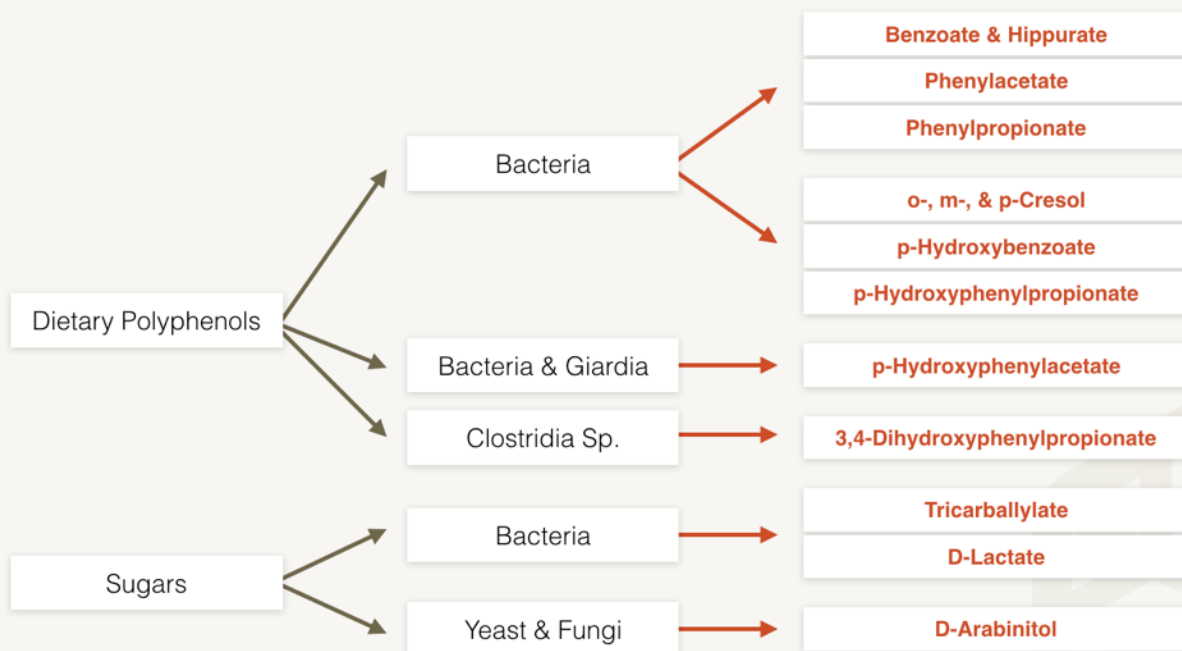


Gut: Organic Acids - Part 1

Hey, everybody, in this presentation we're going to talk about organic acids testing for gastrointestinal health. Organic acids are byproducts of cellular or microbial metabolism. They provide functional markers for metabolic effects of nutrient imbalance, toxic exposure, neuroendocrine activity, and intestinal microbial overgrowth. In the ADAPT Level One course, we're going to focus on using them as markers for microbial overgrowth only. In a future training, I'll cover organic acids testing for metabolic, toxic, and neuroendocrine activity.

Compound Appearing in Urine



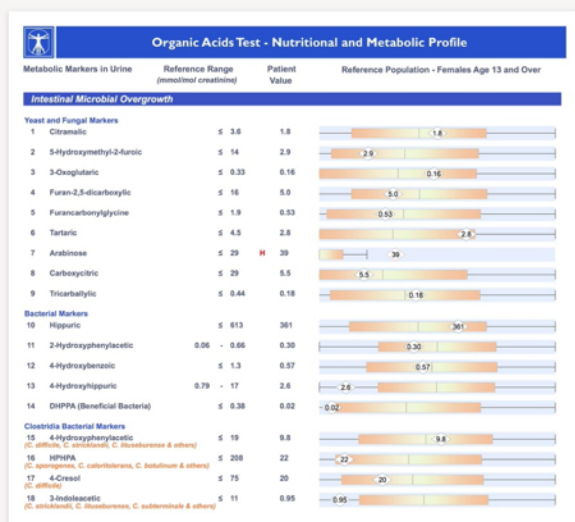
Adapted from: Organix Interpretive Guide: <https://www.gdx.net/core/interpretive-guides/Organix-IG.pdf>

Bacteria in yeast produce metabolites of small molecular weight that can appear in the urine. These compounds reveal the metabolic activities of the microbes that inhabit the mucosal layer and the lumen of the gut. There are a wide range of relative toxicities, cresol being the most toxic and hippurate and benzoate being the least toxic. You'll want to note that production of organic acids most often occurs in the terminal ileum or the ascending colon. The organic acids test therefore cannot tell us whether the problem is in the small intestine or the large intestine, and this is why organic acids testing cannot be used to diagnose SIBO; you need a breath test for that. Specific compounds that are generated by each person depend on available substrates and the species of organisms that are present. Substrates include dietary polyphenols: flavones like parsley, celery, and peppermint; flavonols like cranberries, onions, and peppers; flavanones like citrus;

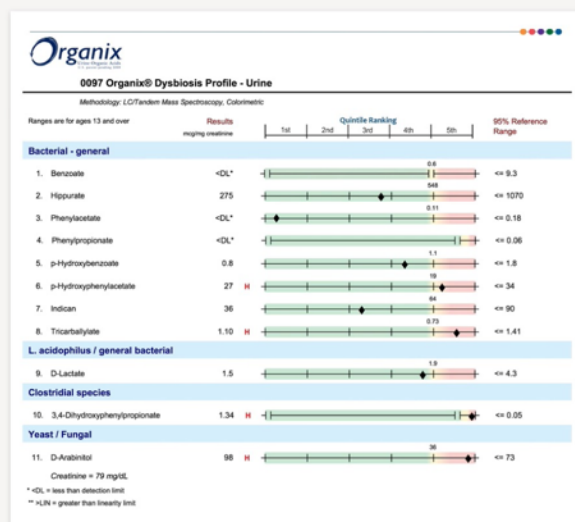
catechins like grapes and plums; anthocyanins like cherries, raspberries, and blueberries; and epicatechins like green and black tea and chocolate. And then amino acids and carbohydrates can also serve as substrates for some organic acids.

Before we jump into test results, I want to tell you a little bit about how I use microbial organic acids testing in practice. I don't think that the research supporting these markers is as strong as stool markers or breath testing. We see a lot of variation in test results depending on what the patient is eating, we've seen some strange variation in results across relatively short time periods, without a lot of explanation for why the results vary that much, and I just feel less confident in organic acids testing overall when compared to stool and breath testing. The other issue is I'm not sure about the ranges that are used by the labs that offer organic acids testing. In the case of metabolic organic acids testing, the ranges on the Genova organics test are much tighter than what you would see in conventional medicine, and the reason for that is they're used to detect functional problems rather than inborn errors of metabolism or serious mitochondrial dysfunction, which is how organic acids testing is used in conventional medicine. So the ranges are tighter, and that may be a good thing for identifying functional issues, but it also means there's less research available to support those ranges. And finally, as I was alluding to earlier, I will sometimes see results on retesting that don't make sense. Other markers, like stool testing and breath testing and signs and symptoms improve, but the organic acids test results might get worse, and I've never been able to fully explain why that is.

Having said all that, there is more evidence for some markers than others, and I'll tell you about these as we go through the presentation, and I do feel that organic acids testing can be a helpful adjunct when combined with other methods of testing. Some markers, like D-lactate, are the subject of a lot of ongoing research right now, they're getting a lot more attention. D-lactate's being investigated, for example, as a marker for SIBO. So we'll talk more about this as we go through the unit, but I just wanted to give you a general overview of how we use organic acids testing for microbial issues in practice right now.

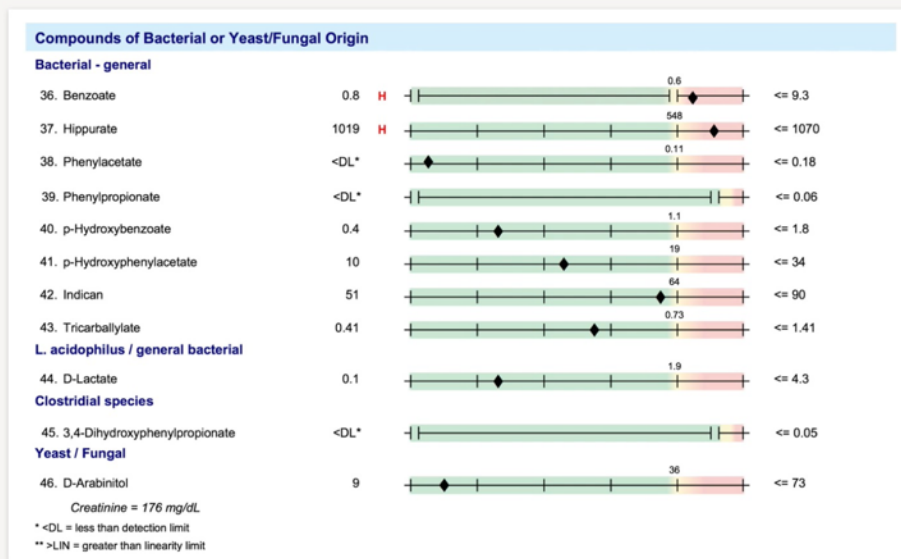


Great Plains



Genova

There are two primary labs that do organic acids testing: Genova, and their panel, called the Organics Dysbiosis or 0097, is specifically the one that just deals with microbial organic acids, and then we have the Great Plains lab, and their microbial panel is called the Microbial Organic Acids Test, or MOAT. And both of these tests, especially the expanded version that contains metabolic markers and neurotransmitter markers, have pros and cons, and the decision about which one to use becomes more complicated when you're doing the entire test, but for microbial markers, here are the main differences: Organics uses D-arabinitol instead of arabinose for yeast, and I think there's a lot more research behind D-arabinitol as a marker, and I'm not convinced by arabinose as a marker for fungal overgrowth, especially if it's the only thing that's elevated on the test, which you'll frequently see with the Great Plains Microbial Organic Acids Test. You can see the result on the left; arabinose is the only marker that's elevated. And given my reading of the research, I don't think that's sufficient evidence to diagnose somebody with fungal overgrowth. Organics also measures D-lactate, which is one of the markers that has the most research behind it. It's, as I said, being investigated as an independent marker for SIBO and for leaky gut. On the other hand, the Great Plains lab test has more clostridial markers and more fungal markers overall, including markers that may indicate exposure to mold, which the organics test does not have, so you can make an argument for both. We use Genova Organics more frequently, but I will use the Great Plains lab in cases of kids with behavioral or cognitive mood disorders, because I think some of the clostridial markers in particular can be helpful in those cases.

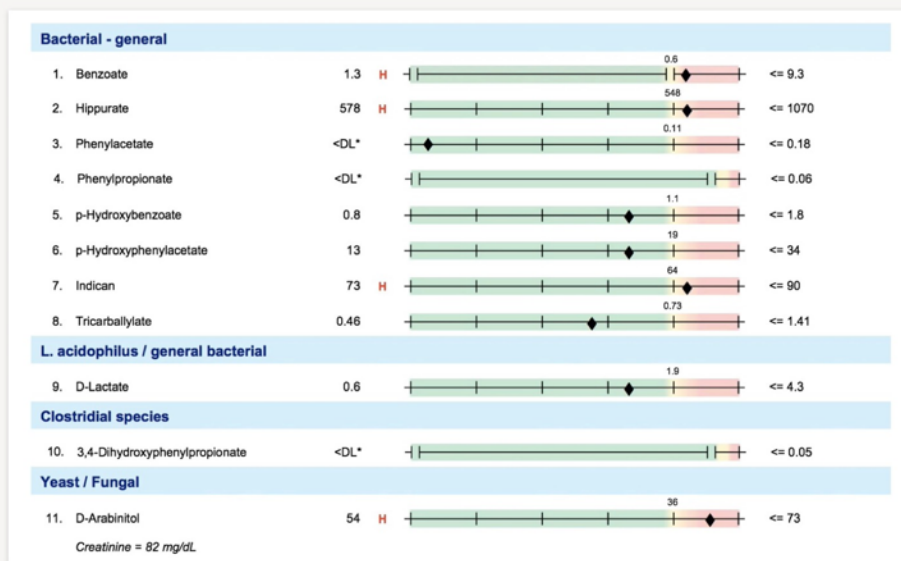


Benzoate

So, the first marker I want to talk about is benzoate. Early studies showed patients with enteritis, celiac disease, or cystic fibrosis have elevated levels of benzoate. It's the product of the dietary catabolism of polyphenols by bacteria. Benzoate is normally conjugated with glycine in the liver to form hippurate. Therefore, benzoate can be a marker for either bacterial overgrowth or impaired Phase 2 detox capacity, specifically due to glycine and/or pantothenic acid, vitamin B5

insufficiency. High benzoate can also be caused by ingestion of a benzoic acid, which is found in processed and packaged foods like pickles, soda, or lunch meats, or naturally in foods like cranberries. If only benzoate is elevated with no other markers, it's less likely to be an indicator of bacterial overgrowth and could just indicate high polyphenol intake. You also need to pay attention to the range. Genova marks high-normal values as high, so if you look at this test result on the slide here, 0.8 is well within the reference range that goes up to 9.3, but it's, in terms of statistical distribution within the population, it's in the high-normal range, so they mark it as high.

The patient on this slide is a 47-year-old female with chronic disequilibrium, muscle aches, and fatigue, GI concerns like gas and bloating, and energy and hormonal imbalance issues. SIBO and stool testing were normal for her, though she did have mercury toxicity, which was probably impairing her Phase 2 detox capacity, so we focused on giving her glycine, pantothenic acid in addition to the mercury detox protocol, and we didn't treat her for bacterial overgrowth or gut issues at all, because there really wasn't much evidence for that, and then these markers did normalize over time.



Hippurate

You'll often see benzoate and hippurate elevated together, as in the last result and this one. The reason is that benzoate is converted into hippurate, so if you have a lot of benzoate and conversion is working, you'll have a lot of hippurate too. Hippurate is one of the most abundant compounds in normal urine, so when no other bacterial markers are high, elevated hippurate is of no clinical consequence. It just indicates higher-than-normal intake of benzoic acid in the diet, and that's especially true when it's only in the high-normal range, as it is here. So, the range goes up to 1,070 and in this patient is at 578. If it's significantly elevated and/or other markers are abnormal, it can be an indicator of microbial overgrowth. Another potential cause of elevated hippurate is exposure

to toluenes, which are widely used as solvents. They're responsible for the distinct smell of paint thinner, for example, and like other solvents, they're sometimes used as recreational drugs.

This patient was a 51-year-old female with insufficiency dysbiosis and fungal overgrowth on the stool test and SIBO on the breath test. So, I may not have treated her for gut issues based on the basis of this organic acids test result alone, because everything is just in the high normal range, nothing is really significantly out of whack, but when you combine this with evidence of fungal overgrowth on the stool test, evidence of dysbiosis on the stool test, and evidence of SIBO on a breath test, I think it's a compelling argument for treatment.

Interpretation of **benzoate** and **hippurate** patterns

Benzoate	Hippurate	Other Bacterial Markers	Interpretation
Low	Low	No elevations	Low intake of benzoate; normal intestinal microbes
		Multiple elevations	Low intake of benzoate; microbial overgrowth w/o polyphenol
High	Low	No elevations	Glycine deficiency; high intake benzoate in diet
		Multiple elevations	Glycine deficiency; microbial overgrowth
Low	High	No elevations	Normal Phase II detox; normal intestinal microbes
		Multiple elevations	Normal Phase II detox; microbial overgrowth
High	High	No elevations	High benzoate intake; partial conversion to hippurate
		Multiple elevations	High benzoate intake; microbial overgrowth

Adapted from: Lord, R & Bralley J. Laboratory Evaluations for Functional and Integrative Medicine. Metamatrix Institute. Duluth, Georgia. 2008.

So, here's a table that summarizes the interpretation of benzoate and hippurate patterns. We'll provide this as a handout for quick reference, so that you have it. We just covered all this, so I'm not going to go through it again, but you can just print this out, and if you ever need to consult it when you get a test result back, you can just have it on hand.