# Neuro-Biogenic Amines; urine first morning void

<table>
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<tr>
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<th>RESULT/UNIT per creatinine</th>
<th>REFERENCE INTERVAL</th>
<th>2.5th</th>
<th>10th</th>
<th>50th</th>
<th>90th</th>
<th>97.5th</th>
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<td>Dopamine, free</td>
<td>111 µg/g</td>
<td>65–400</td>
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<td>Epinephrine, free</td>
<td>1.4 µg/g</td>
<td>1.5–20</td>
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<tr>
<td>Norepinephrine, free</td>
<td>9.7 µg/g</td>
<td>15–78</td>
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<td>Serotonin</td>
<td>531 µg/g</td>
<td>52–155</td>
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<td>Histamine</td>
<td>52 µg/g</td>
<td>12–66</td>
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<td>Gamma-aminobutyrate (GABA)</td>
<td>2.9 µmol/g</td>
<td>1.6–8</td>
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<td>Glutamate</td>
<td>15 µmol/g</td>
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<td>Glycine</td>
<td>538 µmol/g</td>
<td>350–3500</td>
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<td>Phenethylamine (PEA)</td>
<td>279 nmol/g</td>
<td>20–176</td>
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<td>Creatinine</td>
<td>69 mg/dL</td>
<td>30–225</td>
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</table>

Norepinephrine : Epinephrine ratio 6.8 < 11

**SPECIMEN DATA**

- **Comments:**
- **Date Collected:** 06/07/2017
- **Wake-up time:**
- **Volume:**
- **Date Received:** 06/15/2017
- **Time Collected:** 07:00 AM
- **Body Mass Index:** 22
- **Date Completed:** 06/16/2017
- **Collection Period:** first 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:


Kaidanovich-Beilin, O; Cha, DS; McIntyre RS. (2012) Crosstalk between metabolic and neuropsychiatric disorders, F1000 Biology Reports vol. 4 p. 14.


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Zucchi, R; Chiellini, G; Scanlan, TS; et al. (2006) Trace amine-associated receptors and their ligands, British Journal of Pharmacology vol. 149 (8) p. 967-78.

Norepinephrine LOW

The level of norepinephrine is lower than expected in this sample. Norepinephrine is a catecholamine hormone and neurotransmitter secreted by the adrenal gland. It is the principal neurotransmitter in sympathetic nerve endings. Norepinephrine may help regulate vigilant attention, cognition and sleep. Studies indicate that the brain contributes at most 20% of circulating norepinephrine levels.

Low levels of norepinephrine may be associated with conditions such as orthostatic hypotension, dopamine beta-hydroxylase (DBH) enzyme deficiency and Menke’s disease. Alpha-2 agonistic pharmaceuticals decrease sympathetic nerve outflow and norepinephrine levels. Metyrosine therapy may decrease norepinephrine levels. Surgical sympathectomy or medical conditions that disrupt autonomic nerve functions may also decrease norepinephrine levels. Low levels of precursor amino acids phenylalanine or tyrosine, or low levels of the precursor neurotransmitter dopamine may result in low norepinephrine levels.

The synthesis of norepinephrine from dopamine requires Vitamin C and copper. About half of all norepinephrine is produced in the gastrointestinal tract, pancreas and spleen. Most of the norepinephrine produced by these mesenteric organs is removed from portal vein blood by the liver and converted to vanillylmandelic acid (VMA) for excretion.

References:


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.

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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:


Serotonin HIGH

The level of serotonin in this sample is higher than expected. Serotonin signaling in the central nervous system (CNS) may influence mood, appetite, sleep, memory and learning, homeostasis, and sexual behaviors. Altered levels of urinary or plasma serotonin are thought to play a role in many disorders including anxiety, depression, obsessive compulsive disorder and phobias. Elevated plasma serotonin and platelet serotonin levels are a common finding in autistic patients, and may contribute to psychiatric disorders such as schizophrenia. There are a great many serotonin receptors with different affinities, expression and function.

The main diseases that may be associated with elevated levels of serotonin are neuroectodermal tumors, in particular carcinoid tumors arising from gastrointestinal (GI) enterochromaffin cells. Only about 10% of mid-gut carcinoids produce enough serotonin to cause symptoms. Symptoms of serotonin excess (Serotonin Syndrome), are wide-ranging. A triad of symptoms including altered mental status (usually anxiety), neuromuscular hyperactivity or hyperreflexia, and autonomic instability, is suspicious for serotonin excess.

Exogenous estrogens have been shown to raise both serotonin and 5-HIAA levels in post-menopausal women. Serotonin levels may be increased by exercise, increased daylight (or daylight equivalent) exposure, low-protein or high-carbohydrate meals, insulin, or by Tryptophan or 5-hydroxytryptophan 5-HTP supplements. Some studies indicate that therapeutic massage may also elevate serotonin levels. The herbs St. John’s wort and ginseng may elevate serotonin levels. Medications that may increase serotonin include:

- serotonin reuptake inhibitors (SSRIs)
- monoamine oxidase inhibitors (MAOIs)
- antidepressants: bupropion, trazodone
- migraine medications

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- pain medications
- lithium
- dextromethorphan (cough suppressant)
- anti-emetics

The gastrointestinal tract produces about 80% of the body’s serotonin. During the “first pass” through hepatic circulation, monoamine oxidase A (MAO-A) metabolizes 30-80% of GI serotonin to -hydroxyindoleacetic acid (5-HIAA). Serotonin metabolism requires selenium, magnesium and vitamin B3 as cofactors. Mutations, or single nucleotide polymorphisms (SNPs), in MAO-A may affect serotonin degradation. SNPs or mutations in serotonin receptors may affect responses to serotonin.

References:


Field, T; Hernandez-Reif, M; Diego, M; et al. (2009), Cortisol decreases and serotonin and dopamine increase following massage therapy, Informa UK Ltd UK.


Jovanovic, H; Lundberg, J; Karlsson, P; Cerin, et al. (2008), Sex differences in the serotonin 1A receptor and serotonin transporter binding in the human brain measured by PET. NeuroImage vol. 39 (3) p. 1408-19.


Phenylethylamine (PEA) HIGH

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

The interaction of trace amines and trace amine-associated receptors (TAARs) in the brain may play a role in psychiatric and neurological disease processes. Elevated PEA has been associated with
Experiments in humans and animals have associated PEA elevations with stress or anxiety. Very high levels may have amphetamine-like effects and may induce seizures (animal studies). Patients with hypertension or bone disease may also have elevated PEA levels. Elevations in PEA levels have been reported during the use of monoamine oxidase inhibitors (MAOIs) or antipsychotic medications. PEA may alter a cell’s response to dopamine and norepinephrine. PEA may have endocrine effects and inhibit prolactin secretion. Animal studies indicate that PEA may increase glucocorticoid levels and PEA has been shown to stimulate acetylcholine release. Levels of PEA are not associated with neuron responses to serotonin, GABA or glutamate. Monoamine oxidase inhibitor (MAOI) medications may increase trace amine levels without affecting levels of other neurotransmitters. Trace amines may play a role in the activation or regulation of immune responses. PEA excretion may be influenced by diurnal rhythms; larger amounts are excreted during the late evening and early morning hours. Exercise, high protein diets or supplements may also increase PEA levels. High levels of the phenylalanine may result in high PEA levels.

Trace amines may be generated in the gastrointestinal tract by protein-fermenting gut bacteria after a protein-rich meal, and they may be found in a variety of foods as the result of food spoilage or deliberate fermentation. Dietary trace amines are usually metabolized quickly by MAO enzymes. PEA is primarily oxidized by MAO-B which may require selenium.

References:


Husebye, ES; Boe, AS; Rorsman, F; et al. (2000), Inhibition of aromatic L-amino acid decarboxylase activity by human autoantibodies. Clinical and Experimental Immunology vol. 120 (3) p. 420-3.

Licata, AA; Radfar, N; Bartter, FC. (1978), The urinary excretion of phosphoethanolamine in diseases other than hypophosphatasia. The American Journal of Medicine vol. 64 (1) p. 133-138.


Zucchi, R; Chiellini, G; Scanlan, T S; et al. (2006), Trace amine-associated receptors and their ligands. British Journal of Pharmacology vol. 149 (8) p. 967-78.

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.