



LAB #: U000000-0000-0
 PATIENT: Sample Patient
 ID: PATIENT-S-000000
 SEX: Male
 DOB: AGE: 33

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

Neuro-Biogenic Amines, Comprehensive; urine second morning void

	RESULT/UNIT per creatinine	REFERENCE INTERVAL	PERCENTILE				
			2.5 th	10 th	50 th	90 th	97.5 th
Dopamine, free	130 µg/g	52- 320					
3,4-Dihydroxyphenylacetic acid (DOPAC)	764 µg/g	360- 1950					
3-Methoxytyramine (3-MT)	129 nmol/g	65- 215					
Norepinephrine, free	20.1 µg/g	12- 50					
Normetanephrine	116 µg/g	50- 400					
Epinephrine, free	1.7 µg/g	1.2- 16					
Metanephrine	58 µg/g	35- 130					
Serotonin	71.6 µg/g	42- 105					
5-Hydroxyindolacetic acid (5-HIAA)	2203 µg/g	1200- 7200					
Tryptamine	0.16 µmol/g	0.08- 0.9					
Glutamate	12 µmol/g	8- 45					
Gamma-aminobutyrate (GABA)	2.9 µmol/g	1.4- 5					
Tyrosine	45 µmol/g	23- 113					
Tyramine	2.0 µmol/g	1.2- 5.5					
Phenethylamine (PEA)	17 nmol/g	16- 146					
Taurine	2778 µmol/g	170- 1200					
Glycine	804 µmol/g	280- 2800					
Histamine	14 µg/g	10- 48					
Creatinine	178 mg/dL	35- 240					
			PERCENTILE				
			90th	95th			
Norepinephrine : Epinephrine ratio	14.0	< 10					

SPECIMEN DATA

Comments:

Date Collected: 06/12/2017 Wake-up time: Volume:
 Date Received: 06/14/2017 Time Collected: 09:00 AM Body Mass Index: 31
 Date Reported: 06/20/2017 Collection Period: second morning void
 Methodology: LCMS QQQ, Creatinine by Jaffe Method <dL: less than detection limit

Introduction

For the analysis of neuro-biogenic amines excreted in urine, the method employed by Doctor's Data is designed to detect and measure the free, unconjugated forms of these components. The exception is made for Metanephrine and Normetanephrine, for which the standard of care is based upon reference intervals established for the total metanephrines, which includes both the free and sulfur-conjugated forms of these components. Analysis is performed using tandem LC-MS, using calibrators prepared from certified sources.

Urinary neuro-biogenic amines provide an overall assessment of a patient's ability to synthesize and metabolize neurotransmitters, both in the periphery and, for some enzymes, behind the blood brain barrier as well. Alterations in urinary neurotransmitter status may be associated with a variety of conditions including metabolic disorders, mood/behavioral disorders, and in rare occasions the presence of certain tumors. Associations between urinary neurotransmitter levels and health conditions have been documented in scientific literature and may provide valuable insights as part of a comprehensive health assessment.

The activities of many enzymes are expressed differently in specific cells and organs, therefore circulating levels of their metabolites may have distinctive sources. For example, dopamine and serotonin synthesis in the body occurs primarily in the gastrointestinal tract (GIT). Urinary levels of neurotransmitters primarily reflect the activity of the peripheral and GIT enteric nervous systems. Up to 20% of urinary neurotransmitters are estimated as originating in the CNS.

Enzymes and receptors involved in neurotransmitter metabolism may be subject to mutations and single nucleotide polymorphisms (SNPs). A lack of nutritional cofactors (vitamins, minerals) required for normal enzyme function may also decrease enzymatic activity and neurotransmitter levels. Enzymatic defects in synthesis or metabolism may affect levels of neurotransmitters, and normal neurotransmitter receptor function is necessary for normal neurotransmitter activity. Neurotransmitter levels may also be influenced by diet, lifestyle and other health conditions such as high sodium diet, age, gender, body mass index, kidney function, environmental exposures, infection and tobacco use.

References:

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Epinephrine LOW

The level of epinephrine is lower than expected in this sample. Epinephrine is a catecholamine neurotransmitter and hormone synthesized in the adrenal medulla; small amounts are synthesized in the Central Nervous System (CNS) and the vagus nerve. Evidence indicates that epinephrine has neurotransmitter-like functions in the CNS that may affect the regulation of blood pressure, respiration, and pituitary hormone secretion.

Conditions that may be associated with low epinephrine levels include Addison's disease, diabetic nephropathy, congenital 21- hydroxylase deficiency and autonomic failure syndromes. Drugs that can decrease catecholamine levels include clonidine, disulfiram, guanethidine, monoamine oxidase inhibitors (MAOIs), salicylates and Metyrosine therapy. Low levels of precursor norepinephrine may result in low epinephrine levels.

Phenylethanolamine N-methyltransferase (PNMT) methylates norepinephrine to form epinephrine, using S-adenosyl-L-methionine (SAM) as the methyl donor. Individual production and response to epinephrine levels may be influenced in part by genetic polymorphisms (SNPs) in the PNMT enzyme.

References:

Goldstein, DS. (2010) Catecholamines 101. *Clinical autonomic research: Official Journal of the Clinical Autonomic Research Society*, vol. 20(6) p.331-52.

Ji, Y; Snyder, EM; Fridley, BL; et al. (2008) Human phenylethanolamine N-methyltransferase genetic polymorphisms and exercise-induced epinephrine release. *Physiol Genomics* vol. 33 (3) p. 323-332.

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Glutamate LOW

The level of glutamate is lower than expected in this sample. Glutamate is a non-essential amino acid that acts as an excitatory neurotransmitter for metabolic signaling pathways. Glutamate signaling affects neuron maturation, plasticity and higher cognitive functions.

Decreased Glutamate signaling may contribute to apoptosis (death) of immature neurons. Reduced glutamate signaling has also been associated with elevations in dopamine which may contribute to symptoms of schizophrenia. Glutamate signaling may occur through a variety of Glutamate receptors. N-methyl-D-aspartate (NMDA) receptor signals are the most complex, as the receptor requires both

glutamate and glycine to function. Research continues into associations between glutamate signaling and cognitive disorders.

In the central nervous system (CNS), glutamate is recognized as the primary excitatory neurotransmitter and the glutamate signaling system is involved in fast synaptic transmission between neurons. The blood-brain barrier prevents the passage of glutamate. Astroglial cells are the primary source of glutamate in the CNS. Enteric glial cells may be important in glutamate signaling within the gut as neurotransmitter receptors and glial cells respond to dietary L-glutamate and monosodium glutamate (MSG).

References:

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Histamine LOW

The level of histamine in this sample is lower than expected. Histamine is one of the most important neurotransmitters to stimulate and maintain arousal in the central nervous system (CNS). Histamine-acetylcholine signal interactions influence wakefulness (arousal), circadian rhythms, appetite control, learning, memory and emotion.

The essential amino acid histidine is converted to histamine. Histamine synthesis may be influenced by oxidative stress, glucocorticoids and gastrin. Vitamin B-6 deficiency may impair histamine synthesis. Two rare genetic disorders, histidine ammonia-lyase deficiency or histidine decarboxylase deficiency, may prevent the conversion of histidine to histamine. Sedatives such as ethanol, tetrahydrocannabinol, barbiturates and benzodiazepines may also decrease histamine levels.

Alterations in CNS histamine levels may contribute to age-related neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. Low levels of histamine in the CNS may also contribute to Tourette's syndrome, narcolepsy and other hypersomnia disorders. Histamine levels in the CNS may be reduced by nicotinic and serotonergic signaling.

References:

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Phenylethylamine (PEA) LOW

The level of phenylethylamine (B-phenylethylamine or PEA) is lower than expected in this sample. PEA is considered a trace amine neuromodulator; it modifies the effects of neurotransmitter signals on cells or receptors. Trace amines may be found in both the central and peripheral nervous systems ù there are trace amine receptors in vascular and renal tissues. Trace amines and their metabolites are excreted through the kidney into the urine.

Low PEA levels have been associated with Parkinson's disease, depression, attention deficit hyperactivity disorder (ADHD) and autism. Trace amines may play a role in the activation or regulation of immune responses. PEA may alter a cell's response to dopamine and norepinephrine. PEA may have endocrine effects and inhibit prolactin secretion. Levels of PEA are not associated with neuronal responses to serotonin, GABA or glutamate.

PEA is derived from the amino acid phenylalanine. Low levels of phenylalanine may contribute to low PEA levels. Phenylalanine levels may be depleted by stress. PEA synthesis requires vitamin B6. PEA excretion may be influenced by diurnal rhythms; larger amounts are excreted during the late evening and early morning hours.

References:

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N/E Ratio

Elevated N/E ratio may be consistent with poor conversion of norepinephrine to epinephrine. This conversion is driven by the phenylethanolamine N-methyltransferase (PNMT) enzyme that requires SAME, magnesium and cortisol (adequate HPA axis function) as cofactors. Consider the actual levels of both neurotransmitters, and interpret in the ratio in context of cortisol levels/HPA axis function. Optimization of HPA axis function may be clinically warranted.

Taurine (2-aminoethane- sulfonic acid) HIGH

The level of taurine in this sample is higher than expected. Taurine acts as a neuromodulator and exerts, in vitro, an inhibitory effect on the firing rate of neurons in the central nervous system (CNS). Taurine has been shown in human and animal studies to have mild anti-convulsive effects. Taurine promotes neural development in both the embryonic brain and the adult brain.

High plasma taurine may be associated with stress reactions, depression and psychosis. Patients with Cushing's disease may have elevated urinary taurine levels, but low plasma levels. Patients with autism may have elevated urine taurine, glycine and alanine with low glutamate. Elevated urinary taurine levels may result from inherited renal defects, liver disease, heart disease or radiation injury. Gastrointestinal dybiosis with associated excess beta-alanine can cause taurine wasting in the urine (high). Oral supplementation may raise urinary taurine levels. Taurine is an ingredient in many "energy drinks" and taurine supplements are used by some athletes.

Taurine is excreted via urine and bile. A renal wasting condition may result in elevated urine taurine with a low plasma taurine level. The amount of taurine excreted daily is affected by various factors including genetics, age, gender, diet, renal function and medical conditions.

References:

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<http://news.cornell.edu/stories/2008/02/scientists-close-taurines-activity-brain>

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Tyramine LOW

The level of tyramine is lower than expected in this sample. Tyramine is derived from the essential amino acid phenylalanine. Tyramine and the other trace amines are found at low levels in the brain. Trace amines are not considered neurotransmitters; they are believed to act as neuromodulators. Evidence indicates that tyramine may alter neuronal responsiveness,

neuron active transport mechanisms and vesicle dynamics. Low levels of the precursor amino acid phenylalanine or its metabolite tyrosine, may contribute to low tyramine levels. Reserpine may deplete CNS levels of trace amines. Trace amines and their metabolites are excreted through the kidney into the urine.

Multiple studies demonstrate that loss of neurons in specific brain areas or loss of specific types of neurons may result in decreased trace amine levels. Low tyramine levels or deficient trace amine functions may be associated with some depressive disorders. Tyramine has been shown to inhibit the responses of gamma-aminobutyric acid (GABA) receptors (in vitro).

Aromatic L-amino acid decarboxylase (AADC) is the rate-limiting enzyme in tyramine synthesis. Altered AADC activity may alter trace amine levels which may affect dopamine signaling. Loss of specialized dopamine neurons containing AADC have been associated with some forms of schizophrenia. Trace amines are metabolized by monoamine oxidase (MAO A/B).

References:

Berry, MD. (2007), The potential of trace amines and their receptors for treating neurological and psychiatric diseases. *Reviews on Recent Clinical Trials* vol. 2 p. 3-19.

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Metanephrine LOW

Metanephrine is lower than expected in this sample. Metanephrine is a metabolite of epinephrine. Clinically, metanephrine levels provide an indication of adrenal medulla metabolism of epinephrine prior to its release into circulation. The metabolites are usually present in the urine in low and fluctuating levels.

Decreases in epinephrine levels will also decrease metanephrine levels. Pure autonomic failure syndromes decrease adrenomedullar function and may decrease epinephrine and metanephrine levels. Metyrosine therapy may lower both epinephrine and metanephrine levels. There is scant literature describing the symptoms of pure epinephrine and/or metanephrine insufficiency. However, conditions that may be associated with low epinephrine levels include Addison's disease, diabetic nephropathy and autonomic failure syndromes.

Approximately 93% of circulating metanephrine is derived from catecholamine metabolism through the enzyme catechol-O methyl transferase (COMT) in the adrenal medulla. In the normal population, plasma normetanephrine levels are low. Acquired or inherited deficiencies in COMT may result in low metanephrine levels. COMT activity requires S-adenosyl-L-methionine (SAM) and magnesium, and may be suppressed by single nucleotide polymorphisms (SNPs). Phenylethanolamine N-methyltransferase (PNMT) deficiency or 21-dehydroxylase deficiency may decrease epinephrine and metanephrine levels.

Plasma concentrations of total metanephrine (free plus conjugated metanephrine) largely reflect conjugated gastrointestinal metanephrine). Total urinary metanephrine is more clinically relevant and is reported by Doctor's Data.

References:

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Creatinine

The urinary creatinine concentration (CC) presented in this report represents the actual creatinine concentration in the specimen that was submitted. Under normal conditions, the rate of excretion of creatinine is quite constant and highly correlated with lean body mass (muscle). However, the CC can vary significantly as a function of urine volume. An unusually high CC most likely indicates poor hydration of the patient at the time of the urine collection. A very low CC most likely indicates unusually high fluid consumption, or perhaps the influence of diuretics. If the urine specimen is very dilute (extremely low CC), the accuracy of the neurotransmitter analysis may be compromised due to analytical detection limits. It is emphasized that the CC in this specimen should not be utilized to assess renal function or glomerular filtration. For that purpose, one should perform a bona fide creatinine clearance test.

For a given age and gender, intra-individual variability in daily creatinine excretion can vary by as much as two-fold. Therefore, to more accurately assess neurotransmitter status using a random collection, the reported values for each analyte are expressed per gram "normalized" creatinine.