

# TEST REPORT

# 2018 06 10 300 U

Ordering Provider:  
Getuwell Clinic

Samples Received  
06/14/2018  
Report Date  
06/21/2018

Samples Collected  
Urine - 06/05/18 05:30  
Urine - 06/05/18 07:30  
Urine - 06/05/18 18:00  
Urine - 06/05/18 22:00

Patient Name: Advanced Neurotransmitters  
Patient Phone Number: 555 555 5555

|                    |            |       |
|--------------------|------------|-------|
| Gender             | Height     | Waist |
| Male               | 5 ft 11 in | 38 in |
| DOB                | Weight     | BMI   |
| 5/17/1958 (60 yrs) | 200 lb     | 27.9  |

| TEST NAME                                   | RESULTS   06/05/18 | RANGE                                     |
|---|--------------------|---|
| <b>Urinary Inhibitory Neurotransmitters</b> |                    |   |
| Serotonin                                   | 72.6               | 47.6 -140.3 µg/g Cr (Optimal 61.0 -103.2) |
| 5-HIAA                                      | 3857               | 2205 -11816 µg/g Cr (Optimal 2988 -5850)  |
| GABA  | 341                | 167-463 µg/g Cr (Optimal 193 -367)        |
| Glycine                                     | 56                 | 41-295 mg/g Cr (Optimal 61 -159)          |
| <b>Urinary Excitatory Neurotransmitters</b> |                    |   |
| Glutamate                                   | 1436               | 1213 -4246 µg/g Cr (Optimal 1515 -2710)   |
| Histamine                                   | 14.0               | 3.6-44.3 µg/g Cr (Optimal 5.2 -15.3)      |
| PEA   | 20.0               | 3.6-38.8 µg/g Cr (Optimal 5.3 -16.1)      |
| Dopamine                                    | 284 H              | 103 -282 µg/g Cr (Optimal 144 -240)       |
| DOPAC                                       | 1575               | 495 -2456 µg/g Cr (Optimal 658 -1449)     |
| HVA   | 6122               | 3025 -9654 µg/g Cr (Optimal 3737 -7048)   |
| Norepinephrine (pooled)                     | 21.8               | 10.0 -35.7 µg/g Cr (Optimal 15.0 -28.1)   |
| Normetanephrine                             | 18.1               | 13.4 -44.8 µg/g Cr (Optimal 17.9 -31.7)   |
| Epinephrine (pooled)                        | 3.3                | 0.8-6.2 µg/g Cr (Optimal 1.4 -4.2)        |
| Ratio: Norepi/Epi                           | 6.6                | 2.9-25.2 (Optimal 5.2 -13.7)              |
| VMA   | 2849               | 1996 -5939 µg/g Cr (Optimal 2580 -4766)   |
| <b>Urinary Free Diurnal Cortisol</b>        |                    |   |
| Free Cortisol                               | 57.28 H            | 7.8-29.5 µg/g Cr (1st Morning)            |

| TEST NAME                             | RESULTS   06/05/18 | RANGE                            |
|---------------------------------------|--------------------|----------------------------------|
| <b>Urinary Free Diurnal Cortisol</b>  |                    |                                  |
| Free Cortisol                         | 9.54 L             | 23.4-68.9 µg/g Cr (2nd Morning)  |
| Free Cortisol                         | 10.51              | 6.0-19.2 µg/g Cr (Evening)       |
| Free Cortisol                         | 4.13               | 2.6-8.4 µg/g Cr (Night)          |
| <b>Urinary Free Diurnal Cortisone</b> |                    |                                  |
| Free Cortisone                        | 234.25 H           | 31.6-91.6 µg/g Cr (1st Morning)  |
| Free Cortisone                        | 53.48 L            | 63.3-175.8 µg/g Cr (2nd Morning) |
| Free Cortisone                        | 66.80              | 30.6-88.5 µg/g Cr (Evening)      |
| Free Cortisone                        | 25.99              | 15.5-44.7 µg/g Cr (Night)        |
| <b>Urinary Diurnal Melatonin MT6s</b> |                    |                                  |
| Melatonin                             | 6.14 L             | 10.1-26.0 µg/g Cr (1st Morning)  |
| Melatonin                             | 5.79 L             | 6.0-17.0 µg/g Cr (2nd Morning)   |
| Melatonin                             | 1.69               | 0.5-3.6 µg/g Cr (Evening)        |
| Melatonin                             | 1.70               | 1.3-8.4 µg/g Cr (Night)          |
| <b>Urinary Diurnal Norepinephrine</b> |                    |                                  |
| Norepinephrine                        | 40.60 H            | 9.4-22.0 µg/g Cr (1st Morning)   |
| Norepinephrine                        | 22.74              | 12.6-38.2 µg/g Cr (2nd Morning)  |
| Norepinephrine                        | 51.42 H            | 21.1-42.9 µg/g Cr (Evening)      |
| Norepinephrine                        | 29.77              | 16.9-38.8 µg/g Cr (Night)        |
| <b>Urinary Diurnal Epinephrine</b>    |                    |                                  |
| Epinephrine                           | 7.33 H             | 0.5-1.5 µg/g Cr (1st Morning)    |
| Epinephrine                           | 1.24               | 0.7-6.1 µg/g Cr (2nd Morning)    |
| Epinephrine                           | 6.96               | 2.3-8.1 µg/g Cr (Evening)        |
| Epinephrine                           | 4.12               | 1.2-4.2 µg/g Cr (Night)          |
| <b>Urinary Creatinine</b>             |                    |                                  |
| Creatinine (pooled)                   | 0.92               | 0.3-2.0 mg/mL                    |
| Creatinine                            | 0.34               | 0.3-2.0 mg/mL (1st morning)      |
| Creatinine                            | 1.54               | 0.3-2.0 mg/mL (2nd morning)      |
| Creatinine                            | 0.56               | 0.3-2.0 mg/mL (Evening)          |

| TEST NAME | RESULTS   06/05/18 | RANGE |
|-----------|--------------------|-------|
|-----------|--------------------|-------|

Urinary Creatinine

|            |      |                       |
|------------|------|-----------------------|
| Creatinine | 1.24 | 0.3-2.0 mg/mL (Night) |
|------------|------|-----------------------|

<dL = Less than the detectable limit of the lab. N/A = Not applicable; 1 or more values used in this calculation is less than the detectable limit. H = High. L = Low.

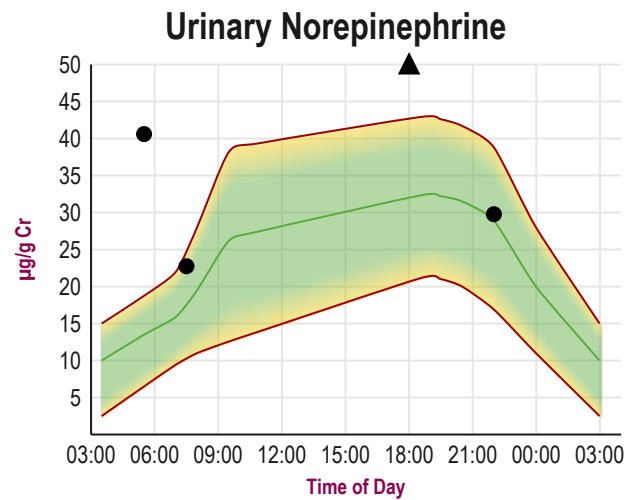
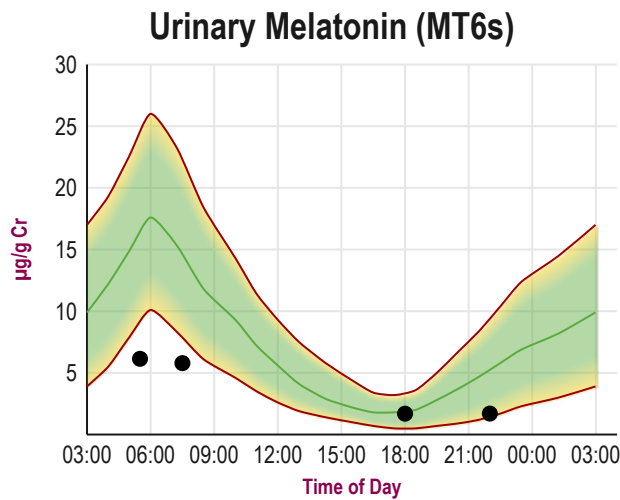
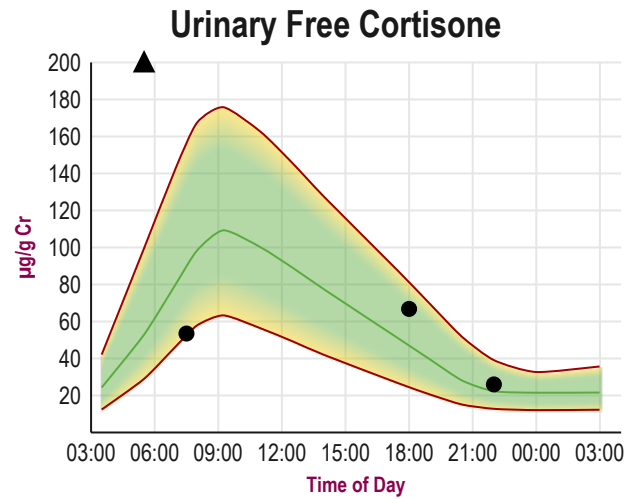
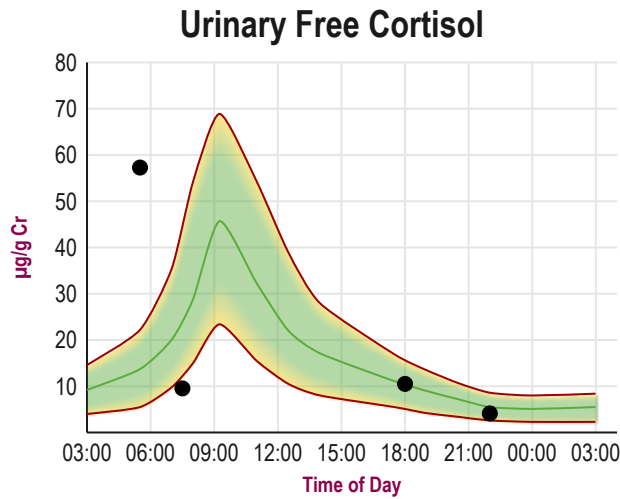
Therapies

BID topical Clobex (clobetasol propionate) (Pharmaceutical) (7 Hours Last Used)

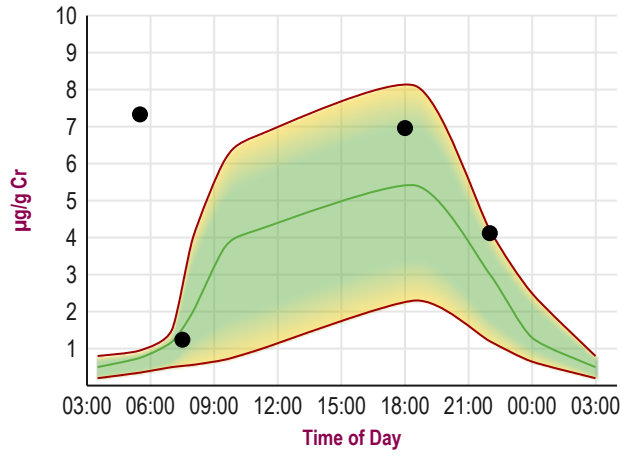
Graphs

**Disclaimer:** Graphs below represent averages for healthy individuals not using hormones. Supplementation ranges may be higher. Please see supplementation ranges and lab comments if results are higher or lower than expected.

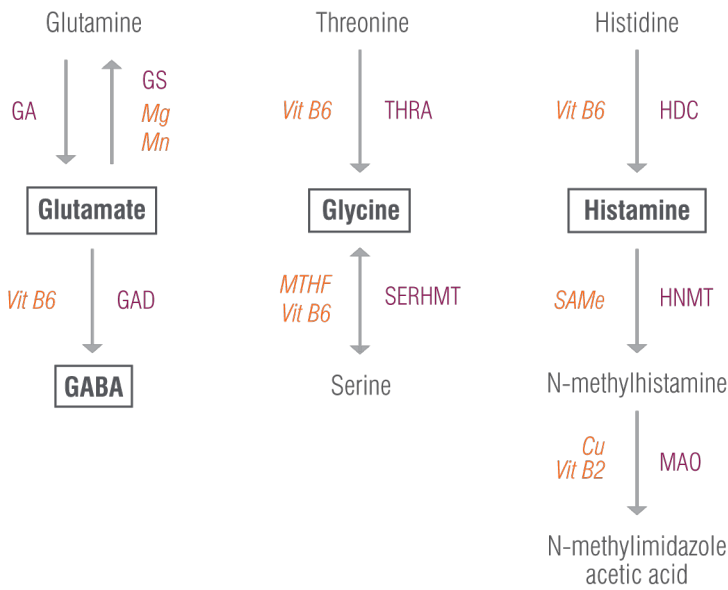
— Average ▼▲ Off Graph



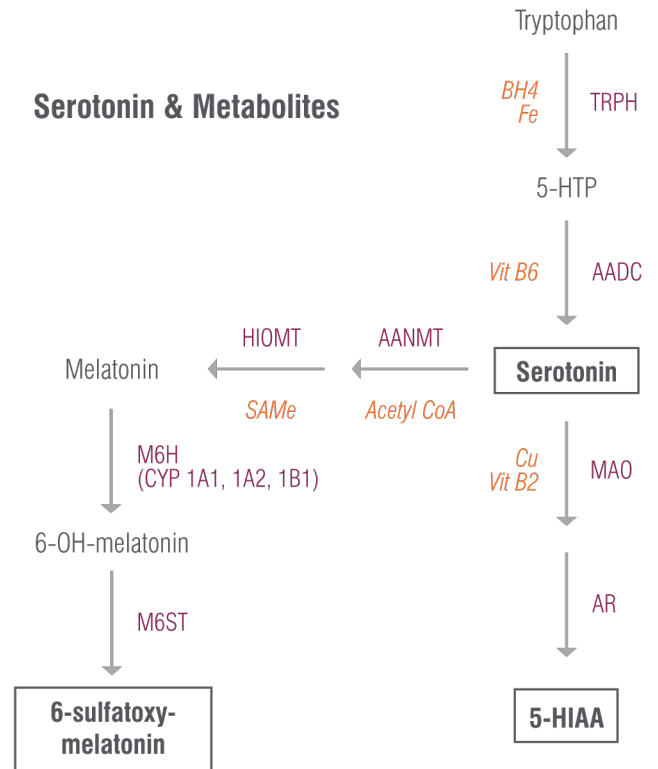
### Urinary Epinephrine



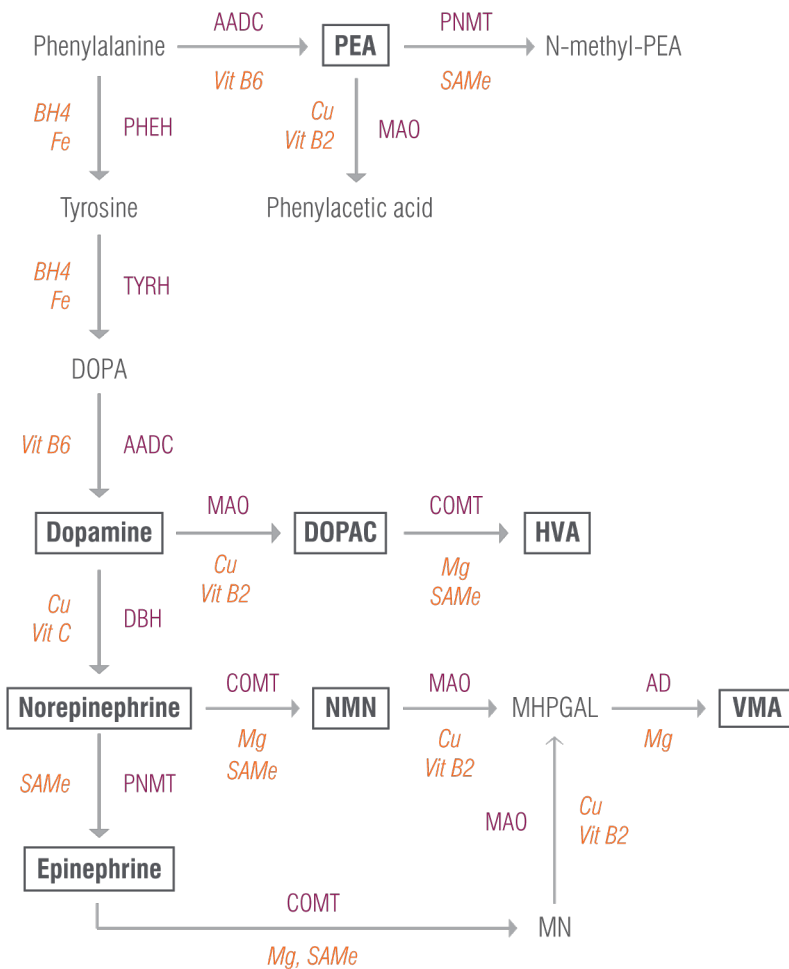
## Glutamate/GABA, Glycine & Histamine



## Serotonin & Metabolites



## Catecholamines & Metabolites



Neurotransmitters & Metabolites:

|        |                               |
|--------|-------------------------------|
| HVA    | homovanillic acid             |
| NMN    | normetanephrine               |
| PEA    | phenethylamine                |
| VMA    | vanillylmandelic acid         |
| 5-HIAA | 5-hydroxyindole 3-acetic acid |

Enzymes:

|        |  |
|--------|--|
| AADC   | aromatic L-amino acid decarboxylase    |
| AANMT  | arylalkylamine N-methyltransferase     |
| AD     | aldehyde dehydrogenase                 |
| AR     | aldehyde reductase                     |
| COMT   | catechol-O-methyltransferase           |
| DBH    | dopamine beta hydroxylase              |
| GA     | glutaminase                            |
| GAD    | glutamate decarboxylase                |
| GS     | glutamine synthetase                   |
| HDC    | histidine decarboxylase                |
| HIOMT  | hydroxyindole-O-methyltransferase      |
| HNMT   | histamine N-methyltransferase          |
| MAO    | monoamine oxidase                      |
| M6H    | melatonin 6 hydroxylase                |
| M6ST   | melatonin 6 sulfotransferase           |
| PHEH   | phenylalanine hydroxylase              |
| PNMT   | phenylethanolamine N-methyltransferase |
| SERHMT | serine hydroxymethyltransferase        |
| THRA   | threonine aldolase                     |
| TRPH   | tryptophan hydroxylase                 |
| TYRH   | tyrosine hydroxylase                   |

Cofactors:

|                       |                        |
|-----------------------|------------------------|
| BH4                   | tetrahydrobiopterine   |
| Cu                    | copper                 |
| Fe                    | iron                   |
| Mg                    | magnesium              |
| Mn                    | manganese              |
| MTHF                  | methyltetrahydrofolate |
| S-Adenosyl Methionine | S-adenosyl methionine  |

**Disclaimer:** Symptom Categories below show percent of symptoms self-reported by the patient compared to total available symptoms for each category. For detailed information on category breakdowns, go to [www.zrtlab.com/patient-symptoms](http://www.zrtlab.com/patient-symptoms).

| SYMPTOM CATEGORIES                           | RESULTS   06/05/18 |
|--|--------------------|
| Estrogen / Progesterone Deficiency           | 14%                |
| Estrogen Dominance / Progesterone Deficiency | 21%                |
| Low Androgens (DHEA/Testosterone)            | 44%                |
| High Androgens (DHEA/Testosterone)           | 25%                |
| Low Cortisol                                 | 44%                |
| High Cortisol                                | 46%                |
| Hypometabolism                               | 36%                |
| Metabolic Syndrome                           | 51%                |

| SYMPTOM CHECKLIST          | MILD  | MODERATE | SEVERE |
|----------------------------|-------|----------|--------|
| Acne                       |       |          |        |
| Aggressive Behavior        |       |          |        |
| Allergies                  |       |          |        |
| Anxious                    |       |          |        |
| Apathy                     |       |          |        |
| Blood Pressure High        |       |          |        |
| Blood Pressure Low         |       |          |        |
| Blood Sugar Low            |       |          |        |
| Body Temperature Cold      |       |          |        |
| Bone Loss                  |       |          |        |
| Burned Out Feeling         |       |          |        |
| Chemical Sensitivity       |       |          |        |
| Cholesterol High           | BLANK |          |        |
| Constipation               |       |          |        |
| Depressed                  |       |          |        |
| Dizzy Spells               |       |          |        |
| Erections Decreased        |       |          |        |
| Fatigue - Evening          |       |          |        |
| Fatigue - Mental           |       |          |        |
| Fatigue - Morning          |       |          |        |
| Flexibility Decreased      |       |          |        |
| Forgetfulness Increased    |       |          |        |
| Goiter                     |       |          |        |
| Hair - Dry or Brittle      |       |          |        |
| Hair or Skin Oily          |       |          |        |
| Headaches                  |       |          |        |
| Hearing Loss               |       |          |        |
| Heart Palpitations         |       |          |        |
| Hoarseness                 |       |          |        |
| Hot Flashes                |       |          |        |
| Infertility                |       |          |        |
| Irritable                  |       |          |        |
| Joint Pain Increased       |       |          |        |
| Libido Decreased           |       |          |        |
| Mental Sharpness Decreased |       |          |        |
| Muscle Size Decreased      |       |          |        |
| Muscle Soreness            |       |          |        |
| Nails Breaking or Brittle  |       |          |        |
| Neck or Back Pain          |       |          |        |
| Nervous                    |       |          |        |
| Night Sweats               |       |          |        |

| SYMPTOM CHECKLIST            | MILD                                  | MODERATE | SEVERE |
|------------------------------|---------------------------------------|----------|--------|
| Numbness - Feet or Hands     | [Progressive bar from Mild to Severe] |          |        |
| Prostate Cancer              | BLANK                                 |          |        |
| Prostate Problems            | [Small bar in Mild]                   |          |        |
| Pulse Rate Slow              | [Progressive bar from Mild to Severe] |          |        |
| Rapid Aging                  | [Small bar in Mild]                   |          |        |
| Rapid Heartbeat              | [Small bar in Mild]                   |          |        |
| Ringing In Ears              | [Progressive bar from Mild to Severe] |          |        |
| Skin Thinning                | [Progressive bar from Mild to Severe] |          |        |
| Sleeping Difficulty          | [Progressive bar from Mild to Severe] |          |        |
| Stamina Decreased            | [Progressive bar from Mild to Severe] |          |        |
| Stress                       | [Progressive bar from Mild to Severe] |          |        |
| Sugar Cravings               | [Small bar in Mild]                   |          |        |
| Sweating Decreased           | [Small bar in Mild]                   |          |        |
| Swelling or Puffy Eyes/Face  | [Small bar in Mild]                   |          |        |
| Triglycerides Elevated       | [Small bar in Mild]                   |          |        |
| Urinary Urge Increased       | [Small bar in Mild]                   |          |        |
| Urine Flow Decreased         | [Small bar in Mild]                   |          |        |
| Weight Gain - Breast or Hips | [Progressive bar from Mild to Severe] |          |        |
| Weight Gain - Waist          | [Progressive bar from Mild to Severe] |          |        |

## Lab Comments

### INHIBITORY NEUROTRANSMITTERS

#### SEROTONIN

Serotonin is within reference range. Serotonin has calming effects and contributes to the feelings of well-being. Serotonin elevates mood, decreases anxiety, appetite, and libido, improves sleep and memory, eases depression, and helps regulate body temperature. Most of serotonin in the human body is produced in the gastrointestinal tract, where it stimulates gut motility.

#### 5-HIAA

5-hydroxyindoleacetic acid (5HIAA) is within reference range. 5HIAA is the primary metabolite of serotonin via the actions of monoamine oxidase and aldehyde dehydrogenase enzymes.

#### GABA

GABA is within the reference range. The brain's major inhibitory neurotransmitter GABA functions as the off switch in the brain. GABA is essential to limiting excitation so that input signals are balanced and not overdone. GABA prevents anxiety, improves mood, promotes sleep, lowers blood pressure, acts as a muscle relaxant, aids in formation and storage of fear memories, increases insulin secretion and decreases blood glucose levels.

#### GLYCINE

Glycine is lower than the optimal range, which may be due to depression (self-reported). Although research on urinary levels of glycine is scarce, levels of glycine in blood are lower in depressed individuals than in controls (Altamura, et. al. 1995).

Glycine is a neurotransmitter and a simple, nonessential (can be made in the body) amino acid that plays a role in the production of DNA, phospholipids, collagen, creatine, heme and glutathione. Glycine serves as an anti-inflammatory agent, calms aggression, improves sleep quality, stabilizes blood sugar, improves metabolic parameters and modulates excitatory signals in the brain. Low levels may be indicative of chronically increased demand for tetrahydrofolate (active folic acid) production, for which glycine serves as a precursor.

Additional research studies show that urinary glycine levels are reduced after intense exercise (Corsetti, et. al. 2016), and in patients with rheumatoid arthritis (Jones, et. al. 2005), or hypometabolic disorders, such as hypothyroidism (Friedrich, et. al. 2017), obesity (Ahmad, et. al. 2016), and diabetes (Sasaki, et. al. 1988).

THERAPEUTIC CONSIDERATIONS: Glycine supplementation, vitamin B6, serine and MTHF may all support optimal glycine levels.

### EXCITATORY NEUROTRANSMITTERS

#### GLUTAMATE

Glutamate is low-normal (< 20th percentile). The brain's major excitatory neurotransmitter glutamate functions as the "on" switch in the brain. Glutamate regulates appetite, thinking, increases gut motility, optimizes learning, modulates memory, improves libido, and decreases sleep. Low urinary glutamate levels have been reported in patients with migraines (Ragginer et al., 2012). Clinically, lower glutamate levels may contribute to agitation, depression, chronic fatigue, lack of concentration, low energy levels, and sleep difficulties.

THERAPEUTIC CONSIDERATIONS:: L-glutamine may be beneficial to restore glutamate to normal values.

**HISTAMINE**

Histamine is within reference range. Histamine plays a dual role in the body as a neurotransmitter and a modulator of the immune system. Histamine has anti-pain properties, plays a neuroprotective role in the brain, and contributes to optimal maintenance of cognition and memory. Histamine stimulates wakefulness and decreases sleep, stimulates gastric acid production, increases metabolism, suppresses appetite, and prevents weight gain. Histamine is a potent vasodilator and a pro-inflammatory agent.

**PEA**

PEA is high-normal (>80th percentile). PEA, also known as phenethylamine, promotes energy, elevates mood, and regulates attention. PEA also contributes to aggression, serves as a biomarker for ADHD, and prolongs the signaling of dopamine, norepinephrine, and serotonin. Urinary PEA levels increase after amphetamine use (Kusaga et al., 2002; Zemetkin et al., 1984), exercise (Szabo et al., 2001), and in the following disorders: bipolar disorder (Karoum et al., 1982), phenylketonuria (Reynolds et al., 1978), schizophrenia (O'Reilly and Davis, 1994), postpartum period (Taylor et al., 1996), and in severe anxiety and insomnia (DeLisi et al., 1984). High PEA is suspected in the etiology of anxiety, inflammation, inability to focus, sleep difficulties, and toxicity.

**THERAPEUTIC CONSIDERATIONS:** Methylation cofactor support to aid metabolism may be beneficial.

**DOPAMINE**

Dopamine is elevated. Dopamine improves attention, focus, and motivation, helps with decision making, modulates movement control, promotes lactation, increases blood pressure, urine output and sodium excretion, and allows for feelings of reward and pleasure. Dopamine also serves as the parent precursor to norepinephrine and epinephrine. Research shows that urinary dopamine levels are elevated in patients with anxiety (Field et al., 2010), increased sodium intake (Gill, Jr. et al., 1991), mercury toxicity (Houston, 2011), primary aldosteronism, post-traumatic stress disorder (Yehuda et al., 1992), and stress (Ghaddar et al., 2014). Supplements including the herb Mucuna (not indicated) may also increase levels. In rare cases, dopamine is elevated in patients with carcinoid tumors and pheochromocytomas (Davidson, 2005). Clinically, high dopamine is associated with anxiety, hyperactivity, inability to focus, mood swings, poor GI function, psychosis, and sleep disturbances.

**THERAPEUTIC CONSIDERATIONS:** Cofactor support with ascorbic acid, magnesium, and SAMe to promote metabolism may be beneficial.

**DOPAC**

DOPAC is high-normal (>80th percentile). DOPAC is the primary metabolite of dopamine formed via the actions of monoamine oxidase. Research shows that DOPAC is elevated in patients with anorexia nervosa (Van Binsbergen et al., 1991).

**HVA**

Homovanillic acid (HVA) is within reference range. HVA is a dopamine metabolite.

**NOREPINEPHRINE**

Norepinephrine is within reference range. Norepinephrine functions both as a neurotransmitter and a hormone, participating in the body's "fight or flight" response. Norepinephrine increases alertness, focuses attention, fine-tunes vigilance, increases blood pressure, heart rate, and blood sugar, reduces digestive activity, pain, and sleep, prevents bladder emptying, and regulates body temperature. Norepinephrine is very similar in structure and physiological effects to epinephrine. The adrenal gland produces approximately 20% of the total output with 80% produced by the sympathetic nerve fibers.

**NORMETANEPHRINE**

Normetanephrine is within reference range. Normetanephrine is a norepinephrine metabolite formed via the actions of catechol-O-methyl (COMT) transferase enzyme in response to stress.

**EPINEPHRINE**

Epinephrine is within reference range. Epinephrine, also called adrenaline, functions both as a neurotransmitter and a hormone, participating in the body's fight or flight response. Epinephrine increases alertness, focuses attention, fine-tunes vigilance, increases blood pressure, heart rate, and blood glucose, reduces digestive activity, pain and sleep, prevents bladder emptying, and regulates body temperature.

**VMA**

Vanillylmandelic acid (VMA) is within reference range. VMA is a norepinephrine and epinephrine metabolite formed via the actions of monoamine oxidase, catechol-O-methyl transferase (COMT), and aldehyde dehydrogenase.

**URINARY FREE CORTISOL (F) AND CORTISONE (E)**

Urinary free cortisol (F) and cortisone (E) are NOT following a normal circadian rhythm and levels are outside the expected reference ranges, particularly in the first two morning voids. F and E are very high in the first morning void, but drop precipitously in the second void but begin to recover to normal reference ranges in the evening and at night before bed. This individual has reported use of a synthetic glucocorticoid, commonly used topically for treating skin conditions associated with inflammation. Synthetic glucocorticoids that enter the systemic circulation suppress endogenous cortisol synthesis by negative feedback to the hypothalamic-pituitary-adrenal axis and lower ACTH/cortisol synthesis. The negative feedback is transient and may result in a rebound with higher synthesis of cortisol several hours afterward. Low second morning cortisol likely results from use of the synthetic glucocorticoid after collecting the first morning void. As seen in these results cortisol recovers to expected levels in the evening and at night before bed. A high F and E in the first morning void suggests that levels are high during sleep at night or rise rapidly just before waking (possible rebound from evening use of the synthetic glucocorticoid).



Overall, these results indicate that endogenous cortisol synthesis is high and is somewhat amplified by use of the topical synthetic glucocorticoid. Self-reported symptoms (e.g. excessive stress, fatigue, depression, irritability, decreased mental sharpness, weight gain most in the waist (belly fat), are consistent with overall high cortisol exposure.

While a normal daily adrenal output of cortisol is essential to maintain normal metabolic activity, help regulate steady state glucose levels (important for brain function and energy production), and optimize immune function, excessive levels of glucocorticoids (natural and synthetic) can have the opposite effect over time. For information about strategies to support adrenal health and reduce stress(ors) that can lead to excess or deficient cortisol synthesis, the following books are worth reading: "Adrenal Fatigue", by James L. Wilson, N.D., D.C., Ph.D.; "The Cortisol Connection", by Shawn Talbott, Ph.D.; "The End of Stress As We Know It" by Bruce McEwen; "The Role of Stress and the HPA Axis in Chronic Disease Management" by Thomas Guillems, PhD.

#### MELATONIN METABOLITE 6-SULFATOXYMELATONIN (MT6s)

The melatonin metabolite 6-sulfatoxymelatonin (MT6s) is not following a normal circadian rhythm. MT6s should be at its highest level in the first morning void, which is reflective of the dark period (night), but instead is low. Lower MT6s in the first morning void may reflect work during a night shift or staying up at night with excessive lighting (e.g. watching television). Some sleep (benzodiazepines, barbituates), pain (ibuprofen, opiates) and blood pressure medications (beta blockers like propranolol) are known to interfere with melatonin production and secretion and lower the circulating and excreted (MT6s) urinary levels of melatonin. Use of any of these medications at night before bed would result in a lower melatonin in the first morning void. The second morning void in this individual is also lower than the reference range. MT6s begins to rise thereafter in the evening and is within normal reference range at night before bed.

In a healthy individual the circadian rhythm of melatonin is inversely related to circulating levels of adrenal cortisol levels, i.e. melatonin rises with darkness and peaks about 2-3 am, while cortisol falls to its lowest level at this time of day. With morning and onset of light exposure, melatonin drops rapidly and cortisol rises, peaking to its highest level about 30 min to 1 hr after waking (referred to as a Cortisol Awakening Response-CAR). By mid-afternoon (evening void) with maximal light exposure melatonin reaches a nadir. It then gradually begins to rise again with nightfall and less light exposure, while cortisol continues to rise. Cortisol and melatonin reach their nadir and peak, respectively, about 2-3 am. Melatonin synthesis by the pineal gland is controlled by light exposure, while cortisol synthesis is controlled by the hypothalamic-pituitary axis in response to stressors. While melatonin and cortisol have opposing circadian rhythms neither hormone directly and acutely controls the synthesis of the other.

Melatonin is known to have many different beneficial effects in the body. For an excellent review of melatonin's many benefits please read: Pandi-Perumal et.al. Melatonin, Nature's most versatile biological signal. FEBS 273: 2813-2838, 2006. Melatonin has multiple roles in maintaining health. It helps slow the aging process, is a potent anti-oxidant, regulates the immune system, inhibits formation and growth of tumors such as breast and prostate cancers, and helps regulate the synthesis of the sex-hormones estradiol and progesterone (melatonin increases progesterone, decreases estrogens by inhibiting aromatase, and down-regulates cellular estrogen receptors, which diminishes response of estrogen-sensitive tissues to estrogens). Low melatonin is also thought to contribute to obesity in people with insomnia or those who do night shift work.

Because of its established role in the regulation of the circadian rhythm, treatment with exogenous melatonin has been found useful in people with circadian rhythm sleep disorders, such as delayed sleep phase disorder, jet lag, shift worker disorder, and the non-24-hour sleep-wake disorder most commonly found in totally blind individuals; however, its utility for the treatment of insomnia is not established and remains controversial.

If melatonin is taken as a supplement (available OTC) to correct low levels or treat a condition, the timing and dosage are important to its effectiveness, especially as a sleep aid. Response to supplemental melatonin can be very individual. For optimal benefit it is best to work with a health care provider familiar with melatonin dosage and timing. Excessive dosing can result in spillover of melatonin into daylight hours, excessive sleepiness during the day, and disruption of the normal melatonin-cortisol circadian rhythms.

For more general information about melatonin please see: <http://www.nlm.nih.gov/medlineplus/druginfo/natural/940.html>

#### DIURNAL NOREPINEPHRINE (NE)

Norepinephrine (NE) is not following a normal circadian rhythm and is fluctuating erratically from high to normal levels throughout the day. Catecholamines are higher in the first morning and lower in the last (night) urine voids. NE is high in the evening. Low levels of NE at night may be caused by use of medications or hormones used prior to bedtime.

Elevated NE generally is reflective of psychosocial (e.g. emotional-psychological) perceived stressors. Increases in urinary norepinephrine reflect stimulation of both adreno-medullary and renal and peripheral sympathetic nerve endings. Excessive and prolonged exposure to NE can lead to downregulation of beta-adrenergic receptors, increased free radical production, and increased risk for diabetes, cardiovascular disease, senile dementia, and overall functional decline (Reuben DB. J Gerontology: Medical Sciences 2000, 55A (10), M618-M624).

High NE Treatment Options: Since norepinephrine is produced by the adrenal glands, sympathetic nervous system and within the brainstem (locus coeruleus), support of these systems with supplements like calming adrenal adaptogens, tyrosine, phenylalanine, cofactor support of SAME, Vitamin C, iron, MTHR, B6, and L-theanine may be beneficial.

DIURNAL EPINEPHRINE

Epinephrine is elevated during the night (1st morning), but returns to normal range in the morning (2nd sample), and remains within normal ranges throughout the day (evening collection) and at night (evening/night sample) before bed. The pooled sample is within range, but the diurnal results are more accurate for true epinephrine status. Epinephrine, also called adrenaline, functions both as a neurotransmitter and a hormone, participating in the body's "fight or flight" response. Epinephrine increases alertness, focuses attention, fine-tunes vigilance, increases blood pressure, heart rate, and blood glucose, reduces digestive activity, pain and sleep, prevents bladder emptying, and regulates body temperature. It is commonly triggered by stress, fear, blood sugar irregularities or anxiety.

Research shows that urinary epinephrine levels are increased in patients with attention deficit disorder (Faraone et al., 2014), anxiety and depression (Hughes et al., 2004), bipolar disorder (Koslow et al., 1983), hyperglycemia (Troisi et al., 1991), hyperinsulemia (Troisi et al., 1991), obstructive sleep apnea (Kheirandish-Gozal et al., 2013), post-traumatic stress disorder (Yehuda et al., 1992), and stress (Holzman et al., 2009; Fujiwara et al., 2004). Fluctuating levels throughout the day have been commonly associated with an inverse relationship with cortisol (e.g. high epi when cortisol is low).

**THERAPEUTIC CONSIDERATIONS:** Because epinephrine is almost exclusively from the adrenal glands, treatments geared to support normal adrenal function and calm the sympathetic nervous system may be beneficial. Supplements such as adrenal adaptogens, B vitamins, essential fatty acids, vitamin C, as well as stress management, blood sugar balance and sleep support may be helpful.

Creatinine is within range throughout the day reflecting normal concentration of urine.