight into adrenal function with details about a patient's cortisol awakening response (CAR) by showing the natural rise and fall of cortisol within the first hour of waking.

# When is the DUTCH Plus recommended?

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

- Sex hormone production and metabolic patterns
- · Adrenal hormones (DHEA and cortisol) production and metabolic patterns
- Diurnal free cortisol and cortisone patterns
- Melatonin production during sleep
- · Micronutrient availability and oxidative stress

# You may be considering the DUTCH Complete or the DUTCH Plus:

Both panels provide the above information but what's the difference? You should use the DUTCH Plus 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.

# Another test is better suited when:

- 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.
- HPA axis dysfunction is not suspected. The DUTCH Complete<sup>™</sup> provides insights into the overall diurnal pattern of free cortisol and the total distribution of cortisol metabolites.

# What does the cortisol awakening response add?

A healthy individual's free cortisol production should rise in a predictable pattern in response to physiologic stress. Cortisol's rise in response to the stress of waking provides insight into hypothalamic-pituitary-adrenal (HPA) axis function and its ability to respond appropriately to daily stressors. The cortisol awakening response (CAR) is a mini-ACTH stimulation test.

During an ACTH stimulation test, the patient is given ACTH and the adrenal cortisol response is recorded. This test and the CAR both test adrenal reserve; in other words, how well an individual adapts to a stressor. HPA Axis dysfunction (abnormal cortisol responses) may be represented as changes in the CAR. An abnormal CAR may arise from chronic stress and is also documented in conditions like depression, chronic pain, insomnia, hypertension, metabolic syndrome, fatigue, and in autoimmune diseases.

# **HIGHLIGHTS FROM THE REPORT**

# Cortisol Production and Metabolism

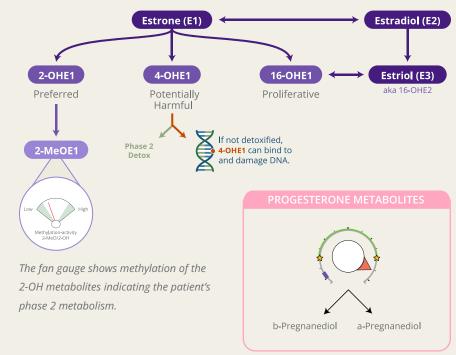
Daily free cortisol patterns can reveal answers to questions about HPA axis health. Cortisol should have a diurnal pattern that is highest in the morning and lowest at night before bedtime. High cortisol production can be associated with stress, anxiety, vigorous exercise, migraines, and acute inflammation.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



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.

# 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.



# PATIENT COLLECTION SCHEDULE

The DUTCH Plus uses 4 urine and 5-6 salivary samples collected throughout the day (and night in some cases).

Caffeine, alcohol, and strenuous exercise may affect results.

## Sample #1: Waking Samples Urine + Saliva

Collect saliva immediately upon waking, complete within 5 minutes, and set a timer for 30 minutes for Sample #2. Collect the first urine sample, do not lay awake in bed before collecting samples.

# Sample #2: +30 Minute Sample

Collect saliva 30 minutes after waking, complete within 5 minutes, then set the timer for 30 minutes for Sample #3.

### Sample #3: +60 Minute Sample Saliva Only

Collect saliva 60 minutes after waking, complete within 5 minutes. Avoid morning food, drink, and brushing your teeth until after this collection.

### Sample #4: 2–3 Hrs After Waking Sample Urine Only

Collect urine only, two to three hours after waking.

# Sample #5: 4–5pm Samples

# Urine + Saliva

Rinse your mouth with water 10 minutes prior to collecting saliva. Collect both urine and saliva between 4-5pm (before your evening meal).

# Sample #6: Bedtime Samples Urine + Saliva

Rinse your mouth with water 10 minutes prior to collecting saliva. Collect both urine and saliva at bedtime, but no later than midnight.

# Sample #7: Optional Extra Sample Saliva Only

If you struggle with staying asleep during the night, keep the collection tube close to your bed and collect at the time of your sleep disturbance.



# Scan the QR Code

to see a full sample report for the **DUTCH Plus** 



Health4life	\$550
CONCIERGE MEDICINE	MSRP

# For female patients experiencing:

- Irregular cycles
- Polycystic ovary syndrome (PCOS)
- Luteal phase defect
- Trying to conceive (TTC)
- Month-long hormonal symptoms
- Partial hysterectomy
- Ablations
- Mirena IUD (no menstrual bleeding due to IUD but still have hormonal symptoms)
- Mood swings that follow a cycle
- PMS
- Mid-cycle spotting
- Migraines

# DUTCH Cycle Mapping measures:

Nine (9) targeted urinary estrogen and progesterone measurements taken throughout the cycle to characterize the follicular, ovulatory, and luteal phases.

# WHAT IS DUTCH CYCLE MAPPING<sup>™</sup>?

The DUTCH Complete<sup>™</sup> and DUTCH Plus<sup>®</sup> are one-day tests. DUTCH Cycle Mapping is designed to detail estradiol, estrone, and alpha- and beta pregnanediol (urinary progesterone markers) over the course of an entire menstrual cycle. DUTCH Cycle Mapping charts nine representative data points across the follicular, ovulatory, and luteal menstrual cycle phases. The nine chosen samples are determined based on variables like current cycle length, date the next menstrual cycle begins, providerdocumented preferences noted on the requisition form, and other factors.

Please Note: Patients using cycle-suppressive therapies such as Lupron or oral contraceptives should be advised against doing DUTCH Cycle Mapping because these drugs decrease cyclic endogenous hormone production, which is what the DUTCH Cycle Mapping test measures.

# When is DUTCH Cycle Mapping recommended?

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

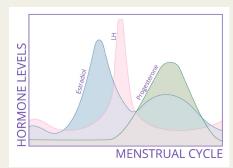
- · Females with symptomatic hormone shifts during the cycle
- Females, as part of a fertility workup
- Females who have menstrual cycle symptoms and who still have one or both ovaries and no uterus (partial hysterectomy)
- Females who have had an endometrial ablation and don't cycle
- Perimenopausal females before beginning hormone replacement therapy

### Another test is better suited when the patient:

- Is a postmenopausal female
- Is taking hormonal birth control
- Has predictable cycles

# Why is Cycle Mapping Important?

For many patients, a one-day test is sufficient to get a picture of their hormones. However, you may wish to see a complete map of their cycle to identify how estrogen and progesterone levels fluctuate. Cycle Mapping is necessary to provide this map.

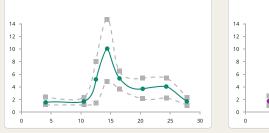


Typical estrogen patterns show relatively low levels early in the cycle, a surge around ovulation, and modest levels in the latter third of the cycle (the luteal phase). Progesterone levels stay relatively low until after ovulation when they typically increase more than tenfold before dropping back down at the end of the cycle.

Determining how a patient's hormone fluctuations compare to this optimal pattern can shed light on cycle-related health concerns. DUTCH Cycle Mapping helps you develop an accurate picture of your patient's hormone patterns throughout their menstrual cycle so you can craft an effective treatment program specific to their individual needs.

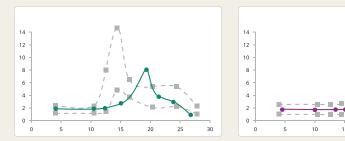
# **READING THE REPORT**

On each report, you'll find four stacked graphs with the reference ranges and the patient's results mapped out. Two graphs represent estrogen (E) production in green, and two graphs represent progesterone (Pg) production in purple. The horizontal axis shows the cycle days and the vertical axis shows the concentration of hormone metabolites being measured (ng/mg). The patient submits many samples over one cycle, and we select the 9 most relevant measurements. Some measurements from longer cycles are from two-day averages to ensure transitory E and Pg peaks are not missed. Below are four different cycle patterns that may help with interpretation: Normal Cycle



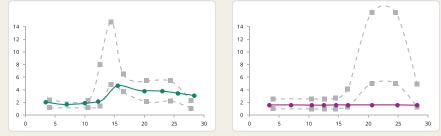
This is a relatively normal cycle. There is an E peak around ovulation and a Pg surge to follow with enough Pg to balance estrogen.

### Luteal Phase Defect



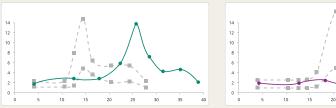
A luteal phase defect may be suspected. The luteal phase is shorter than normal. Ovulation is later than typical, followed by a Pg peak that is less than ideal

### No Ovulation

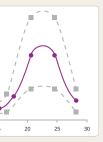


There is likely no ovulation in this case. The E pattern shows no mid-cycle rise. With no ovulation, Pg levels remain flat with no surge.

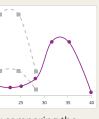
### Long Cycle



A long cycle, over 40 days. E and Pg patterns can still be assessed by comparing the patient values with expected ranges, but peaks may not align horizontally.



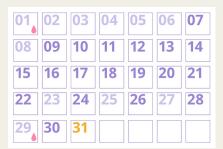




# PATIENT COLLECTION **SCHEDULE**

The schedule on which a patient collects depends on the average length of their cycle. Additional instructions are included in the test kit to help them adjust the schedule according to their cycle.

Here's a look as the collection schedule for a 28-day cycle:



First day of a menstural cycle (first full-flow day)

The patient will begin collecting on the seventh day of the cycle, collecting every **dark purple** day, preferably in the morning. On the day marked with the golden number, about day three of the next period, they will collect the final four samples throughout the day to map their daily hormone fluctuation.

### Normal Cycle or Short Cycle

If the patient's typical cycle is 34 days or shorter, they should collect according to the Normal/Short Cycle collection schedule included in the kit instructions.

### Long Cycle

If the patient's typical cycle is 34 days or longer, they should collect according to the Long Cycle collection schedule included in the kit instructions.

### No Cycle

If the patient has functional ovaries without regular menstrual bleeding (partial hysterectomy, ablation etc.) they can begin collecting on any day and should follow the No Cycle collection schedule included in the kit instructions.



# Scan the QR Code

to see a full sample report for DUTCH Cycle Mapping



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CONCIERGE MEDICINE	MSRP

# For female patients experiencing:

- Irregular cycles
- Luteal phase defect - Brain fog
- Low libido Ablations
- PMS - Weight gain
- Mid-cycle spotting - Fertility concerns

Vaginal dryness

- Migraines
- Partial hysterectomy
- Trying to conceive (TTC)
- Mood swings that follow a cycle
- Month-long hormonal symptoms
- Mirena IUD (no menstrual bleeding due to IUD but still have hormonal symptoms)
- Polycystic ovary syndrome (PCOS)
- Fatigue or low energy
- Hot flashes or night sweats

# DUTCH Cycle Mapping + Complete measures:

Nine (9) targeted urinary estrogen and progesterone measurements taken throughout the cycle to characterize the follicular, ovulatory, and luteal phases. Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9); Cortisol (4), Cortisone (4), and Cortisol Metabolites (3); Creatinine (4), DHEA-S, OATs (9), Melatonin (6-OHMS), and 8-OHdG.

# This test combines the DUTCH Complete and **DUTCH Cycle Mapping.**



# Scan the QR Code

to see a full sample report for the DUTCH Cycle Mapping + Complete

# WHAT IS DUTCH CYCLE MAPPING + COMPLETE™?

DUTCH Cycle Mapping provides information about ovarian reserve, follicle development, ovulation, and luteal sufficiency. In many circumstances, this may be enough information to treat the patient. Adding a DUTCH Complete provides a more complete patient picture by assessing estrogen metabolism, methylation activity, androgens (testosterone and DHEA), androgen metabolites, adrenal cortisol, cortisol metabolites, organic acids, etc., at the same time.

The estrogen, alpha-, and beta-pregnanediol luteal phase samples with the highest beta-pregnanediol is the sample used to report estrogen and progesterone metabolism on the accompanying DUTCH Complete.

# When is Cycle Mapping + Complete recommended?

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

- Estrogen dominance
- Androgen dominance (including PCOS presentations)
- Preconception wellness

### Another test is better suited when the patient:

- Is a postmenopausal female
- Is taking hormonal birth control
- Has predictable cycles

# PATIENT COLLECTION SCHEDULE

The schedule on which a patient collects depends on the average length of their cycle. Additional instructions are included in the test kit to help them adjust the schedule according to their cycle. Here's a look as the collection schedule for a 28-day cycle:

01	02	03	04	05	06	07
08	09	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31	32			

The patient will begin collecting on the seventh day of the cycle, collecting every dark purple day, preferably in the morning. On the day marked with the blue number, day four of the next period, they will collect the final four samples throughout the day to generate their DUTCH Complete report.

First day of a menstural cycle

### FINAL FOUR COLLECTIONS (DUTCH COMPLETE)

**#1: Waking -** Collect within 10 minutes; do not lay awake in bed before collecting.

#2: Two Hours After Waking - No alcohol or caffeine and no more than one cup of fluids between #1 and #2.

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

#4: Bedtime - Approximately 10pm. Do not drink fluids for two hours before.

#5: Optional Extra Sample - Collect at your first waking sleep disturbance with urination, if you wake and urinate a second time during the night, do not collect.

# WHAT IS DUTCH CYCLE MAPPING + PLUS™?

DUTCH Cycle Mapping is the most comprehensive test offered and provides information about ovarian reserve, follicle development, ovulation, and luteal sufficiency. In many circumstances, this may be enough information to treat the patient. Adding a DUTCH Plus maximizes the available information from sex and adrenal hormone production and metabolism and provides an even more complete patient picture by providing additional insight into adrenal function with details about a patient's cortisol awakening response (CAR).

The estrogen, alpha-, and beta-pregnanediol luteal phase samples with the highest beta-pregnanediol is the sample used to report estrogen and progesterone metabolism on the accompanying DUTCH Plus.

# When is Cycle Mapping + Plus recommended?

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

- Estrogen dominance
- Androgen dominance (including PCOS presentations)
- Preconception wellness
- Cortisol awakening response (CAR)

### Another test is better suited when the patient:

- · Is a postmenopausal female
- Is taking hormonal birth control
- Has predictable cycles

# PATIENT COLLECTION SCHEDULE

The schedule on which a patient collects depends on the average length of their cycle. Additional instructions are included in the test kit to help them adjust the schedule according to their cycle. The final 4 urine and 5 - 6 saliva samples are to be collected in one day, on the fourth day of the second cycle OR day 33 if you are using the No Cycle Schedule. See left, for an example of a 28-day cycle collection schedule.

### FINAL SIX COLLECTIONS (DUTCH PLUS)

#1: Waking, Urine + Saliva - Collect saliva immediately upon waking, complete within 5 minutes, and set a timer for 30 minutes for Sample #2. Collect the first urine sample, do not lay awake in bed before collecting samples.

#2: +30 Minutes, Saliva - Collect saliva 30 minutes after waking, complete within 5 minutes, then set the timer for 30 minutes for Sample #3.

#3: +60 Minutes, Saliva - Collect saliva 60 minutes after waking, within 5 minutes. Avoid morning food, drink, and brushing your teeth until after this collection.

#4: 2-3 Hrs After Waking, Urine - Collect urine only, two - three hours after waking.

**#5: 4–5pm, Urine + Saliva -** Rinse your mouth with water 10 minutes prior to collecting saliva. Collect both urine and saliva between 4-5pm (before your evening meal).

#6: Bedtime Samples, Urine + Saliva - Rinse your mouth with water 10 minutes prior to collecting saliva. Collect both urine and saliva at bedtime, but no later than midnight.

**#7: Optional Extra Sample, Saliva -** If you struggle with staying asleep during the night, keep the collection tube close to your bed and collect at the time of sleep disturbance.

# TEST KITS





# For female patients experiencing:

- Irregular cycles
- Luteal phase defect
- Ablations
- PMS
- Mid-cycle spotting
- Migraines
- Vaginal dryness
- Brain fog
- Partial hysterectomy
- Trying to conceive (TTC)
- Mood swings that follow a cycle
- Month-long hormonal symptoms
- Mirena IUD (no menstrual bleeding due to IUD but still have hormonal symptoms)
- Polycystic ovary syndrome (PCOS)
- Depression or anxiety, especially on waking
- Fatigue or low energy, especially on waking
- Hot flashes or night sweats

# DUTCH Cycle Mapping + Plus measures:

Nine (9) targeted urinary estrogen and progesterone measurements taken throughout the cycle to characterize the follicular, ovulatory, and luteal phases. Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9); Cortisol (4), Cortisone (4), and Cortisol Metabolites (3); Creatinine (4), DHEA-S, OATs (9), Melatonin (6-OHMS), and 8-OHdG. Plus salivary cortisol awakening response, Cortisol (5), Cortisone (5), and optional insomnia cortisol measurement.

This test combines the DUTCH Plus and DUTCH Cycle Mapping.



# Scan the QR Code

to see a full sample report for the DUTCH Cycle Mapping + Plus

- Low libido
- Weight gain
- Fertility concerns
- Insomnia
- Chronic fatigue
- High-stress lifestyle
- Loss of resiliency

# **PRICING GRID**

DUTCH TEST	DESCRIPTION	MSRP
<b>dutch</b> COMPLETE	The DUTCH Complete <sup>™</sup> Test Kit Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9); Cortisol (4), Cortisone (4), and Cortisol Metabolites (3); Creatinine (4), DHEA-S, Vanilmandelate, Homovanillate, Kynurenate, Methylmalonate, Xanthurenate, Pyroglutamate, Quinolinate, Indican, b-Hydroxyisovalerate, 8-OHdG, and Melatonin (6-OHMS). This test combines the DUTCH Sex Hormones, Adrenal, and OATs Panels.	\$499
<b>dutch</b> SEX HORMONES	The DUTCH Sex Hormones Panel Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9).	\$399
<b>dutch</b> ADRENAL	The DUTCH Adrenal Panel Urinary Cortisol (4), Cortisone (4), and Cortisol Metabolites (3); Creatinine (4), and DHEA-S.	\$399
<b>dutch</b> organic acids	The DUTCH Organic Acids (OATs) Panel Urinary Vanilmandelate, Homovanillate, Kynurenate, Methylmalonate, Xanthurenate, Pyroglutamate, Quinolinate, Indican, b-Hydroxyisovalerate, 8-OHdG, and Melatonin (6-OHMS). If added to a smaller panel (Sex Hormones/Adrenal), only costs an additional \$50.	\$299
dutch	The DUTCH CAR <sup>™</sup> Test Kit Salivary cortisol awakening response, Cortisol (5), Cortisone (5), and optional insomnia cortisol measurement.	\$299
<b>dutch</b> PLUS	The DUTCH Plus® Test Kit Urinary Progesterone (2), Androgen (8), and Estrogen Metabolites (9); Cortisol Metabolites (3), Creatinine (4), DHEA-S, Vanilmandelate, Homovanillate, Kynurenate, Methylmalonate, Xanthurenate, Pyroglutamate, Quinolinate, Indican, b-Hydroxyisovalerate, 8-OHdG, and Melatonin (6-OHMS). Plus salivary cortisol awakening response, Cortisol (5), Cortisone (5), and optional insomnia cortisol measurement. This test combines the DUTCH Complete and DUTCH CAR.	\$650





PTION	MSRP
sterone measurements taken throughout ory, and luteal phases.	\$550
ones Panel sterone measurements taken throughout ory, and luteal phases; Progesterone (2), and the DUTCH Sex Hormones panel.	\$625
nnel sterone measurements taken throughout ory, and luteal phases; Cortisol (4), eatinine (4), and DHEA-S. <b>and the DUTCH Adrenal panel.</b>	\$625
M Test Kit sterone measurements taken throughout ory, and luteal phases. Urinary Metabolites (9); Cortisol (4), Cortisone (4), HEA-S, Vanilmandelate, Homovanillate, Pyroglutamate, Quinolinate, Indican, n (6-OHMS). nd DUTCH Cycle Mapping.	\$650
: Kit sterone measurements taken throughout ory, and luteal phases. Urinary Metabolites (9); Cortisol (4), Cortisone (4), HEA-S, Vanilmandelate, Homovanillate, Pyroglutamate, Quinolinate, Indican, n (6-OHMS). Plus salivary cortisol 5), and optional insomnia cortisol <b>JTCH Cycle Mapping.</b>	\$700

# Health4life



CONCIERGE MEDICINE

# Thank You!

We know every sample received by our lab comes from a real person, with a real story.

We are incredibly thankful for the opportunity to serve healthcare practitioners and their patients around the world, and we love hearing stories about how the DUTCH Test profoundly changes lives. This is why we do what we do!

# **GET IN TOUCH**









# **TELL US YOUR STORY**



Scan the QR code or visit dutchtest.com/dutch-testimonial/ to tell us about how DUTCH has helped you get to the root cause and profoundly change lives, one life at a time.

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