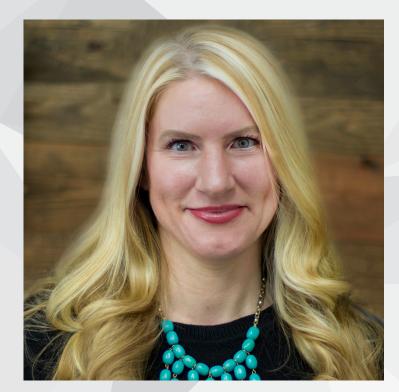


Mark Newman, President and Founder



Dr. Carrie Jones, Medical Director

Organic Acid Testing with DUTCH

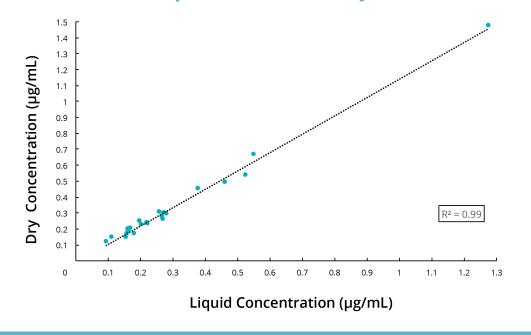
Organic Acid Testing with DUTCH: Putting the puzzle pieces together

Carrie Jones, ND, MPH Medical Director, Precision Analytical, Inc.

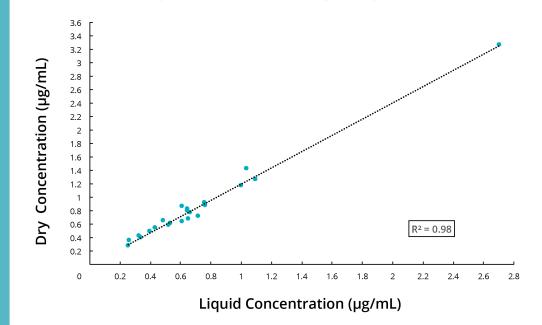


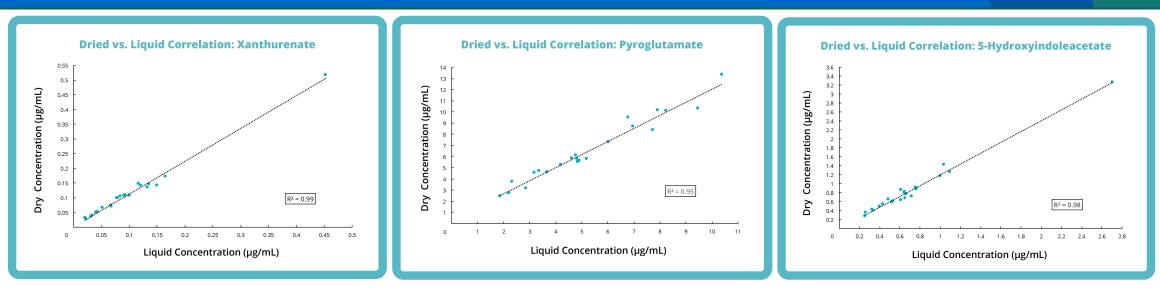
Organic Acid Test (OAT): Validation Data

Dried vs. Liquid Correlation: Methylmalonate

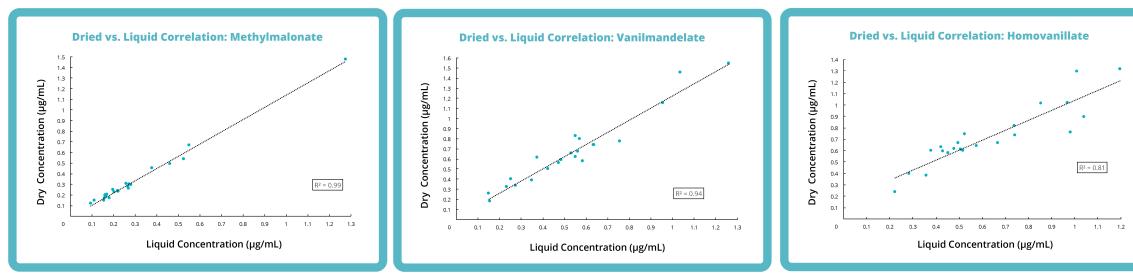


Dried vs. Liquid Correlation: 5-Hydroxyindoleacetate





Organic Acid Test (OAT): Validation Data



Organic Acid Test (OAT): Validation Data

- Dried values correlate to liquid
- Samples are stable at R.T. for weeks
- Precise and accurate
- LC-MS/MS analysis



Medical Disclaimer:

The medical information in this lecture is provided as an information resource only, and is not to be used or relied on for any diagnostic or treatment purposes. This lecture contains general information about medical conditions and treatments. The information is not advice, and should not be treated as such. This information is not intended to be patient education, does not create any patient-physician relationship, and should not be used as a substitute for professional diagnosis and treatment.

The medical information in this lecture is provided "as is" without any representations or warranties, express or implied. Precision Analytical, Inc (DUTCH) makes no representations or warranties in relation to the medical information on this website.



Objectives

□ What OATs are being tested

- □ What each OAT means
- Considerations for treatment
- Understand the relationship to the DUTCH hormone result
- □ Learn OAT patterns to watch out for

□ Clinical case example



What are my testing options?

DUTCH test

- Collection by urinating on 4-5 strips of filter paper throughout the day (Saliva swabs for the CAR)
- ▶ Reports the diurnal cortisol pattern (or CAR)
- ► Reports free cortisol and free cortisone levels
- Reports metabolized cortisol (about 80% of cortisol production)
- ▶ Reports androgens and androgen pathways
- ▶ Evaluates 3 estrogens and estrogen metabolism
- ▶ Tests 80HdG, Melatonin and OATs

Serum

- ► Requires a blood draw
- Tests Estradiol, Progesterone, Testosterone, DHEA-S or DHEA
- ▶ No cortisol diurnal pattern or CAR
- Results are a combination of bound and unbound cortisol in one lump sum
- No androgen pathways or estrogen metabolism
- ▶ Does not test 80HdG, melatonin or OATs

<u>24-hour urine</u>

- ▶ Requires collection of urine in one jug for 24 hours
- ► Reports Estrogen, Testosterone, DHEA and Progesterone
- ► No diurnal pattern or CAR
- ► Does metabolized cortisol
- ► Does report free cortisol
- ► Reports androgen pathways
- ► Evaluates estrogen metabolism
- Some labs test 80HdG, melatonin or OATs (separate tests)

<u>Saliva</u>

- ► Collection by spitting in a tube 4 times throughout the day
- ▶ Reports Estrogen, Progesterone, Testosterone and DHEA-S
- ▶ Reports the cortisol diurnal pattern
- ► Tests free cortisol only
- Some companies evaluate OATs as a separate test
- Does not test metabolized cortisol no good look at cortisol production
- Does not do androgen pathways
- Does not evaluate estrogen metabolism
- Does not test 80HdG or melatonin or OATs



With DUTCH you get it all:

- 1. Androgen Metabolism
- 2. Estrogen Metabolism
- 3. Progesterone Metabolites
- 4. Metabolized Cortisol/Cortisone
- 5. Free Cortisol/Cortisone
- 6. The Diurnal Pattern (Can include the CAR)
- 7. DUTCH Extras: includes OATs, Melatonin and 8-OHdG





DUTCH Complete Test Collection

The Flagship dried urine only test

4 <u>urine</u> samples done throughout the day and dried

- 1. First thing on waking
- 2. 2 hours later
- 3. Around dinner
- 4. Before bed



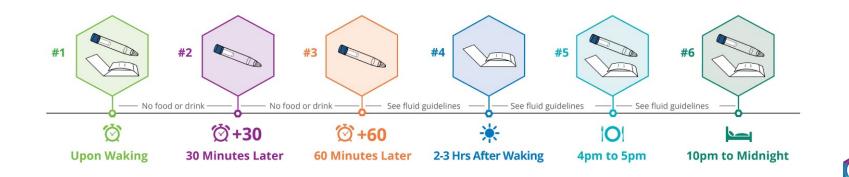
Optional 5th strip if wake and urinate in the middle of the night





5 <u>Saliva</u> collections

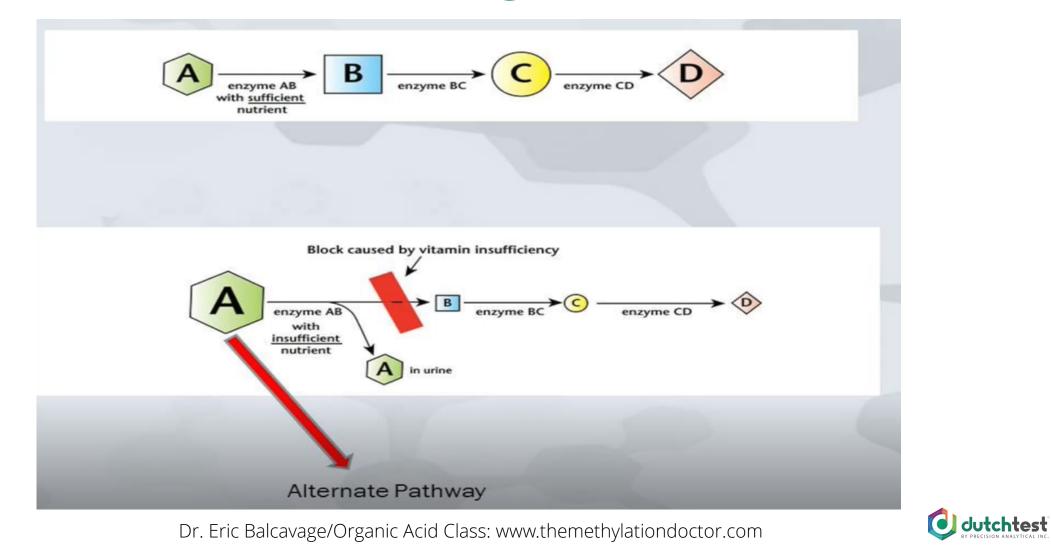
- Waking, +30 min, +60 min, 5pm, Bedtime
- Easier collections using cotton swabs
- 4 <u>Dried urine</u> collections



What are the DUTCH Extras?



What is an Organic Acid?



copyright 2018: Carrie Jones ND, MPH

_ .		UTCH Extras	_					
Category	Test		Result	Units	Normal Range			
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)								
	Melatonin* (Waking)	Low end of range	11.1	ng/mg	10 - 85			
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)								
	8-OHdG (Waking)	Within range	2.8	ng/mg	0 - 5.2			
Nutritional Organic Acids								
Vitamin B12 Marker (may be deficient if high) - (Urine)								
	Methylmalonate (MMA)	Within range	1.2	ug/mg	0 - 2.8			
Vitamin B6 Marker (may be deficient if high) - (Urine)								
	Xanthurenate	Within range	0.4	ug/mg	0 - 1.6			
Glutathione Marker (may be deficient if low or high) - (Urine)								
	Pyroglutamate	Within range	62.2	ug/mg	37 - 70			
Neurotransmitter Metabolites								
Dopamine M	1etabolite - (Urine)							
	Homovanillate (HVA)	Above range	15.6	ug/mg	4.5 - 13			
Norepinephrine/Epinephrine Metabolite - (Urine)								
	Vanilmandelate (VMA)	Below range	0.5	ug/mg	2.7 - 6.4			
Serotonin Metabolite - (Urine)								
	5-Hydroxyindoleacetate (5HIAA)	Below range	1.7	ug/mg	3 - 7.5			



The Basics:

Where do you start?



DUTCH Extras Summary

- Melatonin (6-OH-MS) powerful anti-oxidant made in the pineal gland and gut
- 8-OHdG = oxidative stress and marker of DNA damage

Nutritional Organic Acids:

- **Methylmalonate (MMA) =** if elevated, it reflects insufficient Vitamin B12
- **Xanthurenate =** if elevated, it reflects insufficient Vitamin B6
- **Pyroglutamate =** if decreased or elevated, it reflects insufficient Glutathione



DUTCH Extras

Neurotransmitter Metabolites:

- Homovanillate (HVA) = Dopamine Metabolite, can also reflect genetic mutations and nutritional, neurotransmitter and adrenal problems
- Vanilmandelate (VMA) = Norepinephrine/Epinephrine Metabolite, can also reflect genetic mutations and nutrition, neurotransmitter and adrenal problems
- 5-Hydroxyindoleacetate (5-HIAA) = Serotonin Metabolite, can also reflect nutritional, neurotransmitter, estrogen, inflammation, and adrenal problems.

HVA, VMA and 5-HIAA are particularly sensitive to certain foods, anti-depressant medication and amino acid supplements.

Please read the instructions carefully upon collection of the test.



More Advanced:

Diving deeper down the rabbit hole



Before we get started...

Pay attention to words that are in <u>italics and underlined</u>, They are associated DUTCH markers that can give you additional insight.



Methylmalonate (MMA) Increased = Low Vitamin B12

Not eating it, not absorbing it in stomach/small intestines, not getting into cells, genetics

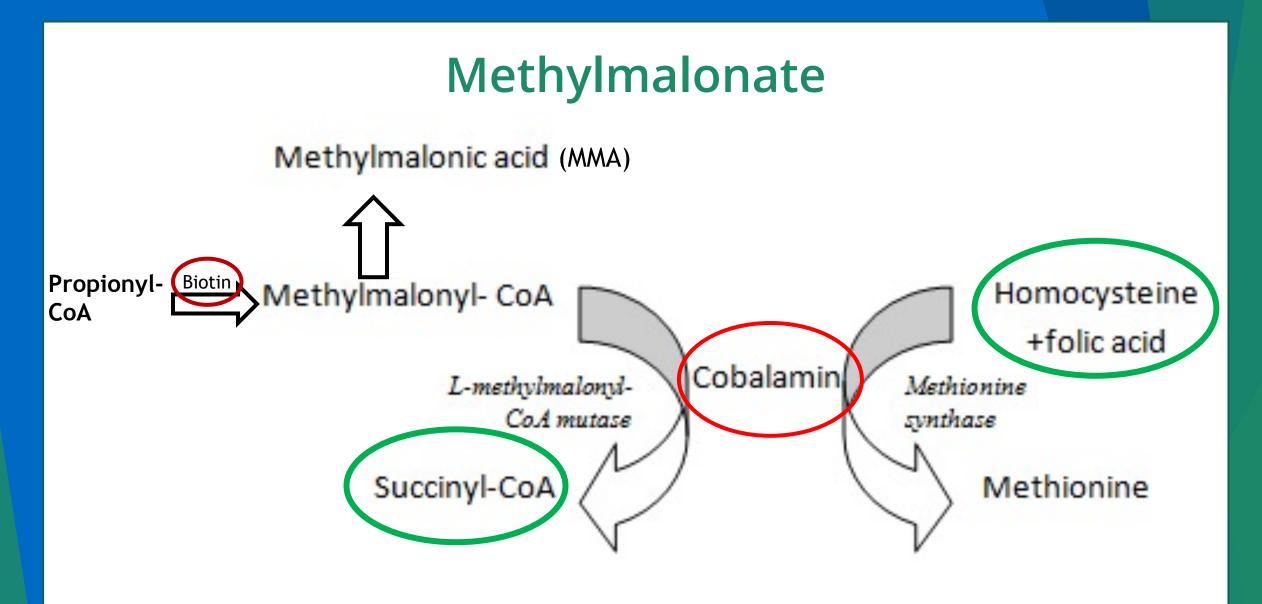
Common sx if low B12:

Fatigue, poor memory, brain fog, unsteady gait, numbness, tingling, and depression

<u>Medications that interfere with or decrease B12:</u>

H2 Blockers and PPIs for acid Metformin/Glucophage Birth Control Pills Hydrocortisone and Ciprofloxacin







When serum B12 is "normal" but cellular levels are low (in this case due to a genetic defect in the transport protein), MMA still increases.

	Tra	Transcobalamin II genotype				
	PP	PR	RR			
N	39	63	26			
Methylmalonic acid (nM)	208 (± 96)	206 (± 80)	264 (± 138)‡			
We conclude that the influences tissue B12		• • • •	•			
BLOOD,	15 JULY 2002 • VOLU	JME 100, NUMBER 2	2 Outcht			

Table 1. Characteristics of study sample by transcobalamin II genotype



Methylmalonate (MMA) How does it relate to the DUTCH Test?

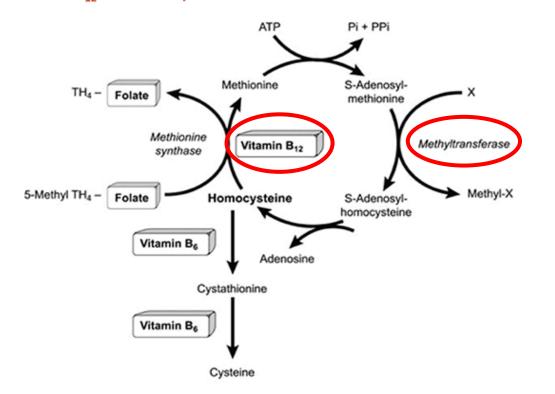
- 1. It's needed as part of the methionine cycle for methylation of <u>Estrogen</u>/COMT with SAM
- 2. COMT also is responsible for Dopamine \rightarrow <u>HVA</u>
- 3. Norepi → Epi uses PNMT
- 4. Norepi and Epi both use COMT to \rightarrow <u>VMA</u>

Pseudo DUTCH Related:

- 1. Needed to break down protein and fats to amino acids and fatty acids
- 2. Needed to create Succinyl CoA for the Krebs Cycle (NADH, FADH, ATP)
- 3. Needed to make methionine which makes SAM which methylates myelin sheath phospholipids



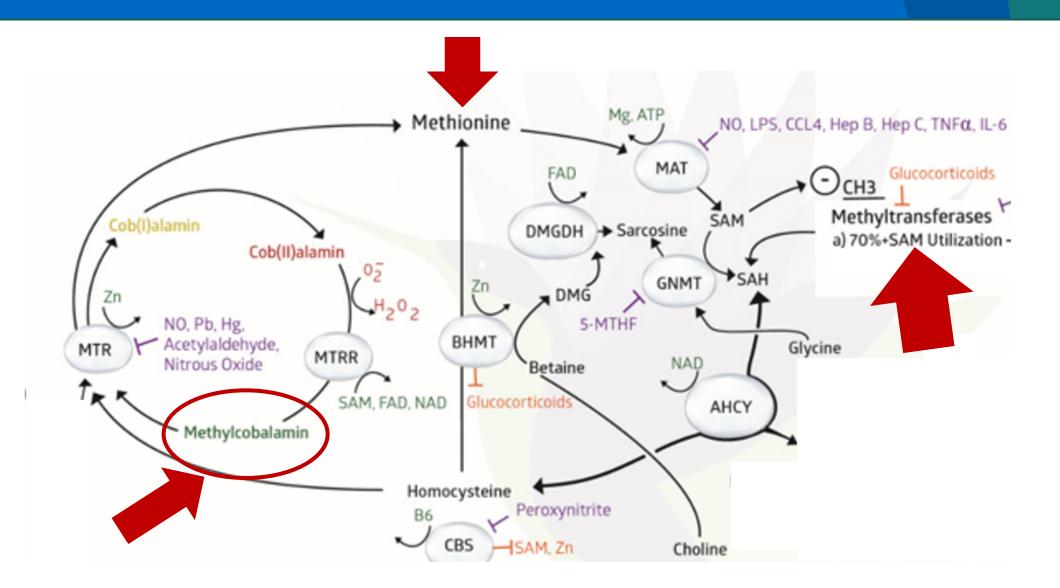
Figure 1. Vitamin B₁₂ and Homocysteine Metabolism



Methionine synthase is a vitamin B_{12} -dependent enzyme that catalyzes the formation of methionine from homocysteine using 5-methyltetrahydrofolate (5-methyl TH₄), a folate derivative, as a methyl donor. Another pathway catalyzed by betaine homocysteine methyltransferase also remethylates homocysteine to methionine using betaine as a methyl donor (not shown here). Methionine, in the form of S-adenosylmethionine, is required for most biological methylation reactions, including DNA methylation.

Photo: Linus Pauling Institute, Oregon State University

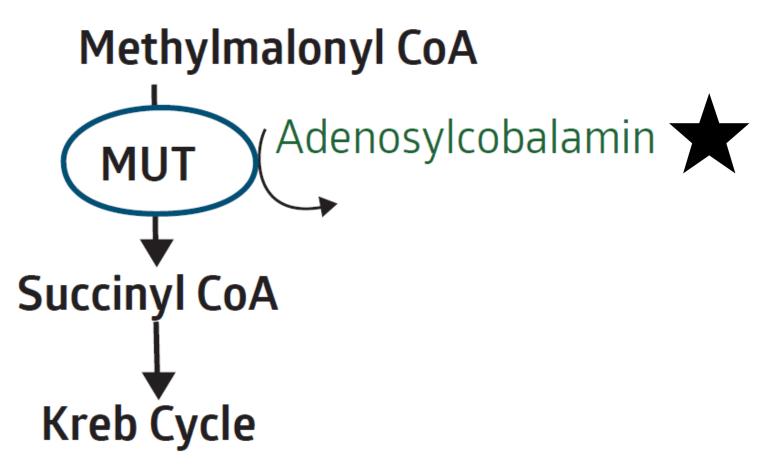




With permission: Dr. Ben Lynch/StrateGene: www.drbenlynch.com



Adenosylcobalamin or Methylcobalamin?



With permission: Dr. Ben Lynch/StrateGene: www.drbenlynch.com



Methylmalonate (MMA) Treatment Considerations:

- 1. Increase B12 foods (liver, sardines, lamb, wild caught-salmon, grass-fee beef, eggs...etc)
- 2. B12 supplementation
 - Methylcobalamin, Adenosylcobalamin, Hydroxycobalamin, Cyanocobalamin
- 3. Improve HCL levels in the stomach (to release B12 bound to proteins in food)
- 4. Consider H.Pylori/SIBO/GUT testing
- 5. Consider serum Intrinsic Factor or Parietal Cell Antibody testing
- 6. Consider Biotin testing (actually causes blunted MMA but B12 symptoms)
- 7. Mutations issues: MMMA, MMAB, MTRR, MTR, TCN-1, GIF (TCN-3) and MUT
 - If they have MUT → they may need Adenosylcobalamin especially if unresponsive to Methyl B12 (see prior slide)



Xanthurenate Increased = Low Vitamin B6

Not eating it, not absorbing it in small intestines, not getting activated to P5P/PLP in liver, low cofactors that help with activation/tissue uptake/circulation, conditions affected (pyroluria)

Common sx if low B6:

It's involved in over 100 enzymatic reactions

Atrophic glossitis, angular cheilitis, impaired glucose intolerance/insulin problems, intertrigo, fatigue, neuropathy, mental confusion, depression

Medications that interfere with or decrease B6:

Birth Control Pills

Anti-convulsant medications

Hydrocortisone and Ciprofloxacin



Xanthurenate

How does it relate to the DUTCH Test?

- 1. P5P is needed for the <u>methylation of estrogen</u>
- 2. P5P is used in the creation of neurotransmitters (HVA, VMA, 5-HIAA)
- 3. P5P used in the transsulfuration pathway to make cysteine and glutathione (Pyroglutamate)
- 4. Can complex with iron to increase <u>8-OHdG</u> (this is bad)
- 5. Higher Xanthurenate = higher risk for diabetes (blood sugar/insulin affect hormones!)
 - Gluconeogenesis needs amino acids via transamination that is B6 dependent
 - Glycogen phosphorylase enzyme to start glycogenolysis is B6 dependent
 - Complexes with insulin so insulin is less effective/available to deal with glucose

Pseduo-DUTCH Related:

- 1. Excess <u>estrogen, inflammation, cortisol</u> and LPS from gram negative bacteria push the Kynurenine pathway away from serotonin. If there is not enough Vitamin B6 on this pathway, Xanthurenate forms
- 2. The Kynurenine pathway makes NAD
- 3. P5P helps enzymes get selenium from dietary form (selenomethionine) thyroid issues



Tryptophan can choose 2 pathways

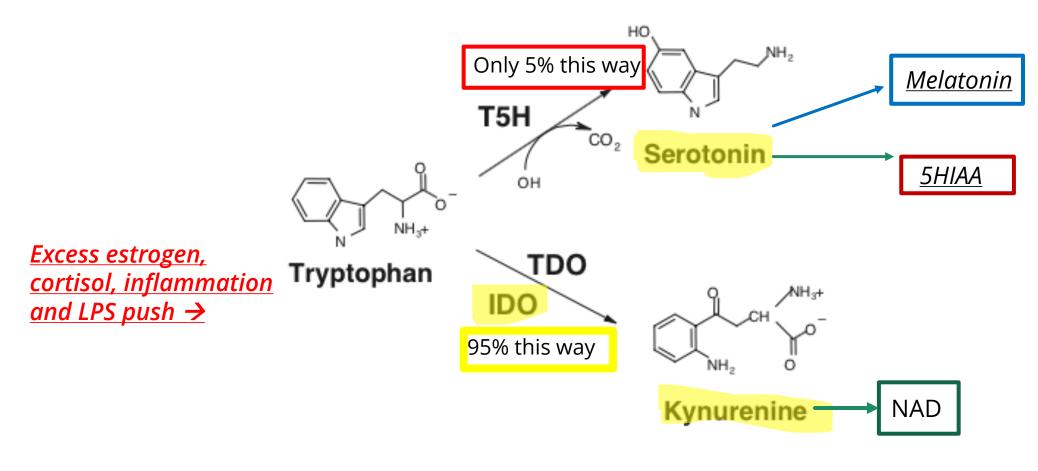
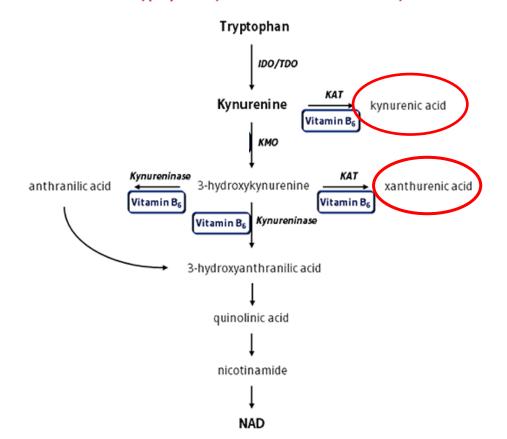




Figure 2. Overview of the Tryptophan-Kynurenine Metabolic Pathway

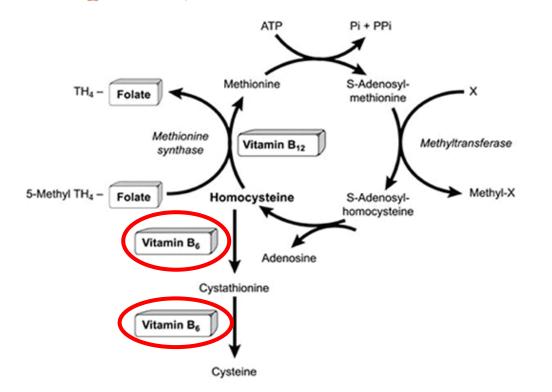


Pyridoxal 5'-phosphate, a vitamin B₆ coenzyme, is required for the activity of several key enzymes in tryptophan catabolic pathway: KAT, KMO, and kynureninase. Dietary restriction of vitamin B₆ most prominently affects kynureninase activity and results in the shift from 3-hydroxykynurenine metabolism and NAD formation to the production of kynurenic acid and xanthurenic acid. *IDO, indoleamine 2,3-dioxygenase; KAT, kynurenine aminotransferase; KMO, kynurenine 3-monooxygenase; NAD, nicotinamide adenine dinucleotide; TDO, tryptophan 2,3-dioxygenase.*

http://lpi.oregonstate.edu/mic/vitamins/vitamin-B6



Figure 1. Vitamin B₁₂ and Homocysteine Metabolism



Methionine synthase is a vitamin B_{12} -dependent enzyme that catalyzes the formation of methionine from homocysteine using 5-methyltetrahydrofolate (5-methyl TH₄), a folate derivative, as a methyl donor. Another pathway catalyzed by betaine homocysteine methyltransferase also remethylates homocysteine to methionine using betaine as a methyl donor (not shown here). Methionine, in the form of S-adenosylmethionine, is required for most biological methylation reactions, including DNA methylation.

Photo: Linus Pauling Institute, Oregon State University



Xanthurenate

Treatment Considerations:

- 1. Increase B6 Foods: Turkey breast, grass-fed beef, pork, pinto beans, avocado, pistachios, chicken, sesame seeds, sunflower seeds, chickpeas
- 2. Supplement with vitamin B6 (Pyridoxine) and/or P5P (PLP)
 - Be aware high doses Pyridoxine (sources vary, 200-1000mg) can damage the dorsal root ganglia causing worse neuropathy symptoms
- 3. Nutrient testing for co-factors: Riboflavin (B2), Zinc, ATP, and Lysine
 - 1. B2 helps activate it to P5P, Zinc and ATP help with absorption/tissue uptake/circulation and lysine sits in its active binding site to act as a Schiff base when it binds to catalyze reactions forward
- 4. Address the small intestines where it is absorbed (SIBO? Leaky gut?)
- 5. Address excess estrogen, inflammation, cortisol and LPS from gram negative bacteria
- 6. Test for Pyroluria (kryptopyrroles bind up B6 check zinc status too)



Pyroglutamate

<u>Increased or decreased = Glutathione (GSH) problem</u>

Either can't be made, recycled or it's being used up Comes from cysteine, glutamate and glycine

Common sx if low Glutathione:

Powerful antioxidant in the body

Can have problems with detoxification, inflammation, infection, illness...etc.

Things that interfere with or decrease Glutathione:

Tylenol (Acetaminophen) and other pharmaceuticals Environmental toxicants/solvents/chemicals/pesticides/herbicides/pollutants/cleaners, Heavy metals, EMF, alcohol...etc.



Pyroglutamate How does it relate to the DUTCH Test?

- 1. Helps prevent <u>4-OH-E1 and 4-OH-E2</u> from going down the Quinone pathway and forming an adduct
- 2. Needs vitamin B6 (<u>Xanthurenate</u>) for transsulfuration pathway to make cysteine (<u>Pyroglutamate</u>)
- 3. Helps handle infection and inflammation
 - Hormones affected by infection and inflammation:
 - 1. <u>5a-DHT/5a-Reductase</u> can increase
 - 2. <u>Estrogen</u> via aromatization
 - 3. <u>16-OH-E1</u> can increase
 - 4. <u>8-OHdG</u> (oxidative stress and DNA damage marker) can increase
 - 5. <u>Metabolized and/or free cortisol</u> can increase
- 4. Glutathione helps recycle CoQ10, Vitamin E and Vitamin C = antioxidants and much more!



Pyroglutamate Treatment Considerations

- 1. Address any exposure, infection, inflammation, oxidative stress...etc
- 2. Glycine and sulfate
- 3. Supplement support:
 - Cysteine via NAC
 - Glutathione
- 4. Co-factor support:
 - FAD (B2), Selenium, ATP, Magnesium
- 5. Mutation issues: CBS, GCL, GSS, GST, GSR, GPX
- 6. Consider serum GGT testing as GGT starts the y-glutamyl cycle (GGC)
- 7. Ask about diet need protein
- 8. Test methionine and homocysteine (high methionine/low homocysteine = likely not making cysteine)



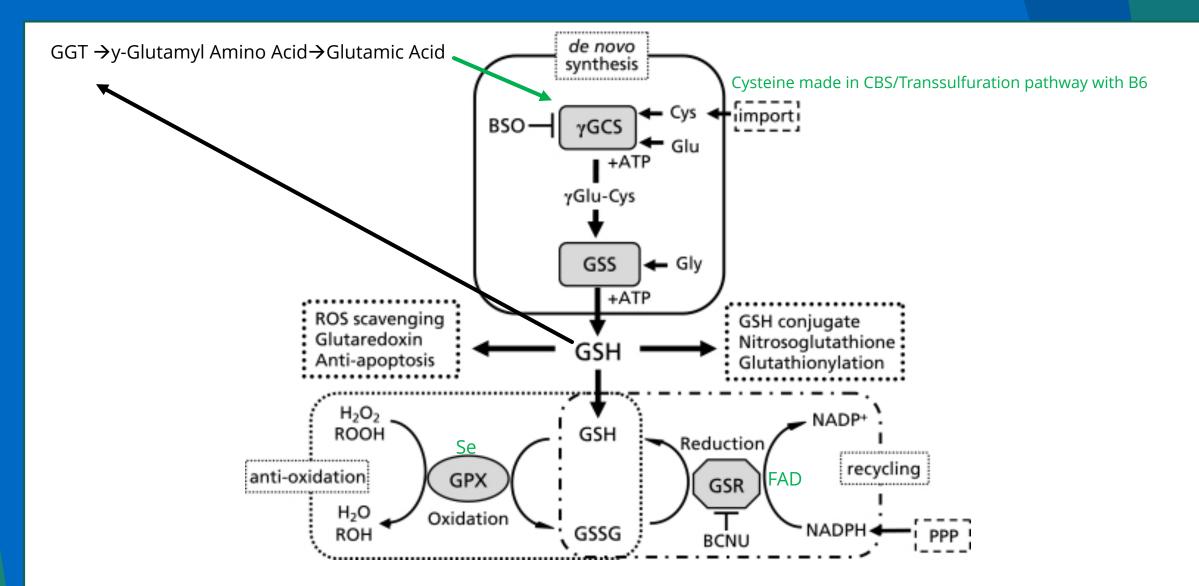


Photo: <u>https://openi.nlm.nih.gov/detailedresult.php?img=PMC3171681_jcbn10-138SRf01&req=4</u> Additional info: Dr. Ben Lynch/Strategene www.drbenlynch.com



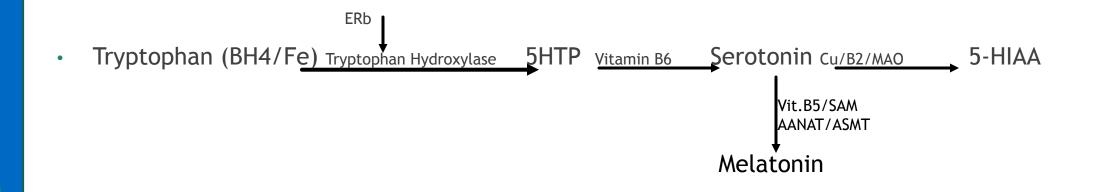
5-Hydroxyindoleacetate (5-HIAA) <u>Primary Serotonin Metabolite</u>

- Approximately: 90% made in the gut (for gut motility and activates smooth muscle activity, can induce vomiting/diarrhea with food poisoning)
- 1% made in the brain
- The rest is made in peripheral tissue
- It's stored in platelets and mast cells
 - Released during injury and inflammation bc of its analgesic, clotting and vasoconstrictive effect



5-Hydroxyindoleacetate (5-HIAA) Primary Serotonin Metabolite: Co-Factors

- TRYPTOPHAN needs BH4, iron and healthy <u>estrogen</u> levels to make 5HTP
- 5HTP needs Vitamin B6 to make serotonin (check Xanthurenate)
- SEROTONIN uses copper and vitamin B2 with MAO to break down to 5HIAA





5-HIAA

Decreased Levels: Address the Cause

- 1. <u>Excess estrogen, cortisol, inflammation</u> and LPS from gram negative gut bacteria push away from serotonin to the Kynurenine pathway (so serotonin and <u>melatonin</u> go down)
- 2. But low estrogen (ie. menopause/amenorrhea) means Tryp. Hydroxylase can't make 5-HTP
- 3. Low Co-factors: BH4, Iron, B6, Copper and B2
- 4. MAO mutation
- 5. Low Tryptophan (ie. low protein diets)
- 6. Recent, even low levels, alcohol consumption (due to a competitive inhibition of aldehyde dehydrogenase by acetaldehyde, which inhibits 5–HIAA formation)
- 7. Low levels of platelets and/or mast cells
- □ IF on SSRI/SNRI and 5-HIAA is <u>LOW,</u> the med is not working, There are low levels of TRYPTOPHAN, it's not serotonin's fault. It may also be a serotonin receptor problem.



5-HIAA

<u> ↑Increased Levels: Address the Cause</u>

- 1. Ate high serotonin foods during testing: butternuts/black walnuts/pecans (and nut butters), plantains, banana, avocado, pineapple (and juice), eggplant, plums
- 2. On 5-HTP, Tryptophan, St. John's Wort, SAMe, SSRI/SNRI or Tricyclic Antidepressant medication
 - This is normal if levels are increased while taking these things
 - If you wanted baseline then you must stop these products (wean medications please!) for weeks.
- 3. Malabsorption/gut issues (celiac is the most studied) causing high serotonin/5-HIAA bc made in the gut
- 4. Stress
- 5. Metabolic Syndrome
- 6. Released from platelets due to injury/inflammation
- 7. Consider Mast cell issues (mixed in research)
- 8. Carcinoid tumor of enterochromaffin cells (very high levels)



Homovanillate (HVA) Primary Central Dopamine Metabolite

- Dopamine is made in the neurons in the brain and in small amounts in the adrenal medulla
 - There is no negative feedback loop
- In the brain, part of the reward center (rewards increase dopaminergic output), motivation, prolactin suppression, sexual gratification and motor control

Dopamine does not cross into or out of the blood brain barrier (L-dopa can).

• <u>In periphery, it acts locally in specific tissues as a vasodilator to inhibit norepi, to increase urine</u> and sodium output, reduce insulin output, reduce GI motility, and reduce lymphocyte activity.



Homovanillate (HVA) Primary Central Dopamine Metabolite

- 1. Comes from TYROSINE with BH4(biopterin) and iron to make \rightarrow DOPAMINE
- 2. DOPAMINE uses B6, B2, Magnesium and SAMe to make \rightarrow HVA
- 3. DOPAMINE is broken down by MAO then COMT to \rightarrow HVA
- 4. DOPAMINE can use copper, Vitamin C and DBH enzyme to make \rightarrow NOREPI



Vanilmandelate (VMA)

Primary Norepinephrine/Epinephrine Metabolite

- Norepi/Epi are made in the brain and in the adrenal medulla
 - Stored in pre-synaptic vesicles to be released immediately on need
 - There is no negative feedback loop
 - Norepi and Epi can not cross into or out of the brain
- Primary action in the brain or the peripheral tissues is to prepare for fight/flight
 - Brain: alertness, attention, anxiety, vigilance, restlessness
 - Periphery: higher blood pressure and heart rate, increases glucose release (via glycogenolysis), diverts blood flow from GI tract to skeletal muscles...etc.
- It's lowest levels are in the night and <u>highest levels in the morning</u> UNLESS stimulated



"Chronic stress, if continued for a long time, can damage many parts of the body.

A significant part of the damage is due to the effects of sustained norepinephrine release, because of norepinephrine's general function of <u>directing resources away from maintenance, regeneration, and</u> <u>reproduction, and toward systems that are required for active</u> <u>movement.</u>

The consequences can include sleeplessness, loss of libido, gastrointestinal problems, impaired disease resistance, slower rates of injury healing, depression, and increased vulnerability to addiction."

> Chrousos, G. 2009. Stress and disorders of the stress system. DOI: 10.1038/nrendo.2009.106 https://en.wikipedia.org/wiki/Norepinephrine



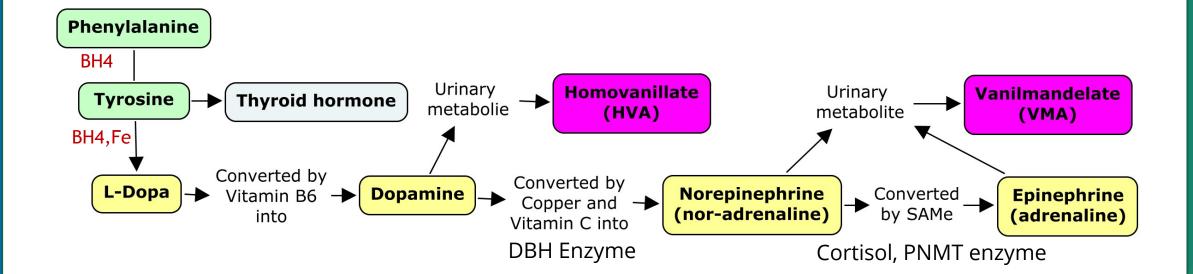


Photo: http://drsaulmarcus.com/mentalillness/Organicacidtestingmental.html



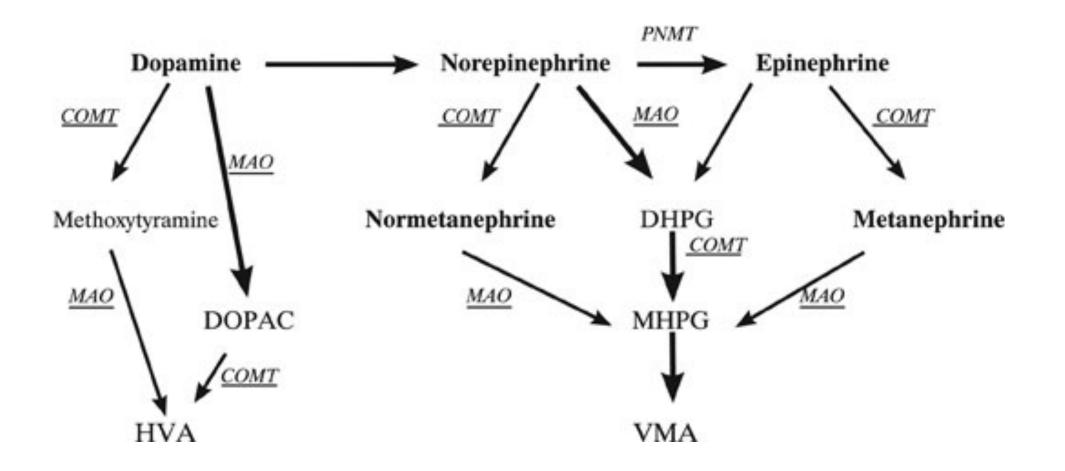


Photo: http://www.hormones.gr/93/article/article.html



If HVA is ↑ high and VMA is ↑ high

- 1. COMT or MAO mutations
- 2. High levels of or taking Tyrosine, DLPA, Dopamine and/or Macuna supplements
- 3. SNRI Medication (Wellbutrin (Bupropion)), Tricyclic Antidepressants (amitriptyline (Elavil))
- 4. Amphetamines/Amphetamine-like medications or drugs, Appetite suppressants (Phentermine), Caffeine (pills or drinks), Ephedrine (ie. Sudafed)
- 5. Opioids (VMA may be normal)
- 6. Elevated adrenal output <u>cortisol</u> address the stress
- 7. <u>Inflammation</u> inflammatory cytokines increase sympathetic output
- 8. Neuroblastic Tumor
- 9. Pheochromocytoma (Very high levels of VMA, maybe HVA)



If HVA is ↑ high and VMA is ↓ Low

- 1. Low copper or vitamin C so DBH enzyme can't move forward (VMA usually quite low)
- 2. Clostridia difficile (inhibits DBH enzyme so can't make VMA)
- 3. Bananas (contain high levels dopamine that doesn't cross BBB VMA likely normal)
- 4. Quercetin supplements/foods turn into HVA in the gut and can show up as artificial high HVA and normal VMA
- 5. Check adrenals low levels of <u>cortisol</u> too? Then VMA is usually low.
- 6. Tetrahydrocannabinol (THC) use short term use raises dopamine (VMA may be normal)
- 7. Opioids (VMA may be normal)
- 8. DBH enzyme deficiency (VMA very low) = orthostatic hypotension, exercise intolerance, ptosis of eyelid, psychological/behavior disorders
- 9. Neuroblastic tumor (very high levels)



If HVA is ↓ Low and VMA is ↑ High

- 1. Check adrenals high cortisol levels too?
- 2. HVA may be normal and VMA elevated with: Amphetamines/Amphetamine-like medications or drugs, Appetite suppressants (Phentermine), Caffeine (pills or drinks), Ephedrine (ie. Sudafed)
- 3. Dopamine reuptake inhibitors (ie. risperidone)
- 4. Pheochromocytoma
- 5. Higher risk for myocardial injury/dysfunction with elevated cardiac troponin I
 - 1. Consider age and CVD risk



If HVA is \downarrow Low and VMA is \downarrow Low

- 1. Low cofactors: BH4, iron, SAMe, Magnesium, Copper, B2, NAD (not eating? Not absorbing?)
- 2. COMT or MAO mutations
- 3. Low Tyrosine (ie. low protein diet or poor protein absorption)
- 4. Check adrenals low <u>cortisol</u> levels too?
- 5. Oxidative stress (pushing PEA down other pathways)
 - 1. Look at <u>8-OHdG</u>
- 6. Fungal/candida infections inhibit Tyrosinase activity (Can't make L-Dopa)
- 7. Glyphosate blocking the Shikamate pathway and depleting/binding co-nutrients (ie. Tyrosine and Tryptophan)
- 8. Tetrahydrocannabinol (THC) use long term use? Possibly suppressive?



Case: Depression and Anxiety on an SSRI

50yo female presents to the clinic with:

- On an SSRI but still reports mild depression and moderate anxiety
- Moderate fatigue
- Irregular cycles
- Does not report hot flashes/night sweats



	D	UTCH Extras						
Category	Test		Result	Units	Normal Range			
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)								
	Melatonin* (Waking)	Low end of range	11.1	ng/mg	10 - 85			
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)								
	8-OHdG (Waking)	Within range	2.8	ng/mg	0 - 5.2			
Nutritional Organic Acids								
Vitamin B12 Marker (may be deficient if high) - (Urine)								
	Methylmalonate (MMA)	Within range	1.2	ug/mg	0 - 2.8			
Vitamin B6 Marker (may be deficient if high) - (Urine)								
	Xanthurenate	Within range	0.4	ug/mg	0 - 1.6			
Glutathione Marker (may be deficient if low or high) - (Urine)								
	Pyroglutamate	Within range	62.2	ug/mg	37 - 70			
Neurotransmitter Metabolites								
Dopamine M	letabolite - (Urine)							
	Homovanillate (HVA)	Above range	15.6	ug/mg	4.5 - 13			
Norepinephrine/Epinephrine Metabolite - (Urine)								
	Vanilmandelate (VMA)	Below range	0.5	ug/mg	2.7 - 6.4			
Serotonin Metabolite - (Urine)								
	5-Hydroxyindoleacetate (5HIAA)	Below range	1.7	ug/mg	3 - 7.5			



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High HVA = Anxiety type symptoms Low VMA = fatigue Low 5HIAA = depression



Treatments to consider:

- High HVA:
 - Given the large discrepancy between HVA and VMA \rightarrow check copper and vitamin C levels
 - Ask about gut issues maybe C. diff?
- Low VMA:
 - Address the copper, vitamin C and C. diff as needed.
 - Look at the adrenals
- Low 5HIAA:
 - The SSRI is not working.
 - There is likely not enough TRYPTOPHAN to make SEROTONIN for the SSRI to work in the first place
 - She's near menopause and DUTCH estrogen (not shown) is in the post-menopausal range
 - Estrogen stimulates ERb to make Tryp. Dehydroxylase to make 5HTP
 - Talk with her about diet (protein) and alcohol



Having the most comprehensive, easy to collect adrenal and hormone test available allows you to make a greater impact on your patients at a deeper level.



References and Resources:

- Richard Lord and Alexander Bralley. Laboratory Evaluations for Integrative and Functional Medicine. (book published 2008). <u>http://functionalmedicinetextbook.com/tag/richard-s-lord</u>
- Ben Lynch, ND StrateGene and Dirty Genes (book published January 2017) <u>www.drbenlynch.com</u>
- Chris Masterjohn, PhD. Testing Nutritional Status: The Ultimate Cheat Sheet. <u>https://chris-masterjohn-phd.myshopify.com/</u>
- Elizma Lambert, ND. <u>https://mthfrandbeyond.com.au/</u>
- Eric Balcavage, DC, CNS, CFMP. The Organic Acid On-Line Class. www.themethylationdoctor.com
- □ Michael McEvoy. https://metabolichealing.com/
- □ Shawn Bean. <u>http://matrixhealthwell.com/</u>
- □ MTHFR Support Australia. How to pick the right B12. 2017. Publication located at <u>www.mthfrsupport.com.au</u>



References:

- Stony Brook University. High sugar intake linked to low dopamine release in insulin resistant patients. ScienceDaily. ScienceDaily, 10 June 2013. www.sciencedaily.com/releases/2013/06/130610223722.htm
- Bonifacic D, Aralica M, Tokmadzic V, Racki V, Tuskan-Mohar L, and Kucic N. Values of vanillylmandelic acid and homovanillic acid in urine as potential prognostic biomarkers in ischaemic stroke patients. BIOMARKERS, 2017;22(8):790–797 https://doi.org/10.1080/1354750X.2017.1351001
- Vander Weele C, Porter-Stransky K, Mabrouk O, Lovic V, Singer B, Kennedy R and Aragona B. Rapid dopamine transmission within the nucleus accumbens: Dramatic difference between morphine and oxycodone deliver. European J Neuroscience. 2014;40:3041-3054.
- Afraideh M, Behdadnia A, Noshad S, Mirmiranpour H, Mousavizadeh M, Khajeh E, Rad MV, MAzaheri T, Nakhjavani M, Esteghamati A, Association of peripheral 5-hydroxyindole-3-acetic acid, a serotonin derivative, with metabolic syndrome and low-grade inflammation. Endocr Pract. 2015;21(7):711-8. doi: 10.4158/EP14442.OR
- Fukui M, Tanaka M, Toda H, Asano M, Yamazaki M, Hasegawa G, Imai S, Makamura N. High Plasma 5-Hydroxyindole-3-Acetic Acid Concentrations in Subjects with Metabolic Syndrome. Diabetes Care. 2012;35(1):163-167. <u>https://doi.org/10.2337/dc11-1619</u>
- Kushnir-Sukhov N, Brown J, Wu Y, Kirshenbaum A, Metcalfe D. Human mast cells are capable of serotonin synthesis and release. J of Allergy and Clinical Immunology. 2007;119(2):498-499. DOI: <u>http://dx.doi.org/10.1016/j.jaci.2006.09.003</u>
- Koch M, Dehghani F, Habazettl, Schomerus C and Horst-Werner K. Cannabinoids attenuate norepinephrine-induced melatonin biosynthesis in the rat pineal gland by reducing arylalkylamine Nacetyltransferase activity without involvement of cannabinoid receptors. JNC. 2006;98(1):267-278.
- Joy T, Walsh G, Tokmakejian S, Van Uum S. Increase of urinary 5-hydroxyindoleacetic acid excretion but not serum chromogranin A following over-the-counter 5-hydroxytryptophan intake. Can J Gastroenterol. 2008 Jan; 22(1): 49–53.
- Stein L and Imai S. They dynamic regulation of NAD metabolism in mitochondria. Trends Endocrinol Metab. 2012 Sep; 23(9): 420–428.
- Shoenfield P. Vitamin B6 The Under-Appreciated Vitamin. The Westin Price Foundation. 2011. Retrieved from https://www.westonaprice.org/health-topics/abcs-of-nutrition/vitamin-b6-the-under-appreciated-vitamin/
- Martin AM, Lumsden AL, Young RL, Jessup CF, Spencer NJ, Keating DJ. Regional differences in nutrient-induced secretion of gut serotonin. Physiol Rep. 2017 Mar;5(6). pii: e13199. doi: 10.14814/phy2.13199
- O'Mahoney S:M, Clarke G, Borre YE, Dinnan TG, and Cryan JF. Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. Behavioural Brain Research. 2015. 277(15):32-48.
- Nowak JZ. Effects of histamine H1- and H2-receptor antagonist on dopamine, noradrenaline and serotonin systems in the rat brain. Pol J PHarmacol Pharm. 1980;32(4):451-61.
- Sadek B, Saad A, Sadeq A, Jalal E, Stark H. <u>Histamine H3 receptor as a potential target for cognitive symptoms in neuropsychiatric diseases</u>". Behavioural Brain Research. 2016;312(1):415–430. doi:10.1016/j.bbr.2016.06.051.



Questions?

If your question(s) aren't answered live, please look for an email or FAQ's we will be sending out after the webinar.

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