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Organic Acids Testing Essentials

Dan Kalish

DC

Founder of the Kalish Institute, an expert in designing practice plans, and a three-time published author, Dr. Kalish has developed practice models for over 1,000 practitioners worldwide.

Organic Acids Testing Essentials

Dr. Daniel Kalish

INTRODUCTION

Principle investigator in a research study conducted with Integrative Medicine Dept., Mayo Clinic on The Kalish Method.

Currently partnering with industry leading scientist Dr. Richard S. Lord, developing curriculum on advanced lab interpretation.

IFM Certified Practitioner with over 25 years of clinical experience.

Lead faculty for IFM's Practice Implementation Program

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LAB INTERPRETATION BOOTCAMP:

Amino Acids and Vitamins Part 2

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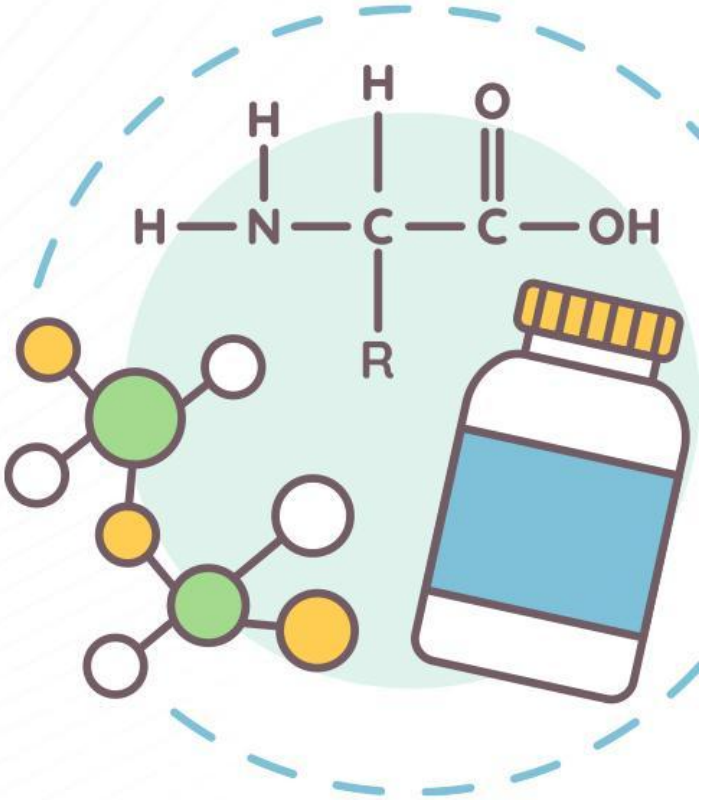

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LEARNING OBJECTIVES

- Review the types of common patient conditions that respond well to organic acids-based treatments such as fatigue, weight gain, depression and anxiety
- Learn the wide array of problems that can be identified on the test including state of inflammation, catabolic physiology, insulin resistance and oxidative stress
- Two approaches: One for practitioners new to this type of test, one for those with 20+ years of experience

WHAT IS ORGANIC ACIDS TESTING?

"Unlike amino acids and fatty acids, the category of compounds called organic acids contains no essential nutrients. Instead of directly measuring nutrient concentrations, abnormal concentrations of organic acids provide functional markers for the metabolic effects of micronutrient inadequacies, toxic exposure, neuroendocrine activity, and intestinal bacterial overgrowth. As such, organic acid testing can indicate the functional need for essential or conditionally essential nutrients, diet modification, antioxidant protection, detoxification, and other therapies" (Lord and Bralley).

ORGANIC ACIDS TEST (OAT)

- Organic acid testing is a way to measure whether your body is getting and using nutrients to drive **optimal health**
- It is designed to assess **metabolic dysfunction**, not diseases
- Like a car's gauges **warn of potential problems, your body has certain chemical indicators, known as organic acids,** that can alert you to potential problems

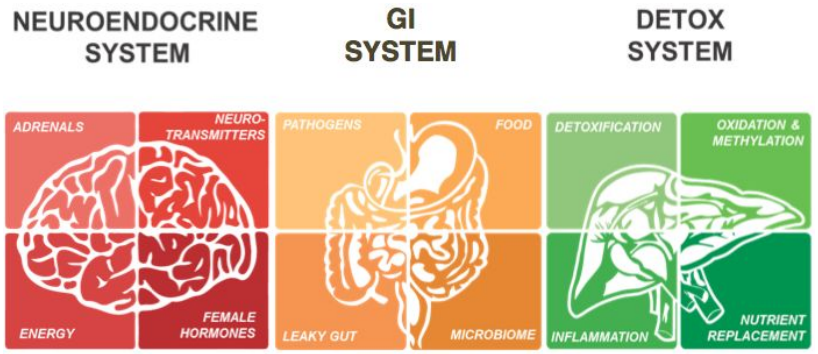
WHO DO WE USE ORGANIC ACIDS TESTING WITH?

EVERYONE…

- Complex patients
- Simple patients
- Annual health assessment for long term maintenance
- Prenatal nutritional programs
- Chemotherapy and radiation recovery programs
- Weight loss
- Fatigue
- Depression/anxiety
- GI factors especially when stool testing normal

WAYS THE OAT CAN BE INTERPRETED

The 4 Horsemen



The 3 Body Systems

Fatty Acid Metabolism

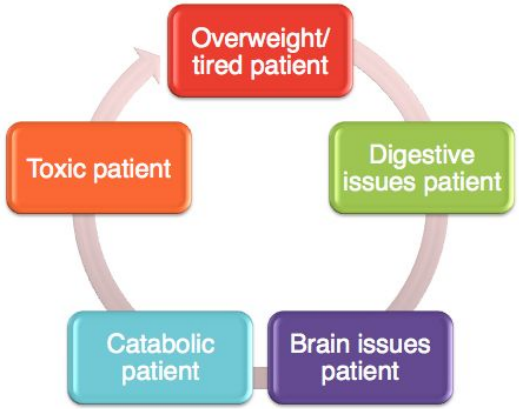
Suberate
Ethylmalonate

Carbohydrate Metabolism

β-Hydroxybutyrate
L-Lactate

Energy Production Markers

Organic Acids Markers



Common Patient Presentations

FOUR HORSEMEN OF PHYSIOLOGICAL DAMAGE

INFLAMMATION

CATABOLIC PHYSIOLOGY

INSULIN RESISTANCE

OXIDATIVE STRESS

PHYSIOLOGICAL DAMAGE IMPACTS

What is getting damaged?

- Mitochondria
- Adrenals
- Neurotransmitters
- DNA
- Gut lining
- Liver

Where is the damage coming from?

- Inflammation
- Oxidative stress
- Catabolic physiology
- Food reactions
- Pathogens
- Toxins

BODY SYSTEMS AND SYMPTOMS

Where is the damage impacting the person?

- Brain inflamed
- Brain chemicals depleted
- Liver toxic/fatty liver
- GI tract inflamed, leaky gut, overgrowth of harmful organisms
- Energy production damaged from oxidative stress
- Carb and fat metabolism damaged from inflammation

UNDERLYING CAUSES

Where is the physiological damage originating from?

- Underlying causes vary and tend to cause the same types of physiological damage
- GI infections, gluten, toxic metals, toxic chemicals, emotional distress all tend to trigger similar patterns of physiological damage

KALISH METHOD TREATMENT MODEL

Underlying Cause	Physiological Damage	Body Systems	Symptoms
Emotional/spiritual (trauma/abuse/chronic stress/addiction)	Inflammation	Neuroendocrine	Weight gain
Dietary (blood sugar, poor diet, nutrient deficiencies, dairy, food allergies)	Catabolic Physiology	GI	Fatigue
Gluten	Insulin Resistance	Liver	Depression
GI infections	Oxidative Stress		Anxiety
Toxins (heavy metals, chemicals)			GI problems (gas, bloating, constipation, diarrhea, heartburn)
Genetics/Epigenetics			Sex hormone imbalance (low sex drive, infertility, hot flashes, nightsweats, PMS, PCOS)
Structural (physical trauma, chronic injury, pain, posture)			Pain
Sleep			Allergies
Exercise			ADHD
Medications/surgery			Insomnia
Dental			Brain fog
Lyme, mold, viral or bacterial (SIBO, environmental exposure)			Sugar cravings
			Skin problems
			Autoimmune

ORGANIC ACIDS MARKERS

Carb Metabolism Markers
- Pyruvate
- Lactate
- b-Hydroxybutyrate

Energy Production Markers
- Citrate
- Cis-Aconitate
- Isocitrate
- a-Ketoglutarate
- Succinate
- Fumarate
- Malate
- Hydroxymethylglutarate

Fatty Acid Metabolism Markers
- Adipate
- Suberate
- Ethylomalonate

B-Complex Vitamin Markers
- a-Ketoisovalerate
- a-Ketoisocaproate
- a-Keto-b-Methylvalerate
- Xanthurenate
- b-Hydroxyisovalerate

NEUROENDOCRINE SYSTEM

Neurotransmitter Metabolism Markers
- Vanilmandelate
- Homovanillate
- 5-Hydroxyindoleacetate
- Kynurenate
- Quinolinate

GI SYSTEM

Bacterial, Clostridial, and Yeast Markers
- Benzoate
- Hippurate
- Phenylacetate
- HPA
- Indican
- Tricarballylate
- D-Lactate
- DHPP
- D-Arabinitol

DETOX SYSTEM

Detoxification Markers
- 2-Methylhippurate
- Orotate
- Glucarate
- a-Hydroxybutyrate
- Pyroglutamate
- Sulfate

Oxidative Damage and Antioxidant Markers
- P-Hydroxyphenyllactate
- 8-hydroxy-2'-Deoxyguanosine

Methylation Cofactor Markers
- Methylmalonate
- Formiminoglutamate

SUPPLEMENTS ASSOCIATED WITH ORGANIC ACIDS

NEUROENDOCRINE SYSTEM

Carb Metabolism Markers
- Lipoic Acid, B1,B2,B3,B5
- Cr, V, Lipoic Acid, Mg, Mn

Energy Production Markers
- Arginine, Mg, lipoic acid, taurine, methionine
- Arginine and Fe
- B1, B3, B5, Asp
- CoQ10, B2

Fatty Acid Metabolism Markers
- Carnitine
- Vitamin B2

B-Complex Vitamin Markers
- B1, B2, B3, B5, Lipoic Acid
- B6
- Pre and probiotics

Neurotransmitter Metabolism Markers
- Tyrosine, Mucuna
- 5HTP
- B6
- Magnesium

GI SYSTEM

Bacterial, Clostridial, and Yeast Markers
- Glycine, pre and probiotics
- Broad spectrum minerals
- Vitamin C
- *S. boulardii*

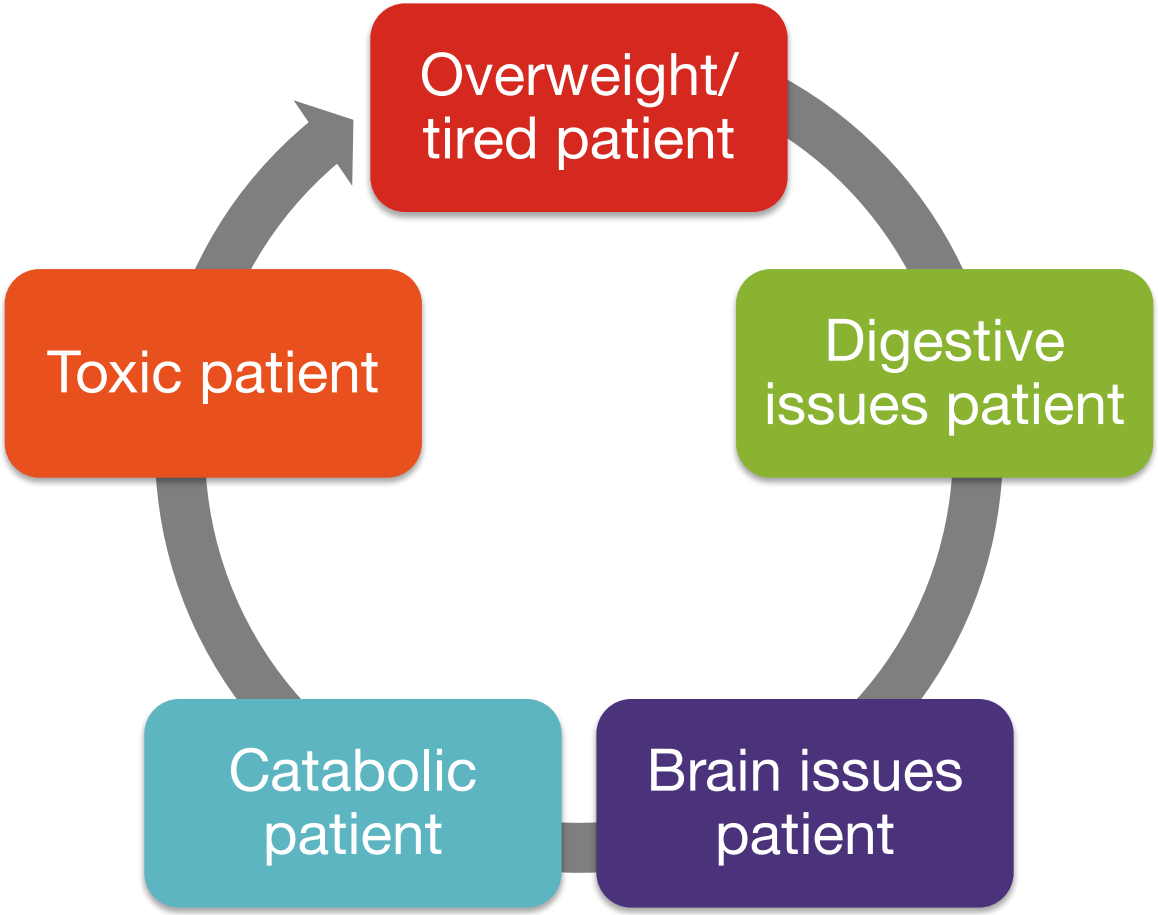
DETOX SYSTEM

Detoxification Markers
- Glycine
- Digestive enzymes, HCl, Mg, Arginine
- Milk thistle, N-acetylcysteine, glutathione
- Taurine, methionine
- Carnitine

Oxidative Damage and Antioxidant Markers
- Antioxidants, vitamin C, and CoQ10
- Vitamin E, lipoic acid

Methylation Cofactor Markers
- B12
- Folate

COMMON PATIENT PRESENTATIONS



MACRO BEFORE MICRO

Think Macronutrients BEFORE you think micronutrients, where are the macronutrients going? What macronutrient imbalances are there? Amino acids, fats, carbs?

MICRONUTRIENT DEFICIENCIES

Labs show depletion and can reveal micronutrient deficiencies

- Depleting serotonin and dopamine from brain
- Depleting B6/B12/Folate leading to methylation problems
- Depleting sulfur amino acids leading to liver detox phase 2 as well as catecholamine imbalances
- Depleting anti-oxidants leading to oxidative stress being placed on DNA, energy production
- Depleting of good bacteria and imbalance of flora in GI tract
- Depleting of carnitine, CoQ10, free form amino acids, B vitamins and other Krebs cycle intermediaries

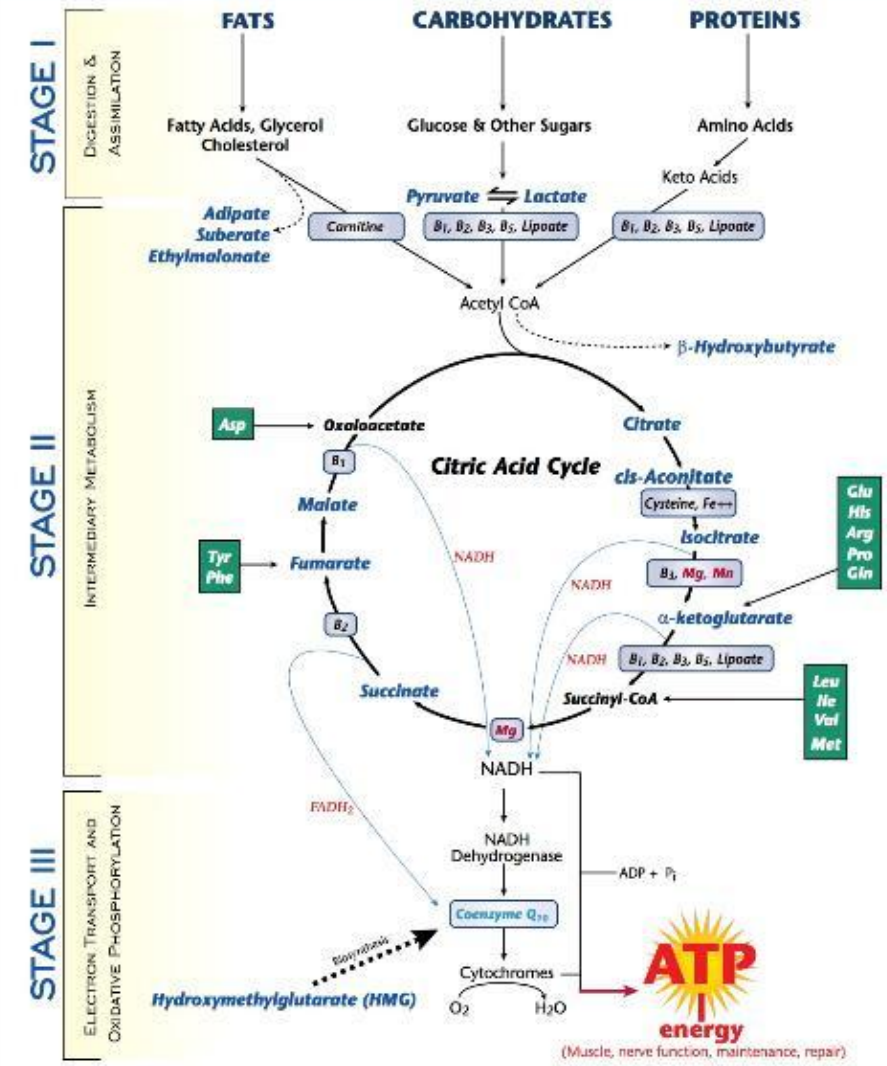


Figure 2 – Urinary Markers of Nutrients Involved in Central Energy Pathways

The Citric Acid Cycle (CAC) and Electron Transport and Oxidation Phosphorylation pathways end in ATP or energy production, which is essential to life. A deficiency of any of the nutrient co-factors involved in these processes may lead to increases of specific compounds.

SUMMARY

KEY CONCEPTS:

- Complex but highly effective tool that allows you as a practitioner to see a variety of your patient's body processes in depth
- Provides the foundation of knowledge behind designing effective treatment programs
- View the results in several ways using the 4 Horsemen, 3 body systems, by individual organic acids markers, and patient archetype
- Invaluable tool in creating an individualized supplementation program

ADVANCED MATERIALS:

ORIGINS STORY OF ORGANIC ACIDS TESTING, USE IN CONVENTIONAL MEDICINE

THE KALISH INSTITUTE
BUILDING SUCCESSFUL FUNCTIONAL MEDICINE PRACTICES

INHERITED METABOLIC DISEASE IN ADULTS

A Clinical Guide

EDITED BY Carla E. M. Hollak

Robin H. Lachmann

Neurology® Clinical Practice | AMERICAN ACADEMY OF NEUROLOGY.

Neurol Clin Pract. 2017 Dec; 7(6): 518–522.
doi: 10.1212/CPJ.0000000000000379

PMCID: PMC5800716
PMID: 29431165

"Think metabolic" in adults with diagnostic challenges

Biotinidase deficiency as a paradigm disorder

Barry Wolf, MD, PhD

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Abstract

Go to:

Neurologists should consider the possibility of an inherited metabolic disorder in adults with neurologic symptoms that may or may not mimic those seen in affected children, such as in the case of biotinidase deficiency. Because many of these disorders are treatable, they must be included in the differential diagnosis. Technologies, such as specific biochemical analysis and whole exomic sequencing, can assist

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WELCOME

Thank you for visiting the SSIEM Adult Metabolic Physicians group website. We are a subgroup of physicians within the SSIEM looking after adult patients with inborn errors of metabolism. Meetings of the group are held during SSIEM meetings/symposia in adult specific sessions.

This website provides information regarding our membership and clinical units, relevant events, as well as education and training in the clinical care of adults with inborn errors of metabolism.

ATM | Annals of Translational Medicine

Ann Transl Med. 2018 Dec; 6(24): 472.
doi: 10.21037/atm.2018.12.39

PMCID: PMC6331355
PMID: 30740403

Organic acid disorders

Jessica Ramsay,[1] Jacob Morton,[1] Marie Norris,[2] and Shibani Kanungo[✉1]

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Abstract

Go to:

Organic acids (OAs) are intermediary products of several amino acid catabolism or degradation via multiple biochemical pathways for energy production. Vitamins or co-factors are often quintessential elements in such degradation pathways and OA metabolism. OAs that result from enzyme defects in these pathways can be identified in body fluids utilizing gas chromatography-mass spectrometry techniques (GC/MS). OAs are silent contributor to acid base imbalance and can affect nitrogen balance and recycling. Since OA production occurs in distal steps of a specific amino acid catabolism, offending amino acid accumulation is not characteristic. OA disorders as inborn errors of metabolism (IEM) are included in differential diagnosis of metabolic acidosis, as the common mnemonic MUDPILES taught in medical schools. High anion gap metabolic acidosis with hyperammonemia is a characteristic OA biochemical finding. VOMIT (valine, odd chain fatty acids, methionine, isoleucine, and threonine) is a smart acronym and a common clinical presentation of OA disorders and can present as early life-threatening illness, prior to Newborn Screening results availability. Easy identification and available medical formula make the field of metabolic nutrition vital for management of OA disorders. Treatment strategies also involve cofactor/vitamin utilization to aid specific pathways and disorder management. Optimal metabolic control and regular monitoring is key to long-term management and prevention of morbidity, disability and mortality. Prompt utilization of acute illness protocol (AIP) or emergency protocol and disorder specific education of family members or caregivers, primary care physicians and local emergency health care facilities; cautiously addressing common childhood illnesses in patients with OA disorders, can help avoid poor short- and long-term morbidity, disability and mortality outcomes.

Introduction

Go to:

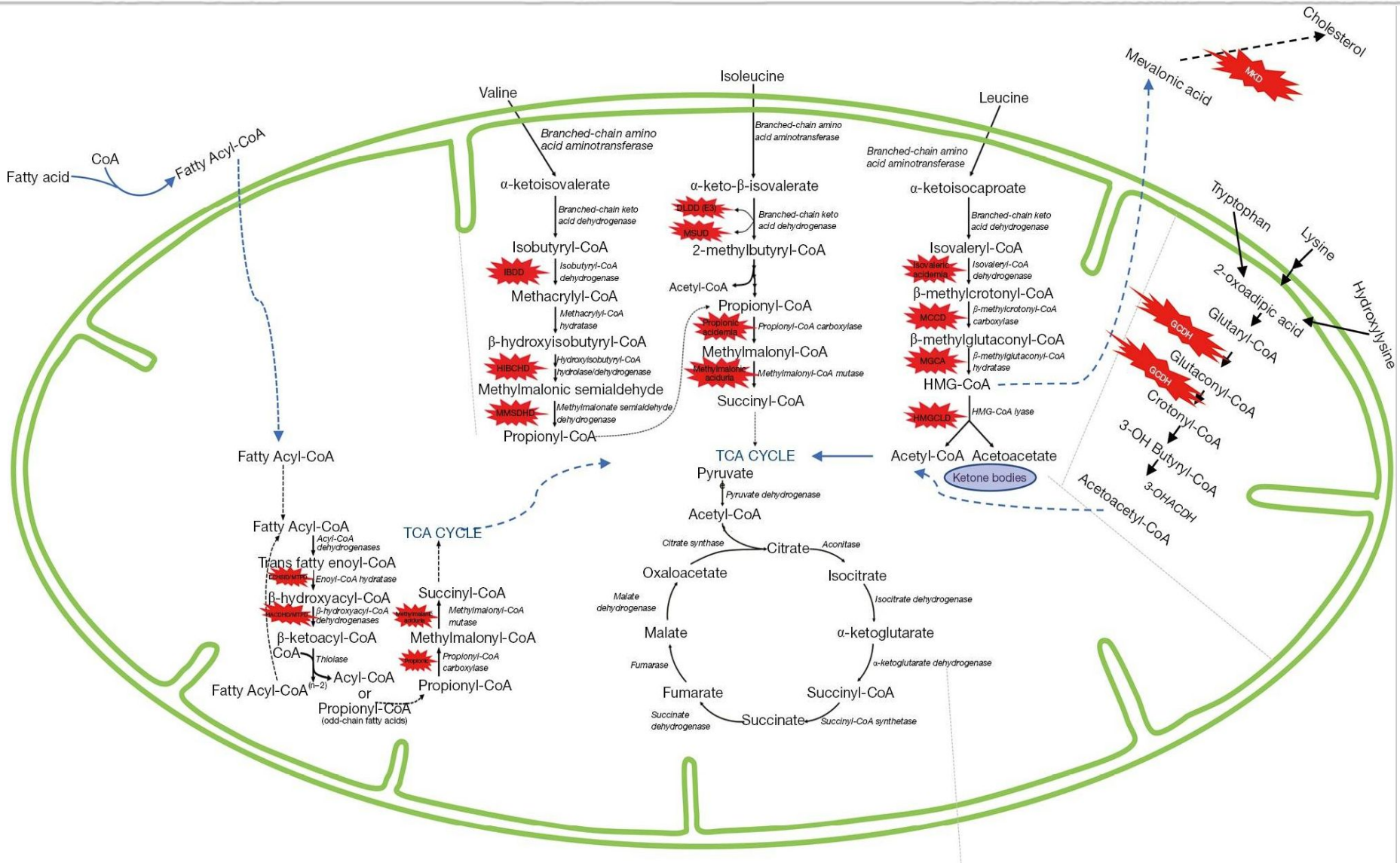
Inborn errors of metabolism (IEM) affecting enzymes and/or transport proteins required for catabolism of amino acids (AAs), lipids, or carbohydrates lead to pathologic buildup of upstream substrates/metabolites resulting in the clinical manifestations of organic acid disorders (OADs), also known as organic acidemias or acidurias. More than 65 specific organic acids (OAs) affecting these pathways have been identified (1). The "classical OAs" refer the most common inborn errors of branched chain AA (BCAA) catabolism, which include maple syrup urine disease (MSUD) and the isovaleric (IVA), propionic (PA), and methylmalonic (MMA) acidemias (or acidurias) (1,2).

SAMPLING OF CONDITIONS POTENTIALLY RELATED TO GENETICS

Mitochondrial Disorders

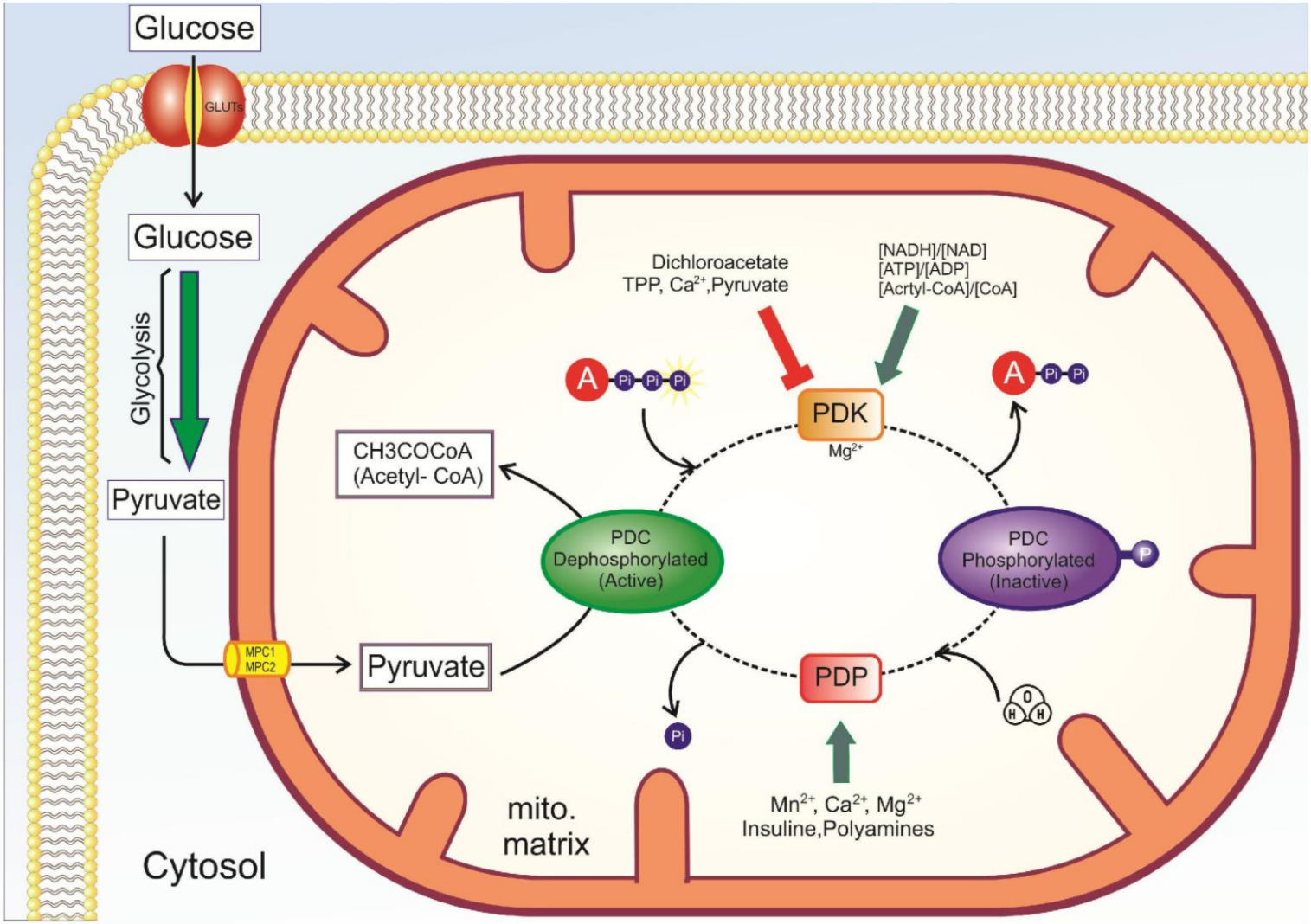
Glycolysis - Insulin Resistance

Urea Cycle and Arginine - Ammonia Toxicity/Nitric Oxide



Overview of organic acid (OA) metabolism. Enzyme names are represented in italics and corresponding intra-mitochondrial enzyme deficiencies are shown in the red star shapes. Green line represents mitochondrial

GLYCOLYSIS


Glucose
GLUTs
Glucose
Glycolysis
Pyruvate
MPC1
MPC2
Pyruvate
Cytosol
mito.
matrix
Dichloroacetate
TPP, Ca2+,Pyruvate
[NADH]/[NAD]
[ATP]/[ADP]
[Acrtyl-CoA]/[CoA]
A
Pi
Pi
Pi
PDK
Mg2+
A
Pi
Pi
CH3COCoA
(Acetyl- CoA)
PDC
Dephosphorylated
(Active)
PDC
Phosphorylated
(Inactive)
P
PDP
Pi
O
H
H
Mn2+, Ca2+, Mg2+
Insuline,Polyamines

PYRUVATE DEHYDROGENASE

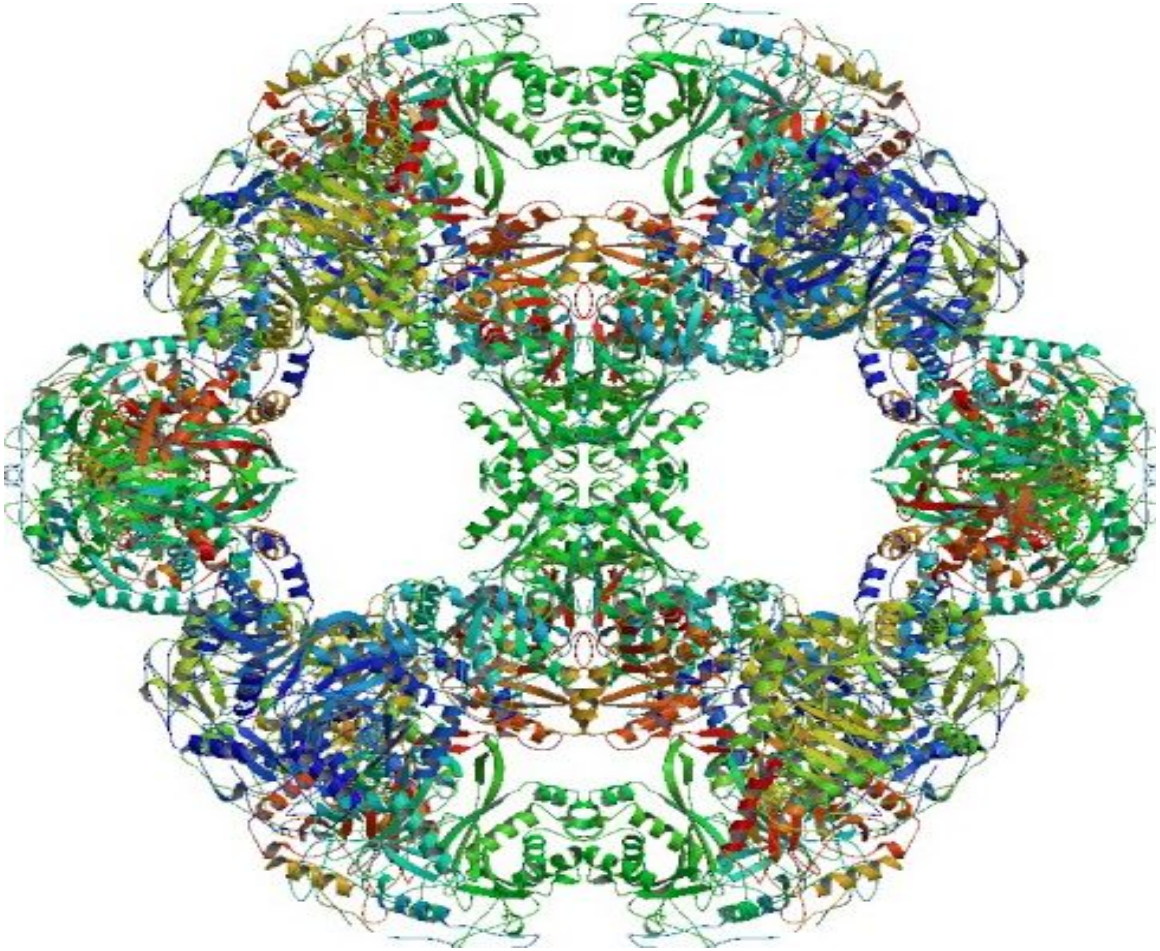
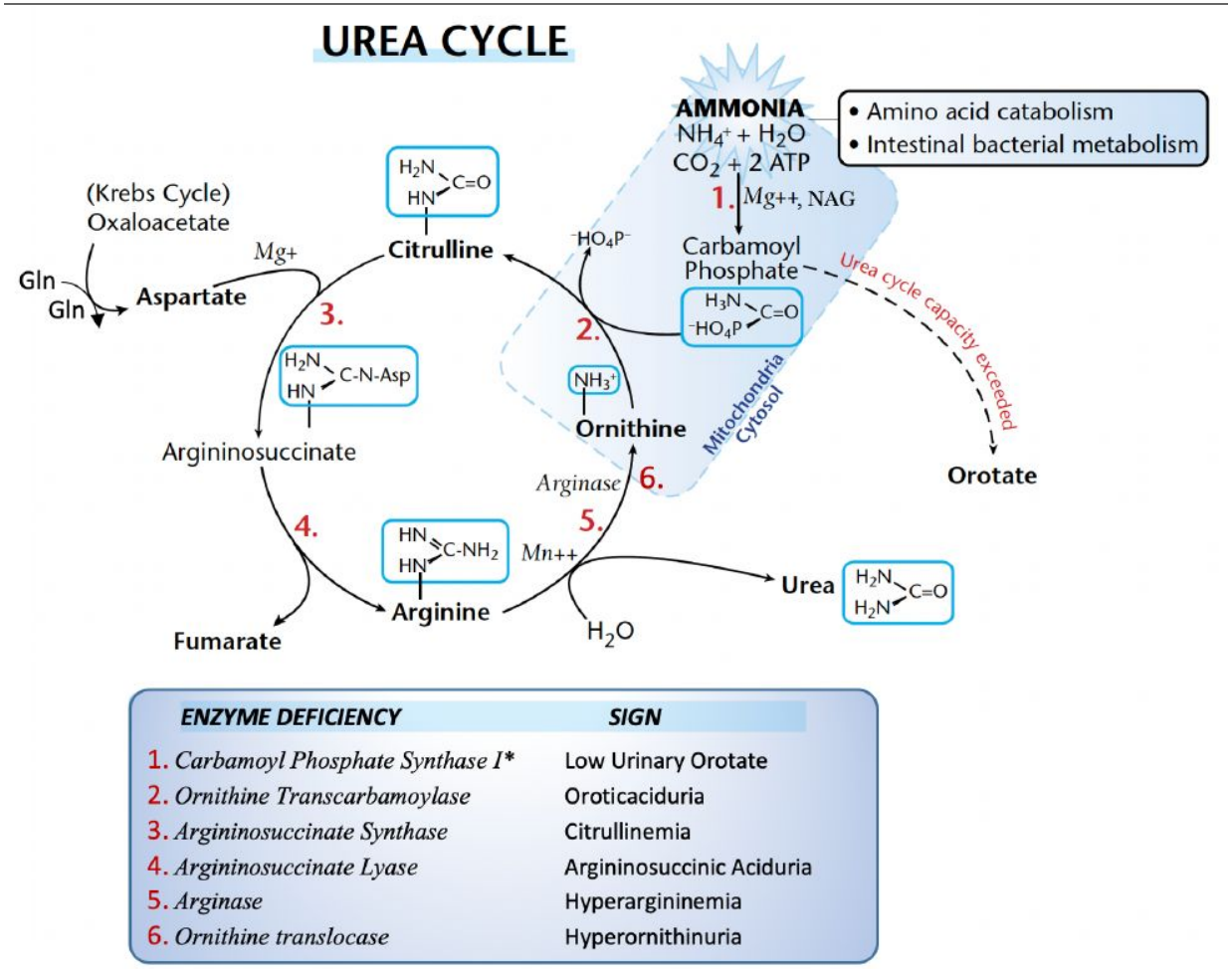


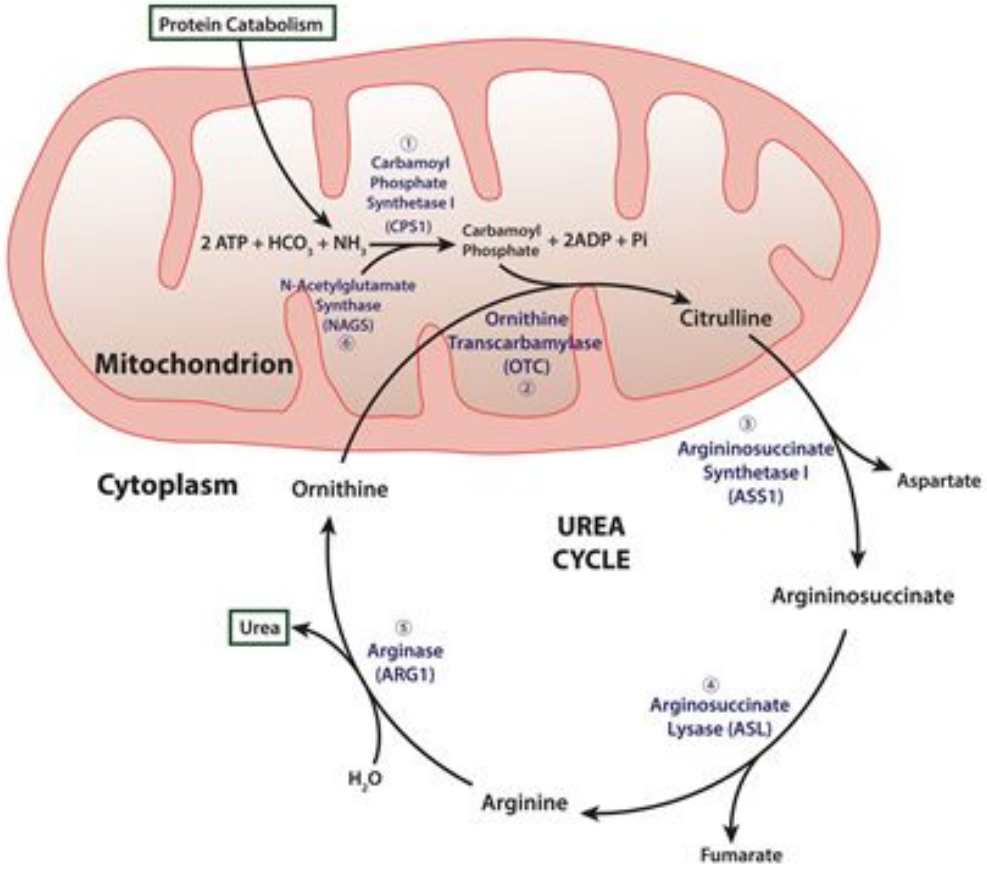
Figure 6.10 – The Urea Cycle



ENZYME DEFICIENCY	SIGN
1. *Carbamoyl Phosphate Synthase I**	Low Urinary Orotate
2. *Ornithine Transcarbamoylase*	Oroticaciduria
3. *Argininosuccinate Synthase*	Citrullinemia
4. *Argininosuccinate Lyase*	Argininosuccinic Aciduria
5. *Arginase*	Hyperargininemia
6. *Ornithine translocase*	Hyperornithinuria

* N-Acetylglutamine (NAG) is an essential cofactor for *CPSI*

The urea cycle produces urea from the nitrogenous waste products of protein metabolism.



Nicholas F Blair et al. Pract Neurol 2015;15:45-48

PN

Urea cycle disorders: a life-threatening yet treatable cause of metabolic encephalopathy in adults

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ABSTRACT

Urea cycle disorders are inborn errors of metabolism that, in rare cases, can present for the first time in adulthood. We report a perplexing presentation in a woman 4 days postpartum of bizarre and out-of-character behaviour interspersed with periods of complete normality. Without any focal neurological signs or abnormality on initial investigations, the diagnosis became clear with the finding of a significantly elevated plasma ammonia level, just as she began to deteriorate rapidly. She improved following intravenous dextrose and lipid emulsion, together with sodium benzoate, arginine and a protein-restricted diet. She remains well 12 months later with no permanent sequelae. Whilst this is a rare presentation of an uncommon disease, it is a treatable disorder and

postoperative pain. She had no previous mood disorder or other psychiatric condition. There was no recent alcohol intake or history of substance abuse.

Her initial blood results showed multiple mild abnormalities (table 1), many of which could be explained by recent pregnancy; in particular, there was no renal or hepatic dysfunction, other than mildly elevated serum alkaline phosphatase, which may have been due to placental production. Her CT scan of head was normal. CSF protein was mildly elevated at 0.58 g/L (0.15–0.45) with normal CSF glucose and cell counts; Gram stain was negative.

By the next morning, her clinical status had completely normalised. Detailed

Table 2 Urea cycle disorders and expected investigation results

Urea cycle disorder	Gene	Inheritance	Plasma amino acids	Urine organic acids
Carbamoylphosphate synthetase I deficiency	CPS1	Autosomal recessive	↓ Arginine ↓ Citrulline	↓/Normal urinary orotic acid
Ornithine transcarbamylase deficiency	OTC	X linked	↓ Arginine ↓ Citrulline	↑ Urinary orotic acid
Argininosuccinic acid synthase deficiency or citrullineamia type I	ASS1	Autosomal recessive	↑ Arginine ↑ Citrulline	
Argininosuccinase acid lyase deficiency or argininosuccinaciduria	ASL	Autosomal recessive	↑ Arginine ↑ Citrulline	
Arginase deficiency	ARG1	Autosomal recessive	↑↑ Arginine	
N-acetylglutamate synthase deficiency	NAGS	Autosomal recessive	↓ Arginine ↓ Citrulline	↓/Normal urinary orotic acid

Plasma amino acid and urinary organic acid levels indicated as being low (↓) or high (↑) relative to the reference range.

PAUSE

WORKSHOP ON PROTOCOLS

- Skills to acquire in this section include how to successfully treat three common, almost ubiquitous types of physiological damage:
- Inflammation – Curcumin, Omega 3's, magnesium
- Catabolic physiology – Free Form Amino Acids, magnesium
- Insulin resistance – Thiamine, niacin, pantothenic acid, lipoic acid and chromium,
- Oxidative Stress - Antioxidants, CoQ10, vitamin E, vitamin C, NAC

PHYSIOLOGICAL DAMAGE TREATMENTS

Physiological damage general body wide treatments

- You can treat for overall body wide problems by addressing Physiological Damage that impacts all cells, tissues and organs, this would include insulin resistance, inflammation, catabolic physiology and oxidative stress

SIMPLE PRESET PROTOCOLS

- As you are learning the detailed physiology behind this lab and how to apply the principles in this portion of the course, you can still effect change with simple protocols
- More complex programs can come later, as with everything in life sometimes the simple approach is actually better

SIMPLE SINGLE SUPPLEMENT PROTOCOLS

Simple single supplement list for organic acids testing:

- You can design a simple supplement program based on results of test using one supplement per section that has abnormal markers or a pattern of borderline abnormal markers. You can choose which area to focus on based on patient symptoms or other factors related to your overall treatment plan.
- Single product mitochondrial supplement
- Single product blood sugar supplement

MULTIPLE SUPPLEMENT PROTOCOL FOR MITOCHONDRIA

- Mitochondrial markers positive
- CoQ10 100mg or more 2x daily
- Magnesium 200mg or more 2x daily
- B Complex 1 capsule daily (can add individual B's as indicated)

MULTIPLE SUPPLEMENTGLYCOLYSIS PROTOCOL

- Carbohydrate Metabolism (insulin resistance) high pyruvate, high lactic acid
- B Complex 1 capsule 1-2 x daily
- Lipoic Acid 300mg 1-2 capsules 2x daily
- Magnesium 200mg 2x daily
- Combination blood sugar stabilizer (herbs and nutrients)

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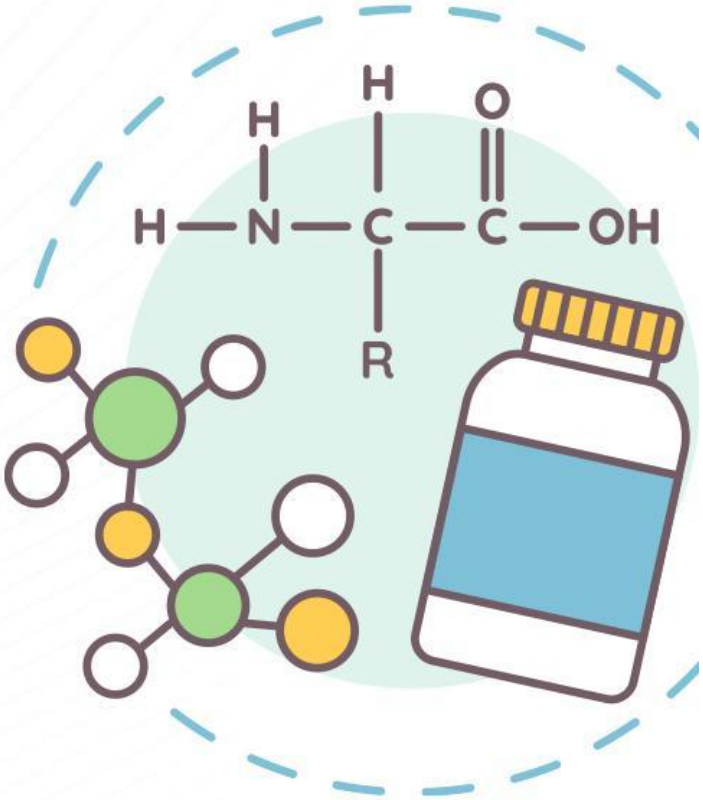

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