Environmental Exposure and Detoxification

Gauge the Body's Ability to Eliminate Toxins

- DNA Oxidative Damage
- Glutathione, Erythrocytes
- Hepatic Detox Profile
- Urine Porphyrins
- DNA Methylation Profile

DOCTOR'S DATA INC.

SCIENCE + INSIGHT

Environmental Exposure and Detoxification

Environmental chemical exposure has never been more pervasive with thousands of chemicals in use around the world. Many chemicals are integrated into our food supply, the air we breathe and the water we drink. Every day, we ingest tiny amounts of these chemicals and our bodies cannot metabolize and clear all of them. Chemicals not metabolized are stored in the fat cells throughout our bodies, where they continue to accumulate.

As these chemicals build up they alter our metabolism, cause enzyme dysfunction and nutritional deficiencies, create hormonal imbalances, damage brain chemistry and can cause cancer. Because the chemicals accumulate in different parts of the body—at different rates and in different combinations—there are many different chronic illnesses that can result.

Doctor's Data offers a spectrum of tests designed to evaluate the exposure to environmental toxins and markers of the body's capacity for endogenous detoxification.

The World Health Organization (WHO) estimates that about
a quarter of the diseases facing mankind today
occur due to prolonged exposure to environmental pollution.

DNA Oxidative Damage

URINE

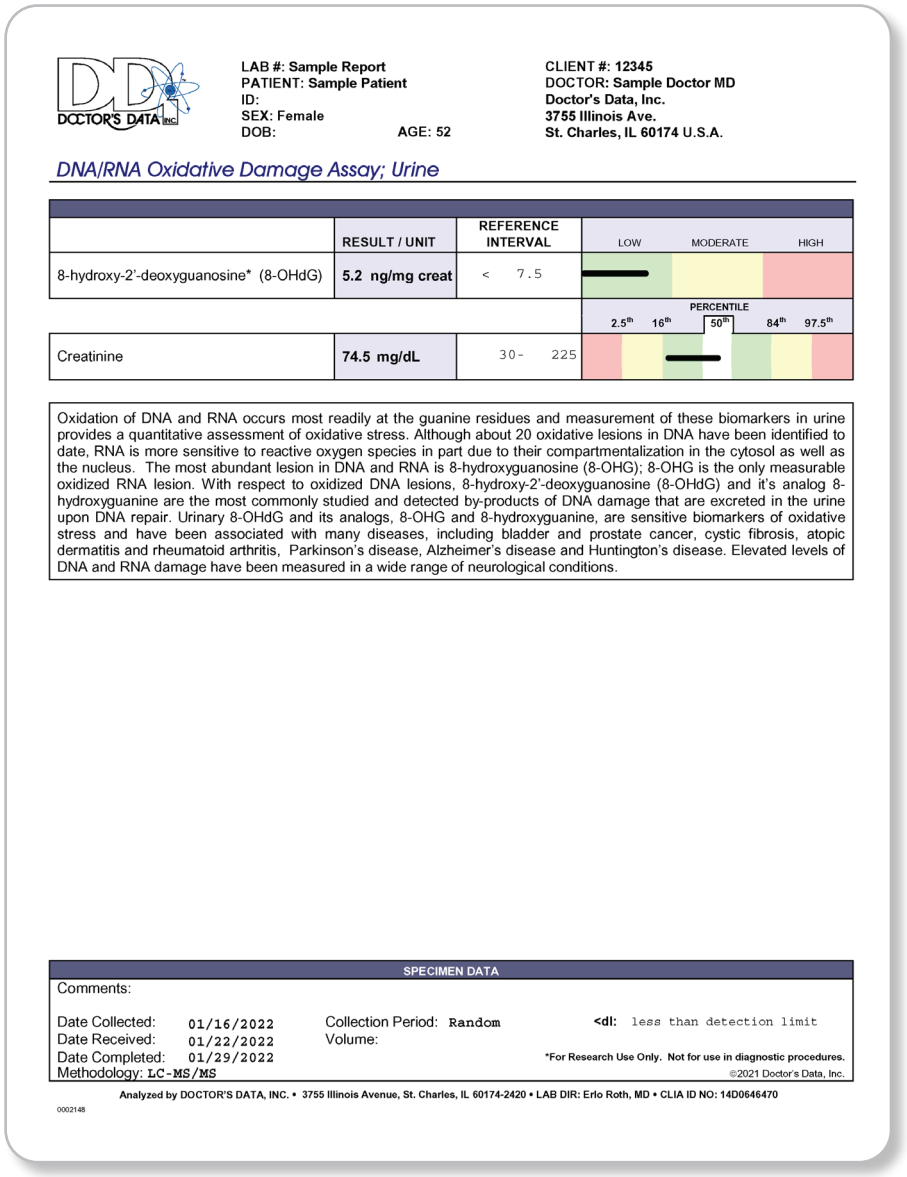
Oxidative stress has been associated with many diseases, including bladder and prostate cancer, cystic fibrosis, atopic dermatitis, rheumatoid arthritis, and a wide range of neurological conditions, including Parkinson's disease, Alzheimer's disease and Huntington's disease. It has also been correlated with the severity of diabetic retinopathy and neuropathy.

Oxidation of DNA occurs readily at the guanosine bases, so measurement of 8-hydroxy-2'-Deoxyguanosine (8-OHdG) in urine provides a quantitative assessment of ongoing oxidative damage or stress in the body.

When 8-OHdG levels are elevated, it's important to identify the sources of oxidative stress and assess the primary intracellular antioxidant glutathione. Taking steps to reduce oxidative stress is valuable in optimizing health and longevity. This non-invasive test requires a single first morning void urine collection.

This marker can be ordered as a standalone test, and is also included in the new Hormone and Urinary Metabolites Assessment Profile (HuMap™). *Learn more about the HuMap™ at doctorsdata.com/humap*

Results are presented in a clear, easy-to-understand report.



LAB #: Sample Report
PATIENT: Sample Patient
ID:
SEX: Female
DOB: AGE: 52

CLIENT #: 12345
DOCTOR: Sample Doctor MD
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

DNA/RNA Oxidative Damage Assay; Urine

	RESULT / UNIT	REFERENCE INTERVAL	LOW / MODERATE / HIGH
8-hydroxy-2'-deoxyguanosine* (8-OHdG)	5.2 ng/mg creat	< 7.5	
			PERCENTILE 2.5th 16th 50th 84th 97.5th
Creatinine	74.5 mg/dL	30- 225	

Oxidation of DNA and RNA occurs most readily at the guanine residues and measurement of these biomarkers in urine provides a quantitative assessment of oxidative stress. Although about 20 oxidative lesions in DNA have been identified to date, RNA is more sensitive to reactive oxygen species in part due to their compartmentalization in the cytosol as well as the nucleus. The most abundant lesion in DNA and RNA is 8-hydroxyguanosine (8-OHG); 8-OHG is the only measurable oxidized RNA lesion. With respect to oxidized DNA lesions, 8-hydroxy-2'-deoxyguanosine (8-OHdG) and it's analog 8-hydroxyguanine are the most commonly studied and detected by-products of DNA damage that are excreted in the urine upon DNA repair. Urinary 8-OHdG and its analogs, 8-OHG and 8-hydroxyguanine, are sensitive biomarkers of oxidative stress and have been associated with many diseases, including bladder and prostate cancer, cystic fibrosis, atopic dermatitis and rheumatoid arthritis, Parkinson's disease, Alzheimer's disease and Huntington's disease. Elevated levels of DNA and RNA damage have been measured in a wide range of neurological conditions.

SPECIMEN DATA

Comments:

Date Collected: 01/16/2022
Date Received: 01/22/2022
Date Completed: 01/29/2022
Methodology: LC-MS/MS

Collection Period: Random
Volume:

<dl: less than detection limit

*For Research Use Only. Not for use in diagnostic procedures.

Analyzed by DOCTOR'S DATA, INC. • 3755 Illinois Avenue, St. Charles, IL 60174-2420 • LAB DIR: Erlo Roth, MD • CLIA ID NO: 14D0646470

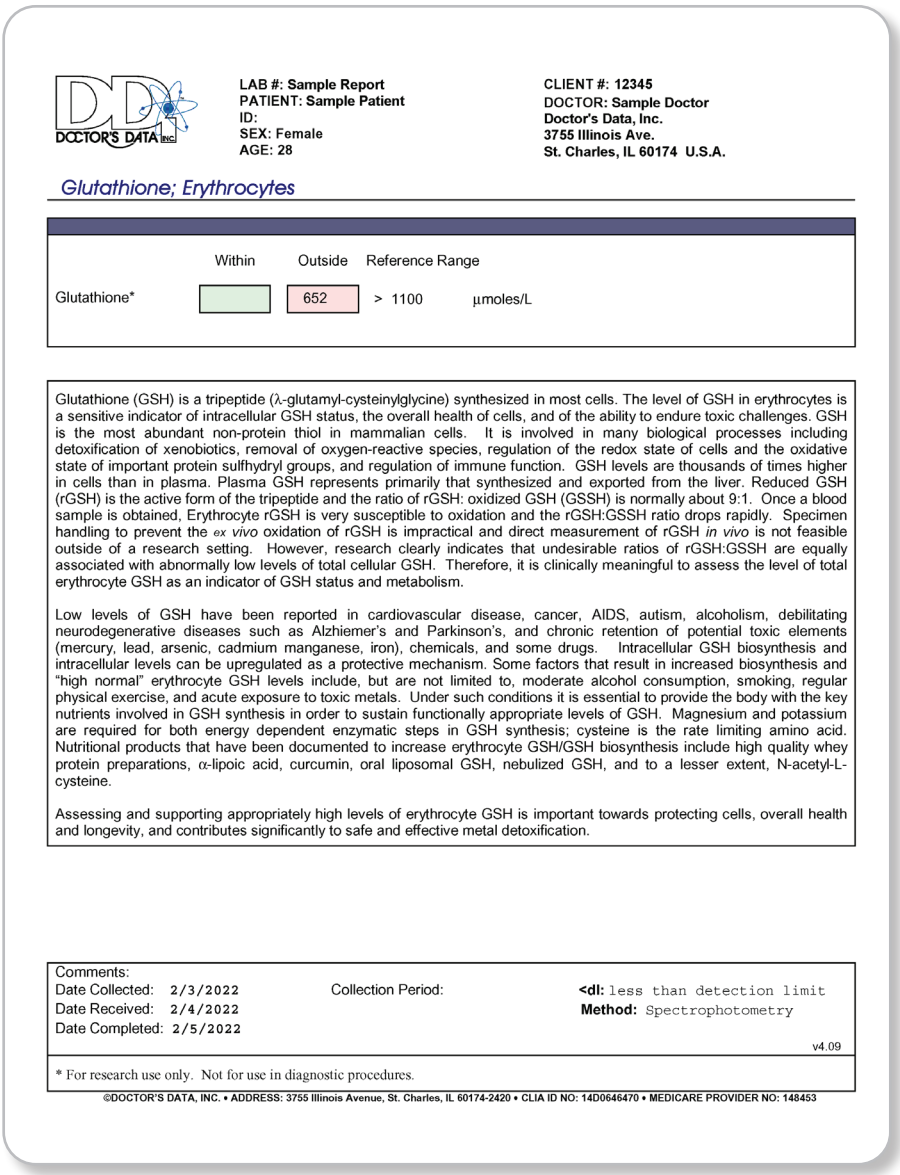
0002148

Glutathione, Erythrocytes

Glutathione (GSH) is the most abundant and important intracellular antioxidant, and GSH levels in erythrocytes can be used to effectively gauge overall health of cells and of the ability to endure toxic challenges.

Low levels of GSH have been reported in cardiovascular disease, cancer, AIDS, autism, alcoholism and debilitating neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. It has also been associated with chronic retention of many potential toxic elements, chemicals and some drugs. Assessment and support of erythrocyte GSH can contribute to healthy aging and effective detoxification of toxic metals and chemicals.

Results are presented in a clear, easy-to-understand report.



DOCTOR'S DATA INC

LAB #: Sample Report
PATIENT: Sample Patient
ID:
SEX: Female
AGE: 28

CLIENT #: 12345
DOCTOR: Sample Doctor
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Glutathione; Erythrocytes

	Within	Outside	Reference Range	
Glutathione*		652	> 1100	µmoles/L

Glutathione (GSH) is a tripeptide (λ-glutamyl-cysteinylglycine) synthesized in most cells. The level of GSH in erythrocytes is a sensitive indicator of intracellular GSH status, the overall health of cells, and of the ability to endure toxic challenges. GSH is the most abundant non-protein thiol in mammalian cells. It is involved in many biological processes including detoxification of xenobiotics, removal of oxygen-reactive species, regulation of the redox state of cells and the oxidative state of important protein sulfhydryl groups, and regulation of immune function. GSH levels are thousands of times higher in cells than in plasma. Plasma GSH represents primarily that synthesized and exported from the liver. Reduced GSH (rGSH) is the active form of the tripeptide and the ratio of rGSH: oxidized GSH (GSSH) is normally about 9:1. Once a blood sample is obtained, Erythrocyte rGSH is very susceptible to oxidation and the rGSH:GSSH ratio drops rapidly. Specimen handling to prevent the *ex vivo* oxidation of rGSH is impractical and direct measurement of rGSH *in vivo* is not feasible outside of a research setting. However, research clearly indicates that undesirable ratios of rGSH:GSSH are equally associated with abnormally low levels of total cellular GSH. Therefore, it is clinically meaningful to assess the level of total erythrocyte GSH as an indicator of GSH status and metabolism.

Low levels of GSH have been reported in cardiovascular disease, cancer, AIDS, autism, alcoholism, debilitating neurodegenerative diseases such as Alzheimer's and Parkinson's, and chronic retention of potential toxic elements (mercury, lead, arsenic, cadmium manganese, iron), chemicals, and some drugs. Intracellular GSH biosynthesis and intracellular levels can be upregulated as a protective mechanism. Some factors that result in increased biosynthesis and "high normal" erythrocyte GSH levels include, but are not limited to, moderate alcohol consumption, smoking, regular physical exercise, and acute exposure to toxic metals. Under such conditions it is essential to provide the body with the key nutrients involved in GSH synthesis in order to sustain functionally appropriate levels of GSH. Magnesium and potassium are required for both energy dependent enzymatic steps in GSH synthesis; cysteine is the rate limiting amino acid. Nutritional products that have been documented to increase erythrocyte GSH/GSH biosynthesis include high quality whey protein preparations, α-lipoic acid, curcumin, oral liposomal GSH, nebulized GSH, and to a lesser extent, N-acetyl-L-cysteine.

Assessing and supporting appropriately high levels of erythrocyte GSH is important towards protecting cells, overall health and longevity, and contributes significantly to safe and effective metal detoxification.

Comments:
Date Collected: 2/3/2022
Date Received: 2/4/2022
Date Completed: 2/5/2022
Collection Period:
<dl: less than detection limit
Method: Spectrophotometry
v4.09

* For research use only. Not for use in diagnostic procedures.

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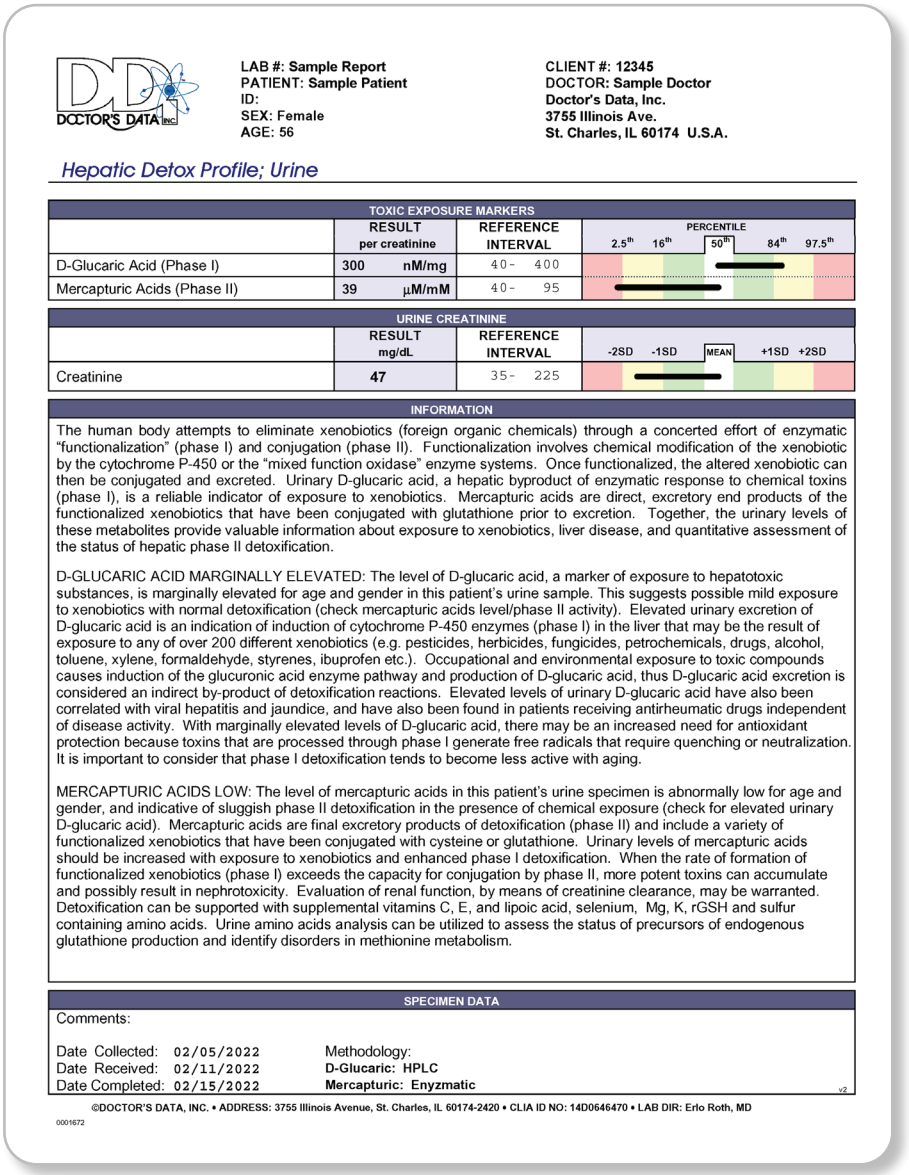
Hepatic Detox Profile

URINE

The body continually attempts to eliminate chemical toxins through enzymatic processes in the liver. Urinary D-glucaric acid, a byproduct of Phase I detoxification, can indicate chemical exposure to over 200 chemicals. Urinary mercapturic acids are excreted end products of Phase II detoxification. Together, assessment of these two analytes provides valuable information about exposure to xenobiotics, liver disease and the ability of the liver to eliminate toxins. This non-invasive test requires a single first morning void urine collection.

Results are presented in a clear, easy-to-understand report which graphically illustrates target ranges and areas of concern.



DOCTOR'S DATA INC

LAB #: Sample Report
PATIENT: Sample Patient
ID:
SEX: Female
AGE: 56

CLIENT #: 12345
DOCTOR: Sample Doctor
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Hepatic Detox Profile; Urine

TOXIC EXPOSURE MARKERS

	RESULT per creatinine		REFERENCE INTERVAL	PERCENTILE 2.5th 16th 50th 84th 97.5th
D-Glucaric Acid (Phase I)	300	nM/mg	40 - 400	
Mercapturic Acids (Phase II)	39	µM/mM	40 - 95	

URINE CREATININE

	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	47	35 - 225	

INFORMATION

The human body attempts to eliminate xenobiotics (foreign organic chemicals) through a concerted effort of enzymatic "functionalization" (phase I) and conjugation (phase II). Functionalization involves chemical modification of the xenobiotic by the cytochrome P-450 or the "mixed function oxidase" enzyme systems. Once functionalized, the altered xenobiotic can then be conjugated and excreted. Urinary D-glucaric acid, a hepatic byproduct of enzymatic response to chemical toxins (phase I), is a reliable indicator of exposure to xenobiotics. Mercapturic acids are direct, excretory end products of the functionalized xenobiotics that have been conjugated with glutathione prior to excretion. Together, the urinary levels of these metabolites provide valuable information about exposure to xenobiotics, liver disease, and quantitative assessment of the status of hepatic phase II detoxification.

D-GLUCARIC ACID MARGINALLY ELEVATED: The level of D-glucaric acid, a marker of exposure to hepatotoxic substances, is marginally elevated for age and gender in this patient's urine sample. This suggests possible mild exposure to xenobiotics with normal detoxification (check mercapturic acids level/phase II activity). Elevated urinary excretion of D-glucaric acid is an indication of induction of cytochrome P-450 enzymes (phase I) in the liver that may be the result of exposure to any of over 200 different xenobiotics (e.g. pesticides, herbicides, fungicides, petrochemicals, drugs, alcohol, toluene, xylene, formaldehyde, styrenes, ibuprofen etc.). Occupational and environmental exposure to toxic compounds causes induction of the glucuronic acid enzyme pathway and production of D-glucaric acid, thus D-glucaric acid excretion is considered an indirect by-product of detoxification reactions. Elevated levels of urinary D-glucaric acid have also been correlated with viral hepatitis and jaundice, and have also been found in patients receiving antirheumatic drugs independent of disease activity. With marginally elevated levels of D-glucaric acid, there may be an increased need for antioxidant protection because toxins that are processed through phase I generate free radicals that require quenching or neutralization. It is important to consider that phase I detoxification tends to become less active with aging.

MERCAPTURIC ACIDS LOW: The level of mercapturic acids in this patient's urine specimen is abnormally low for age and gender, and indicative of sluggish phase II detoxification in the presence of chemical exposure (check for elevated urinary D-glucaric acid). Mercapturic acids are final excretory products of detoxification (phase II) and include a variety of functionalized xenobiotics that have been conjugated with cysteine or glutathione. Urinary levels of mercapturic acids should be increased with exposure to xenobiotics and enhanced phase I detoxification. When the rate of formation of functionalized xenobiotics (phase I) exceeds the capacity for conjugation by phase II, more potent toxins can accumulate and possibly result in nephrotoxicity. Evaluation of renal function, by means of creatinine clearance, may be warranted. Detoxification can be supported with supplemental vitamins C, E, and lipoic acid, selenium, Mg, K, rGSH and sulfur containing amino acids. Urine amino acids analysis can be utilized to assess the status of precursors of endogenous glutathione production and identify disorders in methionine metabolism.

SPECIMEN DATA

Comments:

Date Collected: 02/05/2022
Date Received: 02/11/2022
Date Completed: 02/15/2022

Methodology:
D-Glucaric: HPLC
Mercapturic: Enzymatic

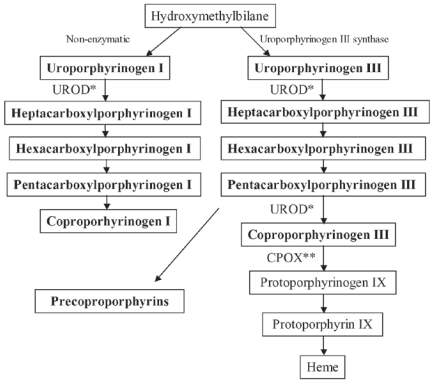
v2

0001672

Urine Porphyrins

Abnormal levels of urinary porphyrins, oxidized metabolites of heme biosynthesis, are associated with genetic disorders, metabolic disturbances and diseases, anemias and oxidative stress, as well as exposure to toxic chemicals or metals. Specific urine porphyrin profiles are associated with high-level exposure to mercury, arsenic, lead and some chemicals and drugs. Precoproporphyrins, associated with mercury, are reported separately and per unit of uroporphyrin to increase detection even when heme biosynthesis is low. This non-invasive test requires a single first morning void or 24-hour urine collection.

Abbreviated Porphyrinogen/Heme Metabolism



*UROD, Uroporphyrinogen decarboxylase
**CPOX, Coproporphyrinogen oxidase

Results are presented in a clear, easy-to-understand report which graphically illustrates target ranges and porphyrinogen/heme metabolism.

DOCTOR'S DATA INC

LAB #: Sample Report
PATIENT: Sample Patient
ID:
SEX: Female
AGE: 26

CLIENT #: 12345
DOCTOR: Sample Doctor
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Porphyrins; Urine

PORPHYRINS	RESULT nmol/g creatinine	REFERENCE INTERVAL	PERCENTILE 95th 99th
Uroporphyrins	69	< 20	
Heptacarboxylporphyrins	2.6	< 4	
Hexacarboxylporphyrins	0.94	< 3.5	
Pentacarboxylporphyrins	1.4	< 3	
Coproporphyrin I	31	< 24	
Coproporphyrin III	100	< 70	
Coproporphyrin I/Coproporphyrin III	0.3	< 0.8	
Total Porphyrins	210	< 110	
Precoproporphyrin I*	1.4	< 2	
Precoproporphyrin II*	1.7	< 1.2	
Precoproporphyrin III*	0	< 1.2	
Total Precoproporphyrins*	3.1	< 4	
Precoproporphyrins*/Uroporphyrins	0.045	< 0.1	

INFORMATION

Urinary porphyrins are oxidized intermediate metabolites of heme biosynthesis and can serve as biomarkers of disorders in heme production. Abnormal porphyrin profiles have been associated with genetic disorders, poor nutritional status, oxidative stress, and high level exposure to toxic chemicals or toxic metals. The ratio of Precoproporphyrins-to-Uroporphyrins is reported to increase the sensitivity for detecting abnormalities in individuals with low heme biosynthesis. Alcohol, sedatives, analgesics, antibiotics estrogens and oral contraceptives can affect the levels of urinary porphyrins. Anemia, pregnancy, and liver disease can also affect porphyrin metabolism. The Urine Porphyrins test is best used in conjunction with urine toxic metals pre- and post-provocation testing.

Porphyrins Pattern Recognition Guide:

Mercury ↑ Penta, ↑ Copro III, ↑ Precopros, ↑ Precorpros : Uros
Arsenic ↑ Uros, ↑ Copro I : Copro III
Lead ↑ Copro III
Hexachlorobenzene, Dioxin ↑ Uros
Methylchloride, Polyvinylchloride, Polybrominated biphenyl ↑Copros

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD -1SD MEAN +1SD +2SD
Creatinine	167	30- 225	

SPECIMEN DATA

Comments:

Date Collected: 01/24/2022
Date Received: 01/31/2022
Date Completed: 02/12/2022

Method: HPLC
<dl: less than detection

Collection Period: Random
Volume:

*Precoproporphyrins are atypical porphyrins associated with high-level mercury exposure as described in Woods, J et al. J. Toxicol. Env. Hlth. 40,235-46(1993) and Morita, Y et al. Porphyrins 14,93-7(2005). Precoproporphyrins are intended for Research Use Only. Not for use in diagnostic procedures.

0001668

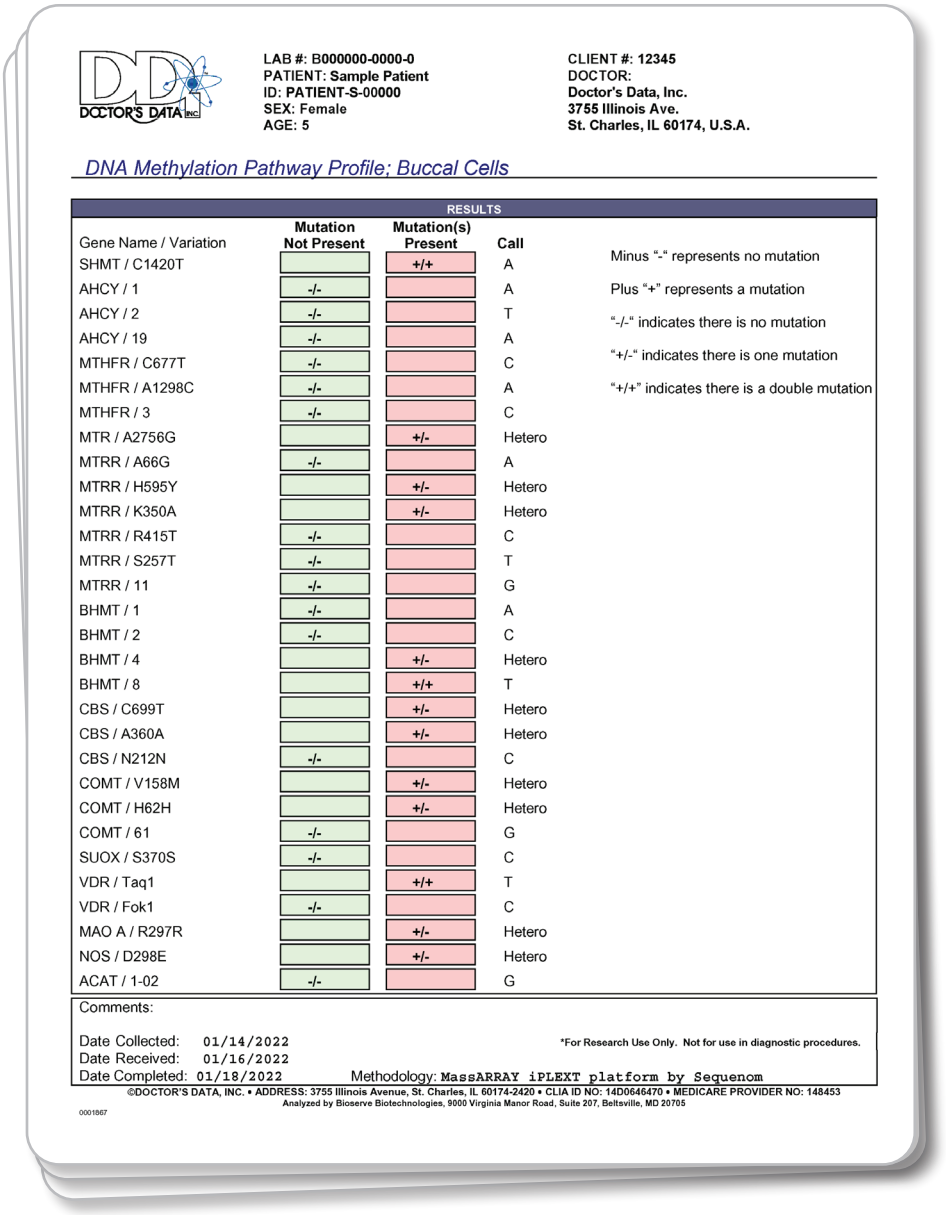
DNA Methylation Profile

The DNA Methylation Profile allows clinicians to screen patients for a variety of genetic variants—single nucleotide polymorphisms, or SNPs—that may impact the function of important biochemical processes such as methionine metabolism, detoxification, hormone balance and vitamin D function. The presence or absence of SNPs may modify disease risk. The risks may be reduced by lifestyle changes, and inefficient biochemical processes can be supported by diet and nutritional supplements to maximize the functions of metabolic pathways.

Identifying single nucleotide polymorphisms (SNPs) that may influence health and rise for diseases facilitates clinical support for patients. The Doctor's Data DNA Methylation Profile includes a variety of SNPs known to influence many aspects of health including:

- Insulin sensitivity
- Bone health
- Cancer risks
- Cardiovascular health
- Detoxification processes
- Fertility
- Mitochondrial function and metabolism
- Methylation
- Neurotransmitter balance

The SNPs affecting detoxification and methylation become even more important if a patient has been exposed to toxicants such as mercury, lead or bisphenol A (BPA). Lead and BPA inhibit the function of methyltransferases, and mercury inhibits methionine synthase, an important enzyme in the re-methylation of homocysteine. Methylation is an essential step in the detoxification and elimination of arsenic and other xenobiotics. Normal methionine metabolism is a critical component of Phase II detoxification processes—the B-12 and folate-dependent transmethylation and B-6 dependent transsulfuration pathways convert homocysteine to cysteine. Cysteine is an important precursor in glutathione biosynthesis.



DOCTOR'S DATA INC

LAB #: B000000-0000-0
PATIENT: Sample Patient
ID: PATIENT-S-00000
SEX: Female
AGE: 5

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174, U.S.A.

DNA Methylation Pathway Profile; Buccal Cells

RESULTS

Gene Name / Variation	Mutation Not Present	Mutation(s) Present	Call
SHMT / C1420T		+/+	A
AHCY / 1	-/-		A
AHCY / 2	-/-		T
AHCY / 19	-/-		A
MTHFR / C677T	-/-		C
MTHFR / A1298C	-/-		A
MTHFR / 3	-/-		C
MTR / A2756G		+/-	Hetero
MTRR / A66G	-/-		A
MTRR / H595Y		+/-	Hetero
MTRR / K350A		+/-	Hetero
MTRR / R415T	-/-		C
MTRR / S257T	-/-		T
MTRR / 11	-/-		G
BHMT / 1	-/-		A
BHMT / 2	-/-		C
BHMT / 4		+/-	Hetero
BHMT / 8		+/+	T
CBS / C699T		+/-	Hetero
CBS / A360A		+/-	Hetero
CBS / N212N	-/-		C
COMT / V158M		+/-	Hetero
COMT / H62H		+/-	Hetero
COMT / 61	-/-		G
SUOX / S370S	-/-		C
VDR / Taq1		+/+	T
VDR / Fok1	-/-		C
MAO A / R297R		+/-	Hetero
NOS / D298E		+/-	Hetero
ACAT / 1-02	-/-		G

Minus "-" represents no mutation
Plus "+" represents a mutation
"-/-" indicates there is no mutation
"+/-" indicates there is one mutation
"+/+" indicates there is a double mutation

Comments:

Date Collected: 01/14/2022
Date Received: 01/16/2022
Date Completed: 01/18/2022

*For Research Use Only. Not for use in diagnostic procedures.

Methodology: MassARRAY iPLEXT platform by Sequenom

Analyzed by Bioserve Biotechnologies, 9000 Virginia Manor Road, Suite 207, Beltsville, MD 20705

0001867

The greatest difficulty in interpreting SNP results is determining the extent to which a DNA genotype is phenotypically expressed. Functional tests combined with evaluation of the patient's symptoms and responses to intervention are necessary to assess the influence of known SNPs on the phenotype. The Doctor's Data Plasma Methylation Profile is one such test—it provides a direct assessment of several major metabolites that indicate genetic and epigenetic affects. The Plasma Methylation Profile is a functional follow-up test when SNPs affecting methionine metabolism are identified.

Results are presented in a clear, easy-to-understand report that graphically illustrates target ranges and areas of concern. Result-specific commentary is provided.

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.

DOCTOR'S DATA INC.

SCIENCE + INSIGHT

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doctorsdata.com

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.