



# New Organic Acids to Improve Patient Protocols

**Precision Analytical  
DUTCH Test**

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# DISCLAIMER

The information shared today is intended for educational purposes and should be not be misconstrued as medical advice.





# Organic Acid Testing (OATs)

- Objectives for our discussion today:
- **What** are Organic Acids?
- **What** are the new Organic Acids on the DUTCH test?
- **How** can we utilize these new markers?





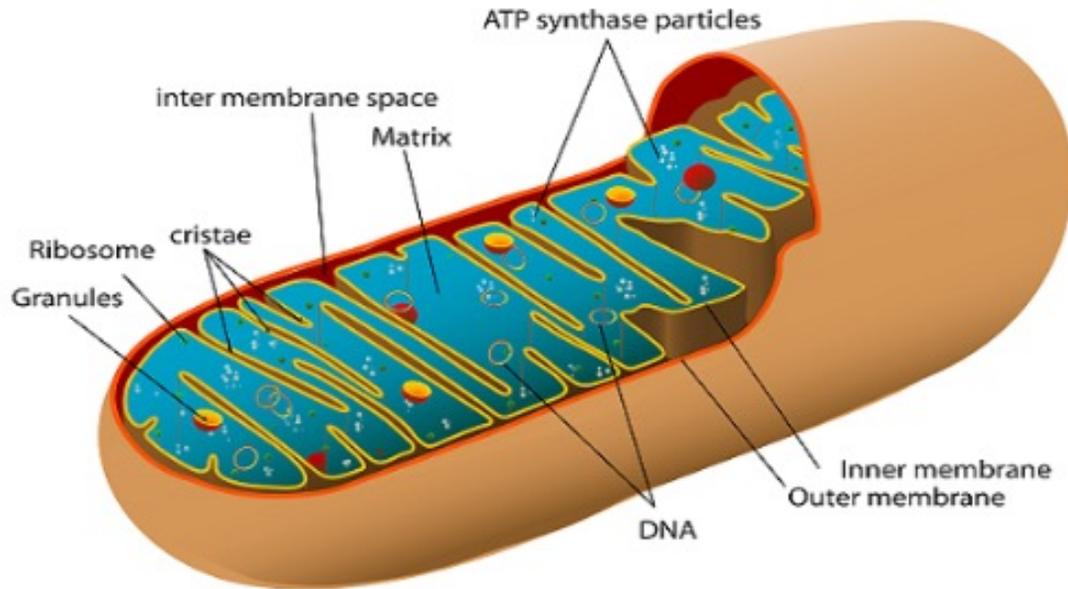
# Organic Acids

- **What are Organic Acids?**
- Let's talk through some definitions so we can better understand the importance of what Organic Acids can offer:
- We need to understand cellular metabolism and the result of metabolism to understand why these markers are important



# Organic Acids

Understanding cells and cellular energy



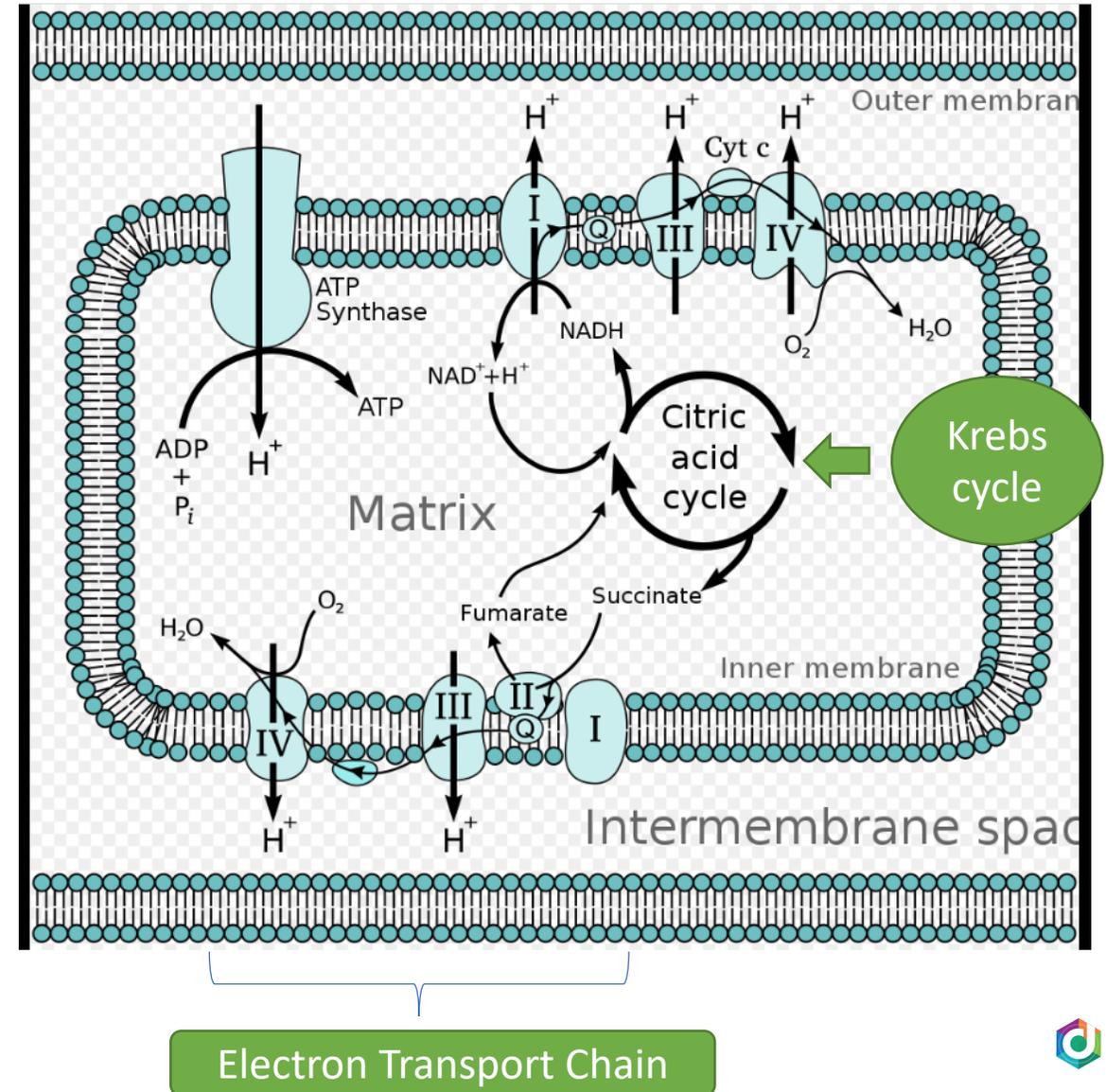
- Cellular energy (energy for the body in general) is produced through **ATP**
- **ATP** is made in the mitochondrial matrix
- Mitochondria are necessary for energy production (**ATP**) which influences how well our cells can create or breakdown



# Organic Acids

## Cellular metabolism

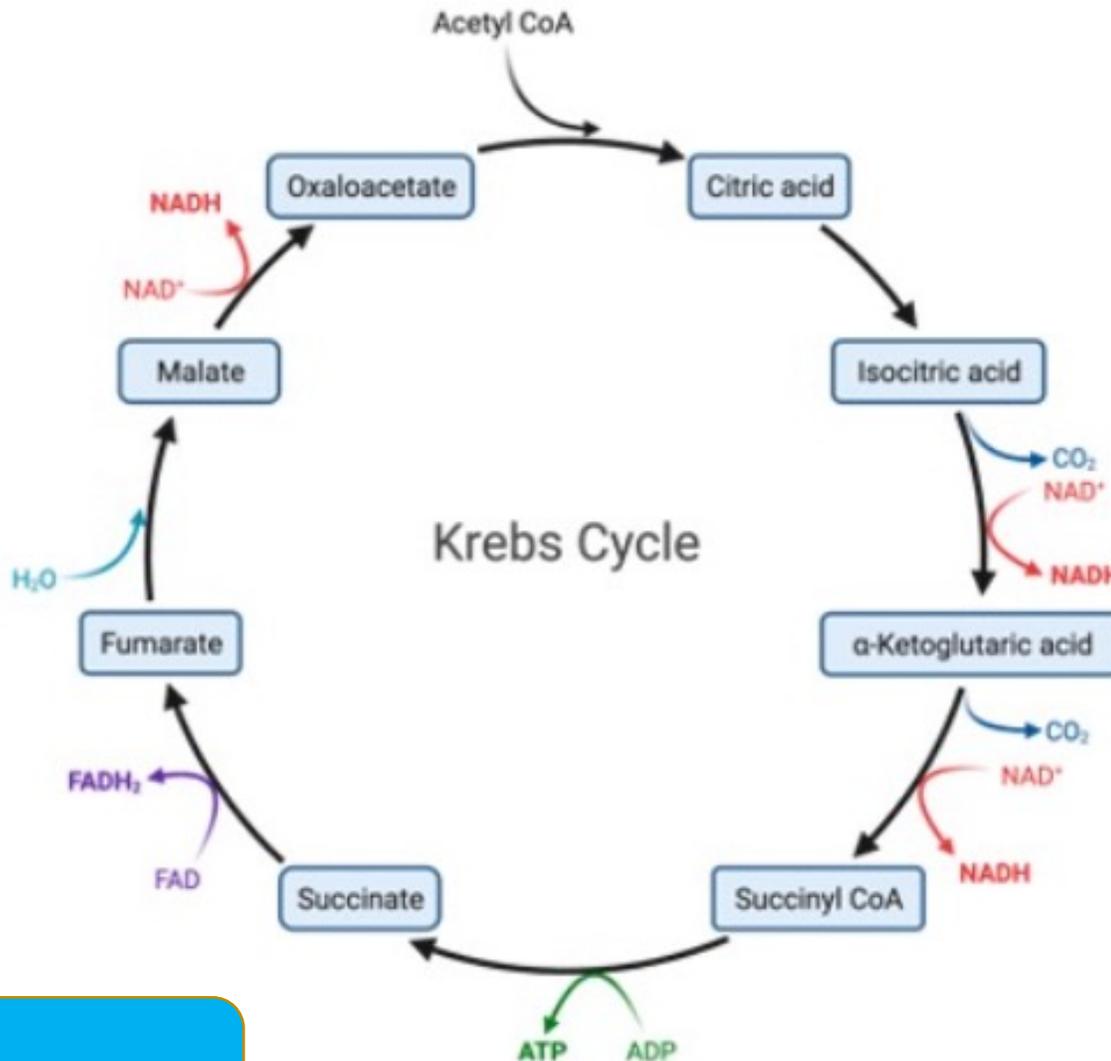
- Most Organic Acids require metabolism through
  - the **Krebs Cycle** (aka: Citric Acid Cycle – CAC) or
  - the **Electron Transport Chain** (ETC) to complete the cycle of steps necessary for our cells to function.
- Each step requires efficient functionality to ensure optimal health.
- Enzymes heavily influence pathway choices in the body



# Organic Acids

## Krebs cycle: TCA Cycle or Citric Acid Cycle

- The Krebs Cycle is an important multi-step process for substrate and metabolite creation for energy and overall metabolism



ENERGY!



PRODUCTS
2 ATP
8 NADH
2 FADH <sub>2</sub>
6 CO <sub>2</sub>



# Organic Acids

## Metabolism

- **Metabolism**
  - The process of chemical transformations in each cells needed for sustaining life
- **Metabolites**
  - Are products of metabolism and may include intermediates
- **Intermediates**
  - Small compounds that are precursors needed for metabolism





# Organic Acids

- **What are Organic Acids?**

- Organic Acids (OA) are compounds the body makes that influence the pH of our cells. Our cells require very specific acid-base balance to ensure they are communicating, or metabolizing, appropriately. How our bodies metabolize compounds can offer:
  - 1) information on nutritional status,
  - 2) the levels of neurotransmitters or metabolites in the body (like dopamine),
  - 3) gut dysbiosis, or
  - 4) more severe disease states.

\*For clarity, most severe disease states are generally found upon newborn testing as severe malfunction can be life-threatening.





# Organic Acids

New markers on DUTCH testing

- **What are the New Organic Acids on the DUTCH test:**
  - Beta-Hydroxyisovalerate ( $\beta$ -Hydroxyisovalerate)
  - Quinolate
  - Indican





# Organic Acids

## New markers on DUTCH testing

- **$\beta$ -Hydroxyisovalerate**
- There is an inverse relationship between Biotin and  $\beta$ -Hydroxyisovalerate levels in the body – as biotin goes down,  $\beta$ -Hydroxyisovalerate increases. DUTCH (dried urine) testing is a very reliable marker to confirm Biotin deficiency.
- **BIOTIN:**
  - Is an important nutrient for skin and hair growth
  - Is water soluble
  - Cannot be synthesized by mammals therefore we depend on nutritional intake
  - A key substrate throughout the Krebs Cycle that influences fatty acid metabolism



# Organic Acids

## New markers on the DUTCH test

- $\beta$ -Hydroxyisovalerate
- Can be depleted from:
  - pregnancy
  - lactation
  - smoking
  - certain medications/antibiotics, lipoic acid (competes with Biotin)
  - gut dysbiosis
  - raw egg white consumption (avidin)
  - depletion
- Low status of other B Vitamins may mimic each other

**Symptoms** associated with low biotin, or elevated Beta-hydroxyisovalerate:

- hair loss
- cracks in the skin along the lips
- dry skin
- eczema
- rashes
- Nerve symptoms and poor cognition





# Organic Acids

New markers on the DUTCH test

- $\beta$ -Hydroxyisovalerate
  - Biotin supplementation can be helpful to replete these levels. It may also be helpful to include an overall B-Complex as B Vitamins work synergistically for overall repletion status.
  - Natural sources from food include egg yolks, liver, and some vegetables.



# Organic Acids

## Case study B-Hydroxyisovalerate

- **How** this will look on a DUTCH test

Category	Test	Result	Units	Normal Range
<b>Nutritional Organic Acids</b>				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Within range	1.32	ug/mg 0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Within range	0.67	ug/mg 0.12 - 1.2
	Kynurenate	Within range	1.28	ug/mg 0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	High end of range	55.3	ug/mg 28 - 58
Biotin Marker (may be deficient if high) - (Urine)				
	b-Hydroxyisovalerate	Above range	13.8	ug/mg 0 - 12.5
Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)				
	Indican	Within range	40.9	ug/mg 0 - 100
<b>Neuro-related Markers</b>				
Dopamine Metabolite - (Urine)				
	Homovanillate (HVA)	Low end of range	4.3	ug/mg 3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)				
	Vanilmandelate (VMA)	Within range	3.7	ug/mg 2.2 - 5.5
Neuroinflammation Marker - (Urine)				
	Quinolate	Within range	7.7	ug/mg 0 - 9.6
<b>Additional Markers</b>				
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
	Melatonin* (Waking)	Within range	32.3	ng/mg 10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
	8-OHdG (Waking)	High end of range	4.19	ng/mg 0 - 5.2





# Organic Acids

## Case study - B-Hydroxyisovalerate

- **Patient complaints:**
  - Fatigue
  - Dry skin
  - Brain Fog
- **Accompanying markers on DUTCH Test:**
  - Elevated pyroglutamate (low glutathione)
  - Elevated 8-OH-dG (oxidative stress - DNA damage)
  - Low HVA (dopamine)

These correlate to **poor detoxification, poor energy, and overall incomplete metabolism support**





# Organic Acids

## New markers on DUTCH testing

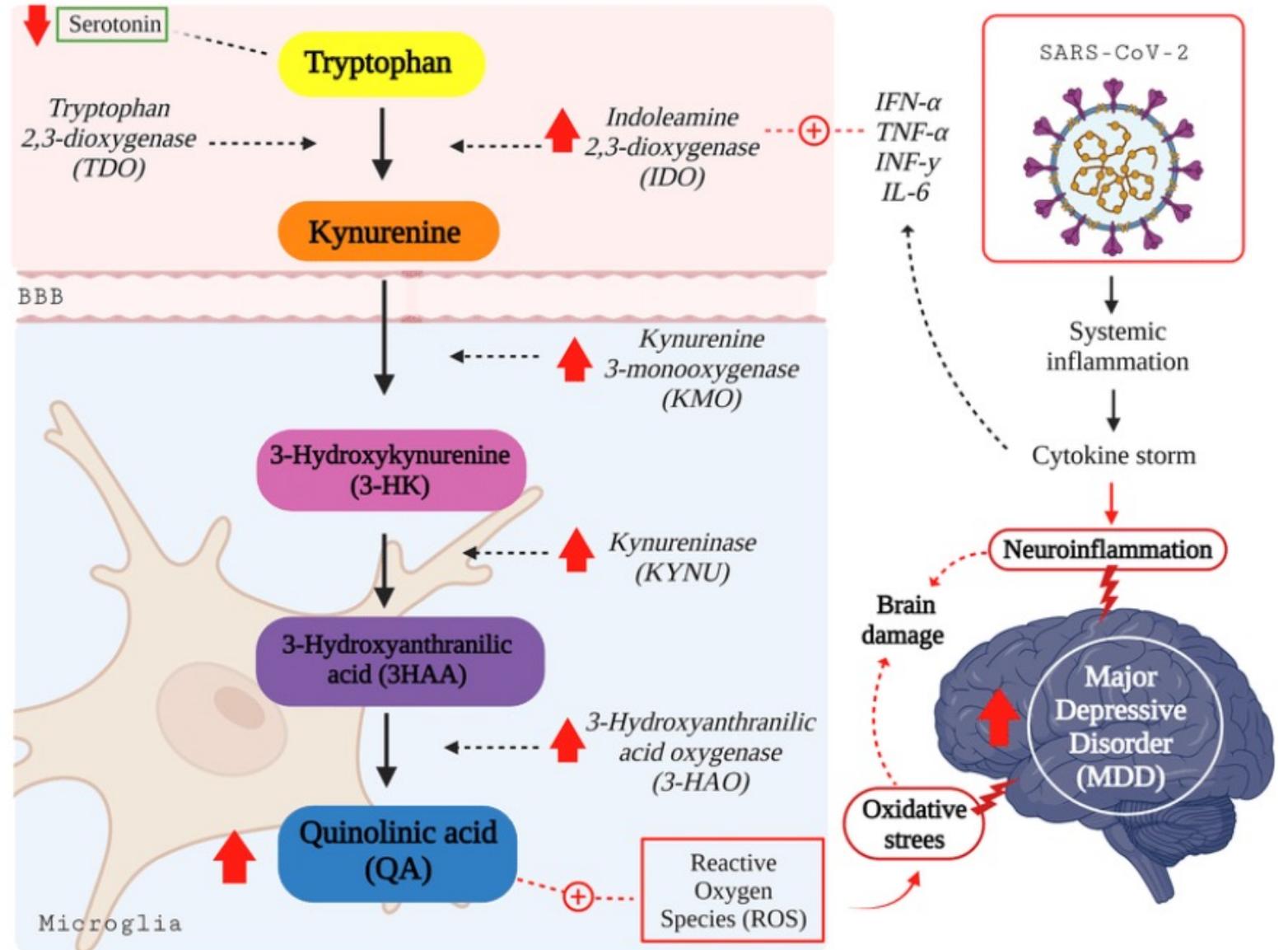
- **Quinolinate** or Quinolinic Acid is elevated when neuroinflammation is present, exposure to phthalates, and generalized inflammation.
- Associated with disease states such as:
  - Amyotrophic Lateral Sclerosis (ALS), Huntington's Disease, motor neuron disease, depression, anxiety, schizophrenia, etc.
  - Neuroinflammatory aggravations that may include Lyme Disease, Covid, post-viral inflammation, etc.
  - False elevations due to tryptophan supplementation



# Organic Acids

## Quinolinate

- Inflammatory Cascade for Quinolinate
- High levels of quinolinate may activate ROS creating oxidative stress on the brain (neural) tissue



# Organic Acids

## Quinolinate

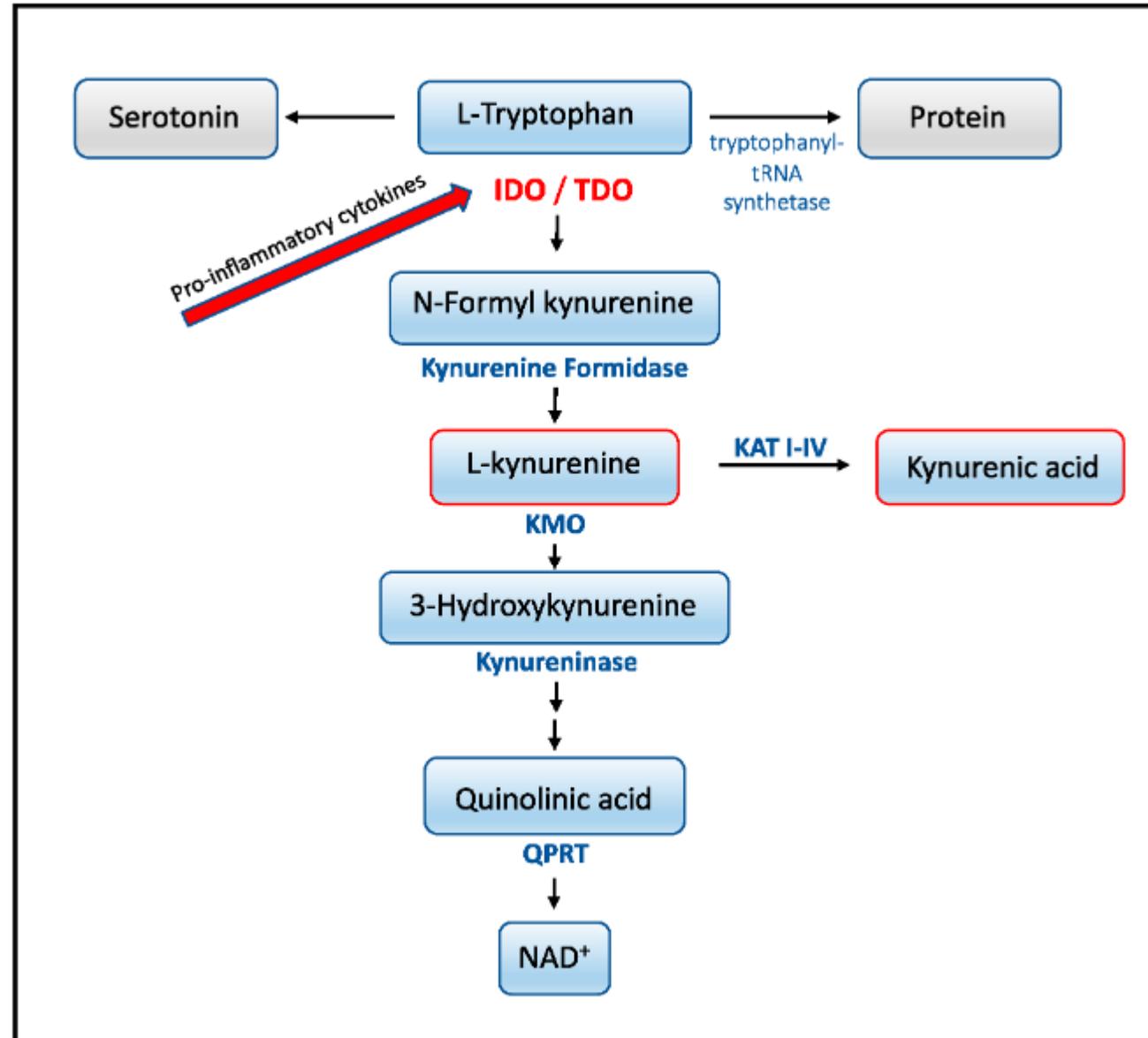
- **Quinolinate** is a precursor, through tryptophan metabolism, to make NAD.
- 1 molecule of NAD equals 3 ATP molecules = **ENERGY**
- NAD is an important molecule that our cells depend on for energy and to reduce oxidation (when cells need to detoxify or get rid of toxins).
- **Quinolinate** is an important intermediary to create NAD for our cells to manage toxicity or inflammation to allow fuel or energy for our cells to fight off toxins.
- There is a delicate balance between activation of quinolinate to help fight off bad toxins, and too much quinolinate if the body is not able to sufficiently fight off toxins or regenerate healthy cells.
- **Quinolinate** is an important factor in evaluating inflammation and inflammatory response in different cell types (usually immune cells from nerve tissue/brain tissue).



# Organic Acids

## Quinolinate

- Quinolinate production of NAD (*de novo synthesis*)
  - Tryptophan is taken from serotonin or protein metabolism due to inflammation
  - Inflammation activates the IDO enzyme down the inflammatory pathway



# Organic Acids

## Case study - Quinolinate

Category	Test	Result	Units	Normal Range
<b>Nutritional Organic Acids</b>				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Within range	1.59 ug/mg	0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Within range	0.89 ug/mg	0.12 - 1.2
	Kynurenate	Within range	3.5 ug/mg	0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	High end of range	53.5 ug/mg	28 - 58
Biotin Marker (may be deficient if high) - (Urine)				
	b-Hydroxyisovalerate	Within range	7.2 ug/mg	0 - 12.5
Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)				
	Indican	High end of range	99.2 ug/mg	0 - 100
<b>Neuro-related Markers</b>				
Dopamine Metabolite - (Urine)				
	Homovanillate (HVA)	Within range	4.7 ug/mg	3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)				
	Vanilmandelate (VMA)	Within range	3.3 ug/mg	2.2 - 5.5
Neuroinflammation Marker - (Urine)				
	Quinolinate	Above range	12.4 ug/mg	0 - 9.6
<b>Additional Markers</b>				
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
	Melatonin* (Waking)	Low end of range	23.0 ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
	8-OHdG (Waking)	Within range	3.16 ng/mg	0 - 5.2



# Organic Acids

## Case study - Quinolinate

- **Patient symptoms:**
  - Fatigue
  - Significant stress
  - Poor sleep
  - PMS/Anxiety/Irritability
  - Pulling it all together:
- **Associated markers on DUTCH testing:**
  - Low melatonin (anti-oxidant)
  - High pyroglutamate (oxidative stress)
  - High indican (gut health imbalance)

These results suggest that we need to evaluate levels of stress and triggers that may be contributing to elevated quinolinate such as oxidative stress, inflammation, or more. Remember to rule out tryptophan supplementation.





# Organic Acids

## New markers on DUTCH testing

- **Indican**
- every person makes indican!
- Indican is a tryptophan by-product.
- In the gut, our bacteria metabolize tryptophan, an amino acid.
- There is high correlation between gut dysbiosis and elevated (not normal) levels of Indican.
  - When there is more bacteria present to break down our tryptophan we have higher levels of Indican





# Organic Acids

## Indican

- Indican levels elevate when:
  - the body is unable to break down proteins efficiently (putrefaction)
  - the gallbladder and/or pancreas are not meeting the enzyme production demands to break down food well (putrefaction) due to poor break down of proteins
  - poor intestinal motility (putrefaction)
  - there is high intake of animal protein



# Organic Acids

## Indican

- Indican can readily be found in stool
- Because Indican is easily found in stool and everyone makes Indican, when this is found elevated in urine this means there is enough Indican available to go through circulation, through the kidneys, and dump into the urine.
- This [extra] is what can be found in urine testing and why elevated levels should encourage further evaluation.



# Organic Acids

## Indican

- Symptoms or presentations associated with elevated Indican:

- Small Intestinal Bacterial Overgrowth (SIBO)
- Overgrowth of anerobic bacteria in the colon
- Malabsorption
- Bloating
- Discomfort



- Constipation
- Pancreatic insufficiency
- Celiac Disease
- *Rarely:* cancers, ulcers, obstruction





# Organic Acids

## Indican

- Indican
- Special Considerations:
- Low protein diets – Vegan/Vegetarian diets
  - small amounts may indicate significant dysbiosis due to generally low putrefaction levels
- Unabsorbed antibiotics
  - killing off bacteria
- High amounts of *Lactobacillus* spp





# Organic Acids

## Indican

- **Indican** itself is not a sufficient enough marker to know what types of treatment may be needed, but it is a wonderful indicator that further work up should be completed to understand what is happening in the gut.
- **Indican** levels are not reliable to understand how *severe* gut dysbiosis levels are due to variability in diet, gut health in general, microbiome, etc.





# Organic Acids

## Indican

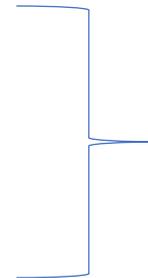
- Indican and correlations with Estrogen metabolism
  - Estrogen Detoxification occurs in **3 Phases**
  - **Phase I** = metabolism
  - **Phase II** = conjugation
  - **Phase III** = excretion



# Organic Acids

Indican

- Estrogen Detoxification occurs in 3 Phases
- Phase I = metabolism
- Phase II = conjugation
- Phase III = excretion



We test these on the  
DUTCH Test





# Organic Acids

Indican

- Estrogen Detoxification occurs in 3 Phases
- Phase I = metabolism
- Phase II = conjugation
- Phase III = excretion



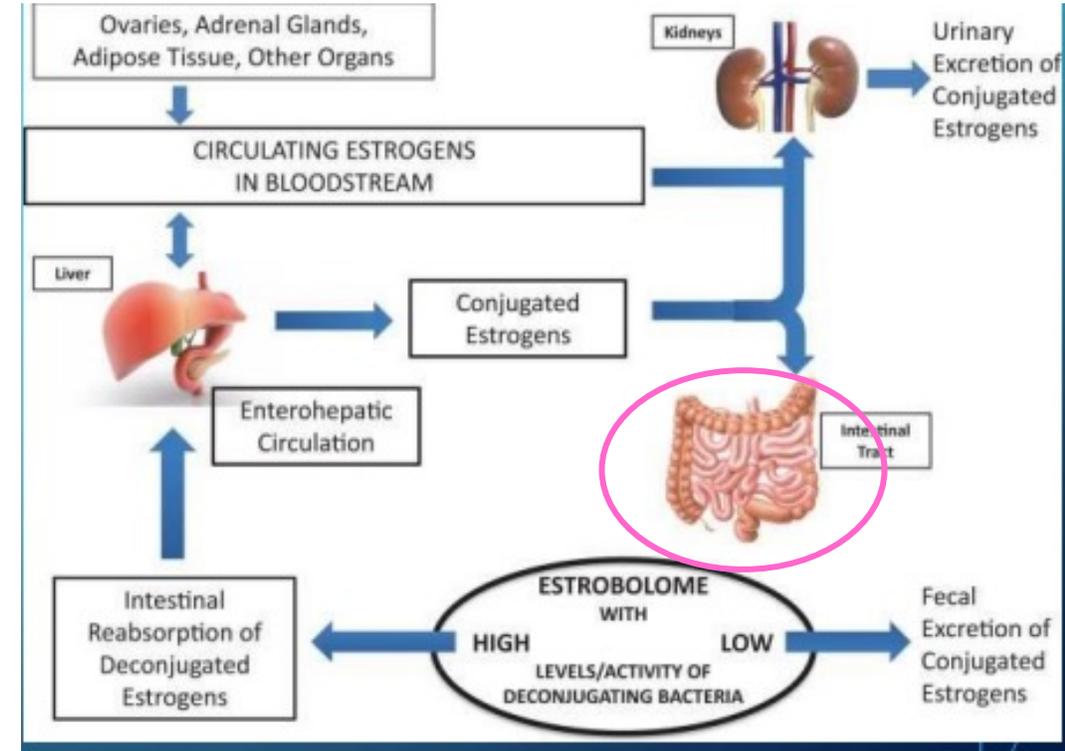
Seen in stool testing



# Organic Acids

Idican

- Gut metabolism of estrogen is managed by the **estrobolome**, which is comprised of its own unique group of enteric bacteria.
- We know the gut microbiome can influence estrogen metabolism through particular enzymes, like  **$\beta$ -glucuronidase**





# Organic Acids

## Indican

- Since the estrobolome influences estrogen, and these are bacteria in the gut, it makes sense that Indican can also show correlations with hormone (more specifically estrogen) dysfunction or imbalance.
- ...and we have seen this on DUTCH testing!



# Organic Acids

## Case study - Indican

Category	Test	Result	Units	Normal Range
<b>Nutritional Organic Acids</b>				
Vitamin B12 Marker (may be deficient if high) - (Urine)				
	Methylmalonate (MMA)	Above range	2.77	ug/mg 0 - 2.5
Vitamin B6 Markers (may be deficient if high) - (Urine)				
	Xanthurenate	Below range	0.06	ug/mg 0.12 - 1.2
	Kynurenate	Below range	0.71	ug/mg 0.8 - 4.5
Glutathione Marker (may be deficient if low or high) - (Urine)				
	Pyroglutamate	High end of range	54.2	ug/mg 28 - 58
Biotin Marker (may be deficient if high) - (Urine)				
	h-Hydroxyisovalerate	Within range	3.6	ug/mg 0 - 12.5
Gut Marker (potential gut putrefaction or dysbiosis if high) - (Urine)				
	Indican	Above range	133.0	ug/mg 0 - 100
<b>Neuro-related Markers</b>				
Dopamine Metabolite - (Urine)				
	Homovanillate (HVA)	Below range	1.9	ug/mg 3 - 11
Norepinephrine/Epinephrine Metabolite - (Urine)				
	Vanilmandelate (VMA)	Above range	6.6	ug/mg 2.2 - 5.5
Neuroinflammation Marker - (Urine)				
	Quinolate	Within range	5.4	ug/mg 0 - 9.6
<b>Additional Markers</b>				
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
	Melatonin* (Waking)	Above range	10813.8	ng/mg 10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
	8-OHdG (Waking)	Within range	2.11	ng/mg 0 - 5.2





# Organic Acids

## Case study - indican

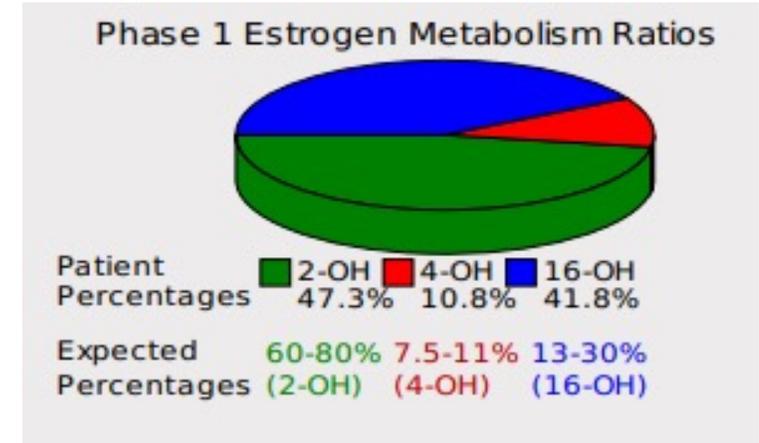
- Patient symptoms:
- + constipation
- + fatigue
- + migraines
- + hormone symptoms
- + poor sleep



# Organic Acids

## Case study - Indican

- Correlative Markers:
  - Estrogen metabolism:
    - Phase I of liver clearance/detoxification is poor
- Poor absorption:
  - MMA elevated (low B12)
  - Elevated pyroglutamate
  - Imbalanced HVA/VMA (poor adrenal/stress response)





# Organic Acids

- **How** we can utilize these new markers
- Multifactorial in reviewing:
  - Nutritional deficiencies
  - Neuroinflammation
  - Gut health





# Organic Acids

- **How** we can utilize these new markers:
- Complementary to other markers on the DUTCH test as well as other testing modalities (stool testing, nutritional evaluation, etc.)
- They tell a story. With each layer of information, we are able to understand how to approach healing on a deeper level.
- We can create better overall healing

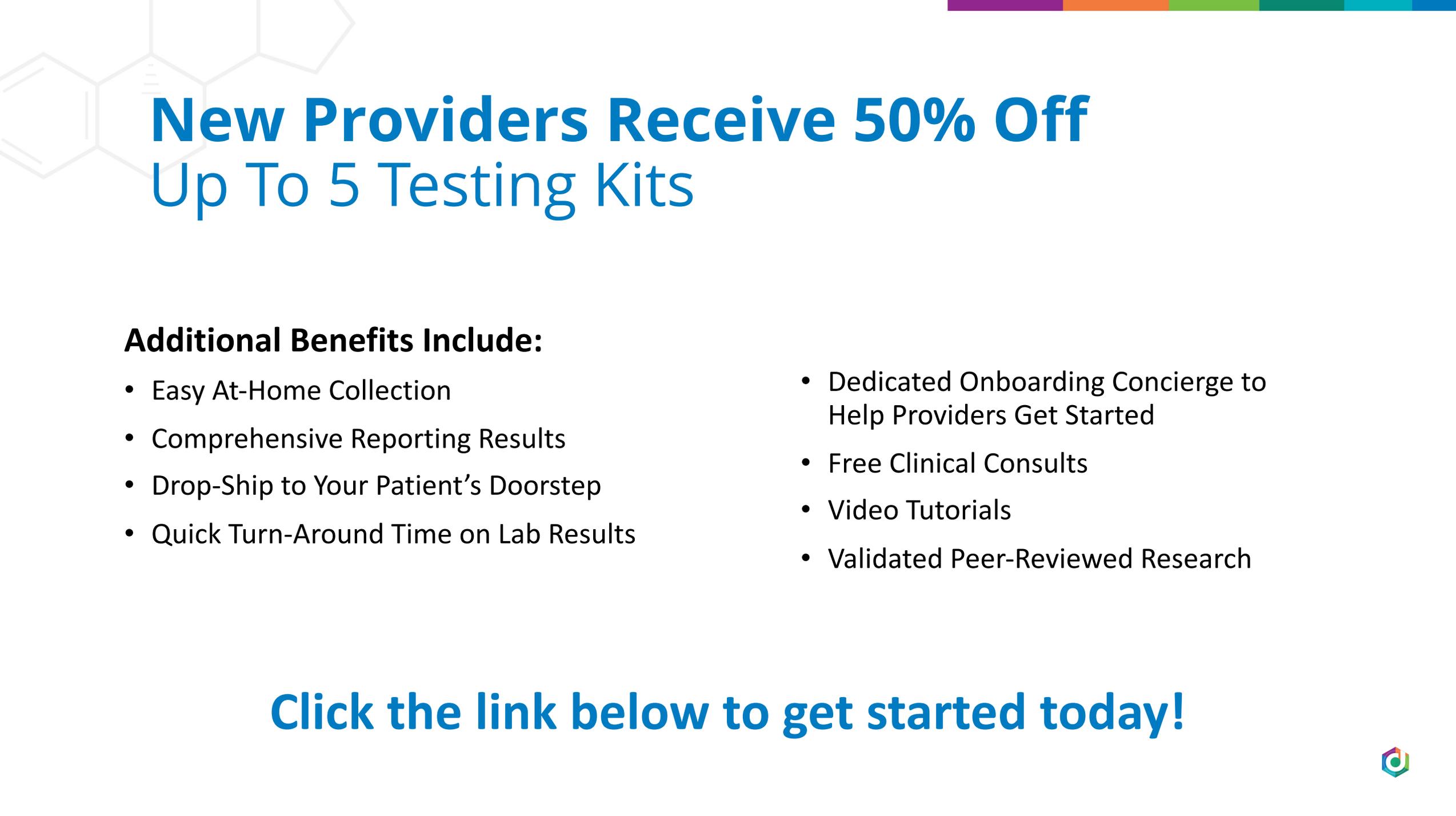


# Organic Acids

- Thank you for your time and attention today!
- We look forward to learning more with you in the future!
- Dr. Debbie Rice







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