# Endocrinology



#### **Comprehensive Assessment of Neuroendocrine Status**

- Salivary Sex Steroid Hormones and Adrenal/HPA Axis Function
- Hormone and Urinary Metabolites Assessment Profile (HuMap<sup>TM</sup>)
- Neurotransmitter and Metabolites Profiles
- Thyroid Profile



SCIENCE+INSIGHT

## Endocrinology

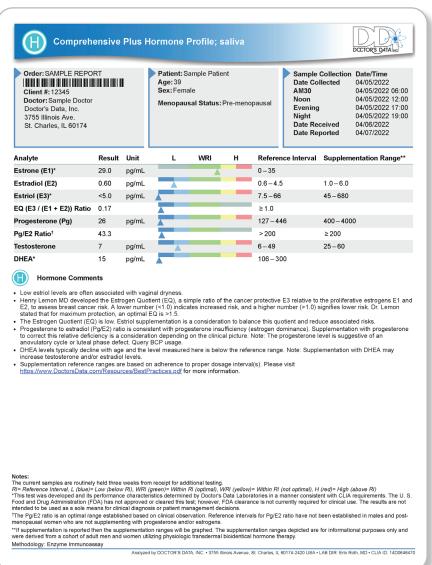
Doctor's Data offers analysis of hormones, neurotransmitters, and metabolites that may impact symptoms, metabolic function, mood or behavior.

## Salivary Sex Steroid Hormones and HPA Axis/Adrenal Function



#### Saliva Testing

Saliva contains only the active, bioavailable portion of the body's hormones, which are secreted in a pulsatile manner. Doctor's Data salivary testing accounts for the normal pulsatile secretion of hormones by averaging 4 collections to give a better idea of how best to treat. This method is noninvasive, and easy to collect, which is particularly beneficial for diurnal cortisol, CAR (Cortisol Awakening Response), and luteal surge testing. Many providers consider saliva testing for determining clinical diagnosis and to monitor any route of hormone replacement therapy. Saliva testing is the matrix of choice to monitor transdermal and sublingual hormone therapies.



#### **HPA Axis/Adrenal Function Testing**

Cortisol profiles from Doctor's Data require four saliva samples taken at 30 minutes post-awakening, noon, dinner and bed time. These points capture the diurnal rhythm of cortisol secretion and can identify dysregulation in the natural cortisol circadian rhythm.

The cortisol awakening response (CAR) is the natural rise in cortisol that is seen minutes after awakening, followed by a noticeable drop within 60 minutes. CAR can be utilized as a biomarker for assessment of the HPA axis function in routine clinical practice—it can be influenced by overall HPA reactivity, as well as a person's anticipation of stress. Combined with the 30-minute postawakening collection, Doctor's Data measures CAR with two additional saliva collections—one immediately upon waking and the other at 60 minutes post-awakening. The CAR Profile can be ordered alone or added to any cortisol profile with an AM30 collection.

#### Secretory IgA (slgA)

SIgA is most often measured in stool or saliva. Measuring sIgA in stool can reveal information about gut immunity, inflammation, recent or current infections, and potential acute or chronic stress generally associated with GALT (gut-associated lymphoid tissue). SIgA measured in the saliva primarily provides insight into the body's stress response. However, there is some evidence that activated B cells can migrate from GALT to salivary glands, which could potentially demonstrate systemic inflammation and possibly link GI pathology via salivary sampling.

#### Comprehensive Adrenal Function Profile + CAR; saliva Patient: Sample Patient Sample Collection Date/Time Age: 39 Sex: Female Date Collected 04/05/2022 AM30 04/05/2022 06:00 Doctor: Sample Doctor Noon 04/05/2022 12:00 Menopausal Status: Pre-menopausa Doctor's Data, Inc 04/05/2022 19:00 3755 Illinois A St. Charles, IL 60174 04/07/2022 Date Reported Analyte Result Unit WRI H Optimal Range Reference Interval 6.0-20 Cortisol Waking 12-17 7.0 nmol/L Cortisol AM30 15 nmol/L 14.0 - 25.0 7.0 – 30.0 Cortisol AM60 nmol/L 12 10.0 - 18.04.9 - 22.0CAR Rise (Calculated) 35 - 60114.3 % % -33 - 0 Cortisol Noon 5.0 - 10.021-140 1.8 nmol/L Cortisol Evening 1.2 nmol/L 2.0 - 5.01.5-8.0 Cortisol Night 0.44 nmol/L 1.0-4.0 0.33 - 7.0DHEA\* 15 106 - 300 pg/mL Secretory IgA pg/mL 75 – 330 125 Cortisol Graph AM cortisol level appears adequate, although the suboptimal diurnal cortisol pattern is suggestive of early (Phase 1) HPA axis (adrenal gland) dysfunction. Cortisol Awakening Response (CAR) is the expected maximum rise in cortisol levels observed at 30 minutes (AM30) post awakening (approximately 93-60% above the waking value). This is followed by an expected decline sixty minutes after waking. The behavior of cortisol is a critical marker to understand the HPA axis physiologic responsiveness and is a key indicator of HPA axis adaptability and reactivity. This patient's CAR Rise (the percent change from waking to AM30) exceeds the This patient's CAR Decline (the percent change from waking to AM60) is observed as an unexpected increase. an unexpected increase. DHEA levels typically decline with age and the level measured here is below the reference range. Note: Supplementation with DHEA may increase testosterone and/or estradiol levels. Every mucosal membrane surface such as the eyes, nose, throat, and gastrointestinal system represent a large portal of entry for pathogenic bacteria, viruses, and yeasts. Secretory [gA (sigA) is the predominant antibody found on the mucosal membranes, and represents the body's first line of defense. SIgA levels change in response to stress. Adrenal Phase: 1 **Melatonin Report** Patient: Sample Patient Sample Collection Age: 39 Sex: Female Date Collected 04/05/2022 Date Received Client #: 12345 Doctor: Sample Doctor **Date Reported** 04/07/2022 Menopausal Status: Pre-menopausal Doctor's Data, Inc 3755 Illinois Ave. St. Charles, IL 60174 Analyte Result Unit L WRI н Reference Interval 5.3 3.0 - 25Melatonin Morning pg/mL Melatonin Evening pg/mL 1.4-19 pg/mL Melatonin Night\* <1.4 4.3-25

#### Melatonin

Melatonin is a hormone that also acts as a neurotransmitter. It is the major indole compound synthesized by the pineal gland and is converted from serotonin. Melatonin levels follow a diurnal rhythm in response to the light/dark cycle, with melatonin and light occurring at opposite times. Endogenous melatonin production begins rising approximately two hours before bedtime, provided light is dim. Melatonin and cortisol share an inverse relationship—when melatonin levels are low, cortisol levels should be high, and vice versa.

## Clinical Relevance and Patient Compliance

Free, unbound sex steroid hormones can fluctuate throughout the day and thus have many peaks and troughs. In order to obtain the most clinically accurate and truly representative results of an individual's hormone status, Doctor's Data averages four saliva specimens,

collected throughout the day, to minimize the risk of reporting a peak or trough. We go an extra step to deliver the most clinically relevant results—a fifth tube of saliva is created by pooling an equal amount of saliva from each of the four submitted samples. This pooled tube is mixed thoroughly to provide homogenization and becomes the saliva

source from which estriol, estradiol, estrone, progesterone, testosterone and DHEA are measured. This additional effort provides a far superior reflection of each patient's hormonal status. Convenient, easy and low-stress sample collection, with no needles or 24-hour urine collection, greatly increases patient compliance.



## a more precise illustration of your patients' sex hormone status

## Salivary Hormone and HPA Axis/Adrenal Function Profiles



	Comprehensive Plus Profile	Comprehensive Hormone Profile	Basic Hormone Profile	Comprehensive Adrenal Function Profile	Adrenal Function Profile	Diurnal Cortisol Profile	CAR Profile	Melatonin Profile
Estrone	/							
Estradiol	✓	✓	✓					
Estriol	<b>✓</b>							
Progesterone	✓	✓	✓					
Testosterone	1	1	1					
DHEA	✓	✓	1	✓	✓			
Cortisol	х4	<b>x4</b>	<b>x2</b>	<b>x4</b>	<b>x4</b>	х4	х3	
Melatonin								х3
slgA				✓				
PG/E2 Ratio	✓	✓	✓					
Estrogen Quotient	✓							

## Hormone and Urinary Metabolites Assessment Profile (HuMap™)



The Hormone and Urinary Metabolite Assessment Profile (HuMap™) provides a complete overview of steroid hormones, their metabolites, and the efficiency of the enzymes that metabolize these hormones. This non-invasive test requires only 4 or 5 separate urine collections. Because the breakdown of hormones relies so heavily on processes within the liver, this test can also elucidate areas of interest as it pertains to conjugation of each metabolite. Additionally, testing urinary hormone metabolites can contribute to further understanding of endogenous hormone secretion, supplemental hormone utilization, enzyme activity, oxidative stress, and insight into whether your body is safely metabolizing hormones.

- Color-coded results and expanded metabolic pathways specific to each patient
- Summary page to highlight important findings
- Key enzyme activity
- Full commentary



## Comprehensive Hormone and Metabolite Markers Available in the HuMap™

- Extensive estrogen metabolites available: E1, E2, E3, 2-OH-E1/E2, 4-OH-E1/E2, 16-OH-E1, 2-M-E1/E2, 4-M-E1/E2
- Comprehensive androgens and metabolites
- Progesterone and metabolites
- Daily cortisol (5), Daily cortisone (5)
- Metabolized cortisol, cortisone, and corticosterone
- Key enzyme activity: COMT, 11βHSD2, aromatase, and 5α-reductase
- Biomarker for Oxidative DNA Damage: 8-hydroxy-2'deoxyguanosine (8-OHdG)

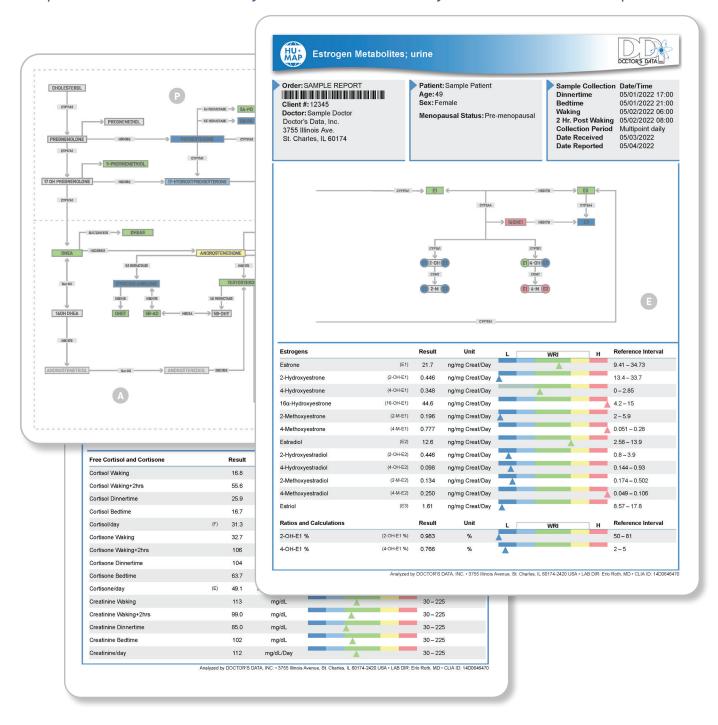


The HuMap™ is the most comprehensive urinary metabolite profile offered by Doctor's Data and is designed to provide deep insight into the secretion and metabolism of unconjugated sex hormones and their metabolites, and the enzymes that

fuel these conversions. Doctor's Data also offers smaller, more concise profiles that are designed for targeted assessment and follow-up testing.

	Hu+ MAP HuMap™	Sex Hormones Profile	Androgens and Progesterones Profile	Adrenal Corticoids Profile	Estrogen Metabolites Profile
Estrogens Fractionated: E1, E2, E3, 2-OH-E1, 4-OH-E1, 16-OH-E1, 2-M-E1, 4-M-E1, 2-OH-E2, 4-OH-E2, 2-M-E2, and 4-M-E2	✓	/	Tionic		✓
Androstenedione (A4)	<b>✓</b>	✓	<b>✓</b>		
EPI-Testosterone (EPI-T)	<b>✓</b>	<b>√</b>	/		
Testosterone (T)	<b>✓</b>	✓	<b>✓</b>		
Androsterone (AN)	/	<b>✓</b>	/		
11-hydroxy-Androsterone (OHAN)	<b>✓</b>	<b>✓</b>	<b>✓</b>		
5a-Androstanediol (5A-AD)	/	<b>✓</b>	<b>✓</b>		
5-Dihydrotestosterone (5A-DHT)	<b>✓</b>	<b>✓</b>	<b>✓</b>		
Etiocholanolone (ET)	/	<b>✓</b>	✓		
11-hydroxy-Etiocholanolone (OHET)	/	<b>✓</b>	<b>✓</b>		
5-Androstanediol (5B-AD)	<b>✓</b>	<b>✓</b>	1		
Dehydroepiandrosterone (DHEA)	<b>✓</b>	<b>✓</b>	<b>✓</b>	/	
Dehydroepiandrosterone Sulfate (DHEAS)	<b>✓</b>	<b>✓</b>	1	1	
Progesterone	<b>✓</b>	<b>✓</b>	<b>✓</b>		
5-Pregnanediol (5A-PD)	<b>✓</b>	<b>✓</b>	1		
5-Pregnanediol (5B-PD)	<b>✓</b>	<b>✓</b>	<b>✓</b>		
Allopregnanolone (ALLOP)	<b>✓</b>	<b>✓</b>	<b>√</b>		
21-Hydroxyprogesterone (21-OHP)	<b>✓</b>	<b>✓</b>	<b>✓</b>		
17-Hydroxyprogesterone (17-OHP)	<b>✓</b>	<b>✓</b>	<b>√</b>		
5-pregnanetriol (metabolite of 17-OHP)	<b>✓</b>	<b>✓</b>	<b>✓</b>		
Cortisol and Cortisone	х5			<b>x5</b>	
Corticosterone (B)	<b>✓</b>			<b>✓</b>	
Tetrahydrodehydrocorticosterone (THA)	<b>✓</b>			<b>√</b>	
5-Tetrahydrocorticosterone (5B-THB)	/			<b>✓</b>	
5a-Tetrahydrocorticosterone (5A-THB)	/			/	
11-Deoxycortisol (11-DOC)	✓ ·			<b>✓</b>	
5a-Tetrahydrocortisol (5A-THF)	<b>✓</b>			<b>✓</b>	
5-Tetrahydrocortisol (5B-THF)	✓ ·			<b>✓</b>	
Tetrahydrocortisone (THE)	✓			✓	
8-hydroxy-2'-deoxyguanosine (8-OHdG)	✓ ·				
Key Enzyme Activity	<b>✓</b>				

## Expanded Metabolic Pathways and Full Commentary included in the HuMap™



Much like a human fingerprint, metabolism is inherently unique to everyone. Understanding how the major hormones of the body are metabolized, as well as the activity of the enzymes responsible for metabolism, is a rare glimpse into a patient's health.

## Convenience, Clinical Utility and Researched Methodology of the HuMap™

#### **Enhanced Specificity and Specificity**

Liquid chromatography (LC) tandem mass spectrometry (MS) is an extremely sensitive and specific way to measure many substances. In the case of urinary steroid hormone testing, LC-MS is used to determine both free hormone and their metabolite amounts in urine. Put simply, both parts work together to figure out the exact amount of each hormone component in a patient sample. LC separates hormones in a liquid urine sample, which are then injected at various times for MS analysis. MS technology monitors the injected sample for specific hormones based on their molecular weights and expected injection times (commonly called retention times). Tandem MS verifies each hormone identity based on fragmentation and determines its amount. The combination of LC and tandem MS allows for extremely sensitive and specific hormone measurements, even in samples containing similar substances that would interfere with other methods.

#### Ability to Test Neurotransmitters from HuMap Urine Specmens

Many of the symptoms that would drive one to test urinary metabolite imbalance in a patient (fatigue, sleep difficulties, stress, mood concerns, cognitive concerns, vasomotor symptoms) can also be influenced by neurotransmitter imbalance. Additionally, the COMT (Catechol-O-Methyltransferase) enzyme plays an essential role in estrogen metabolism as well as catecholamine metabolism. Issues with COMT activity can result in both estrogen metabolite and neurotransmitter imbalance. Adding neurotransmitter testing to HuMap provides a deeper dive into the biochemistry that may be contributing to a patient's symptom picture. Providers can choose to add on the NeuroBasic or Comprehensive Neurotransmitter Profile to the same urine samples for additional convenience to the patient.

#### Advantages of Liquid Urine Collection

The main advantage of liquid urine collection is enhanced sensitivity, especially for low concentration metabolites. Dried urine must be reconstituted from the filter paper once the sample arrives. This reconstitution can lead to loss of polar steroid metabolites or creatinine for some patient samples. With liquid urine, samples can be shipped after being frozen for 4-6 hours, can be processed faster, and concentrated further to enhance the detection of low-level analytes. Steroids are also quite stable in properly preserved liquid urine.



## When to Consider the HuMap™ for your Patients

#### Women

Breast Health Endometriosis

**PCOS** 

PMS/PMDD

Menopausal Symptoms

#### Men

**Erectile Dysfunction** 

Prostate Health

Loss of Muscle Mass

**Breast Health** 

#### General

Metabolic Syndrome

**Thyroid Pathologies** 

Inflammation

**Oxidative Stress** 

Fatique/Insomnia

Libido

**Mood or Cognitive Concerns** 

Family History of Hormone-Driven

Cancers

HRT/BHRT Utilization

Weight Gain

#### Urine and Saliva Testing for BHRT

Urinary hormone and metabolite testing is uniquely suited to provide insight into how hormones and their metabolites are moving through the body as well as risk assessment from the generation of certain metabolites. When using urinary metabolite testing, the level of detectable unconjugated sex hormone levels is not representative of circulating or bioavailable tissue hormone levels, because urine is not reflective of tissue uptake. When the goal of testing is to understand bioavailable levels of hormones, salivary testing may be a better option, especially if utilizing topical hormones.

#### Neurotransmitter Profiles



Urinary neurotransmitter profiles provide insight into a patient's overall ability to synthesize and metabolize neurotransmitters. Neurotransmitters are secreted from pre-synaptic neurons into the synapse between nerve cells to stimulate receptors on post-synaptic neurons. These chemical messengers regulate many physical and emotional processes including movement, stress response, cognition, emotions, energy, cravings, pain and more. Doctor's Data Neurotransmitter profiles help identify alterations in urinary neurotransmitter status which may be associated with a variety of conditions from metabolic to behavioral disorders.

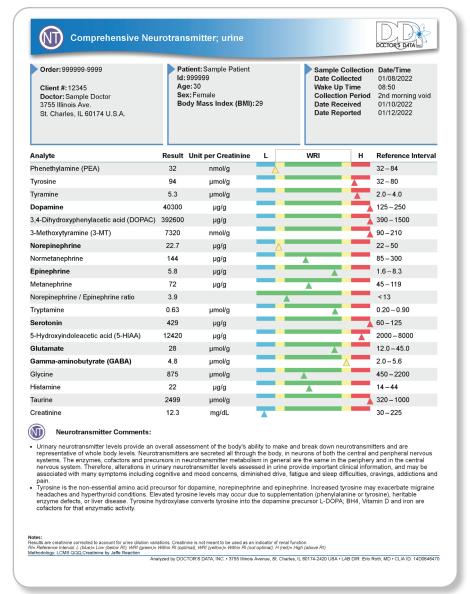
#### Value in Clinical Practice

Analysis of neurotransmitters and their metabolites provides a non-invasive assessment of neurotransmitter status. A review of current scientific literature indicates that neurotransmitter testing may be useful in a variety of areas:

Identification of Imbalances—Research indicates that urinary neurotransmitter levels may correlate with conditions such as depression and PTSD. Further clinical associations have also been made with imbalances in neurotransmitters and:

- Other mood disorders
- HPA axis (adrenal) dysfunction: fatigue, insomnia
- Loss of mental focus: ADD, ADHD, cognitive concerns
- Cravings, addiction and dependency
- Hormonal imbalances: estrogen dominance (progesterone insufficiency), estrogen deficiency, androgen imbalance
- Loss of appetite control: obesity and insulin resistance

**Functional Testing** - Neurotransmitter metabolism is mediated by catechol-Omethyltransferase (COMT), monoamine



oxidase (MAO), and other enzymes. Test results may provide functional information about these important enzymes.

#### Response to Therapy—

Neurotransmitters (serotonin, for example) may be altered by the addition of precursor amino acids such as 5-hydroxytryptophan (5-HTP). These changes may be apparent in the urine.

**Toxicology Risk Assessment**—Changes in urinary neurotransmitters like serotonin, dopamine, and glutamate may be clinically relevant outcomes for neurobehavioral toxicology resulting from chemical or environmental exposures.

### Which Profile to Consider

The NeuroBasic Profile offers a broad-brush assessment that covers most clinical needs and which many providers find highly clinically relevant and useful. For providers interested in a more comprehensive look at neurotransmitter secretion and the metabolism of these markers, the Comprehensive Neurotransmitter Profile includes catecholamine and serotonin metabolites, trace amines, and additional markers that expand the clinical view.

	Comprehensive Neurotransmitter Profile	NeuroBasic Profile	NeuroAdrenal Profile
	URAGE	URINE	UIINE BAINA
Serotonin	✓	✓	✓
GABA	✓	✓	✓
Dopamine	✓	✓	✓
Norepinephrine	✓	✓	✓
Epinephrine	✓	✓	✓
Glutamate	✓	✓	✓
Histamine	✓	✓	✓
PEA (Phenethylamine)	✓	✓	✓
5-HIAA (5-Hydroxyindolacetic acid)	✓		
Glycine	✓	✓	✓
Taurine	✓		
Tryptamine	✓		
Tyroamine	✓		
Tyrosine	✓		
DOPAC (3,4 Dihydroxyphenylacetic acid)	✓		
3-MT (3-Methoxytyramine)	✓		
Metanephrine Fractionation (Metanephrine, Normetanephrine)	✓		
Creatinine	✓	✓	✓
Cortisol			x4
DHEA			✓

## Thyroid Profile

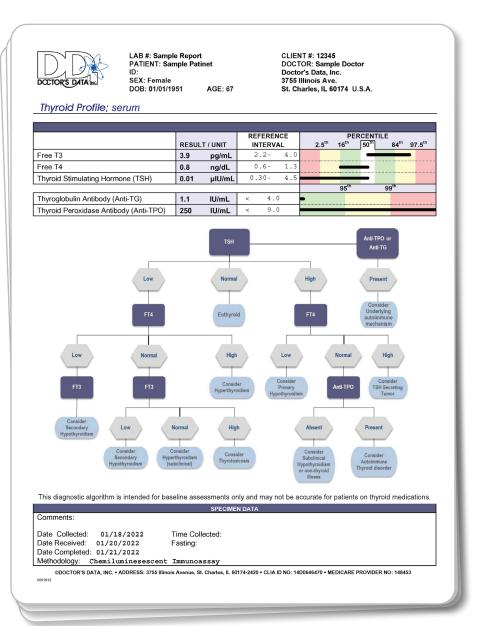


The analysis of thyroid hormones and auto-antibodies together may improve the accuracy diagnosis and clinical success. The American Thyroid Association estimates that approximately 20 million Americans have thyroid disease, and approximately 60% of those with thyroid disease are unaware of their condition. Many patients with thyroid disorders may remain undiagnosed in many patients with asymptomatic or non-specific clinical presentations. The recognition of auto-immunity as a leading cause of thyroid dysfunction has led to the evaluation of auto-antibodies in thyroid testing.

Measuring only thyroid stimulating hormone (TSH) may be misleading in a variety of circumstances, including the recent treatment of thyrotoxicosis, pituitary disease, non-thyroid illness, thyroid hormone resistance or rare, TSH-secreting tumors. Under these circumstances, and in many other cases, the evaluation of thyroid hormones and thyroid antibodies may clarify the diagnosis of thyroid conditions and improve clinical success.

#### This test is useful for

- Hypothyroid conditions
- Hyperthyroid conditions
- Autoimmune conditions
- Arrhythmia
- Infertility
- Cholesterol disorders
- Fatique
- Pituitary disorders



## **OUR MISSION:**

To research, develop and offer innovative specialty tests that help doctors identify health risks and improve outcomes for patients with chronic conditions.

To educate and support healthcare professionals.

To improve lives through science.



**SCIENCE+INSIGHT** 

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#### About Doctor's Data

Doctor's Data, Inc. has provided innovative specialty testing to healthcare practitioners around the world from our advanced, CLIA-licensed clinical laboratory since 1972.

As a pioneer in the laboratory testing industry, Doctor's Data provides a wide array of testing solutions to aid in decision making and better patient outcomes. Choose Doctor's Data to help you assess and treat heavy metal burden, nutritional deficiencies, gastrointestinal function, hormone status, cardiovascular risk, liver and metabolic abnormalities, and more.