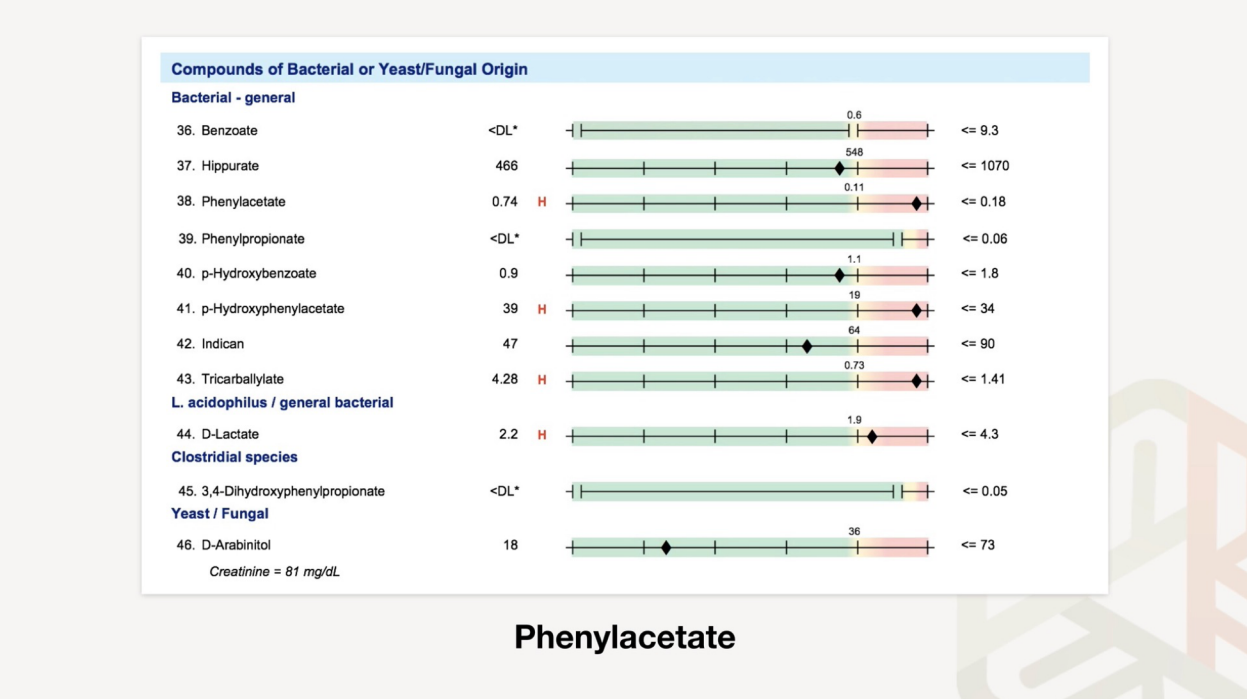
Gut: Organic Acids - Part 2

Phenylacetate is a byproduct of intestinal microbial action on polyphenols or the amino acids tyrosine and phenylalanine.

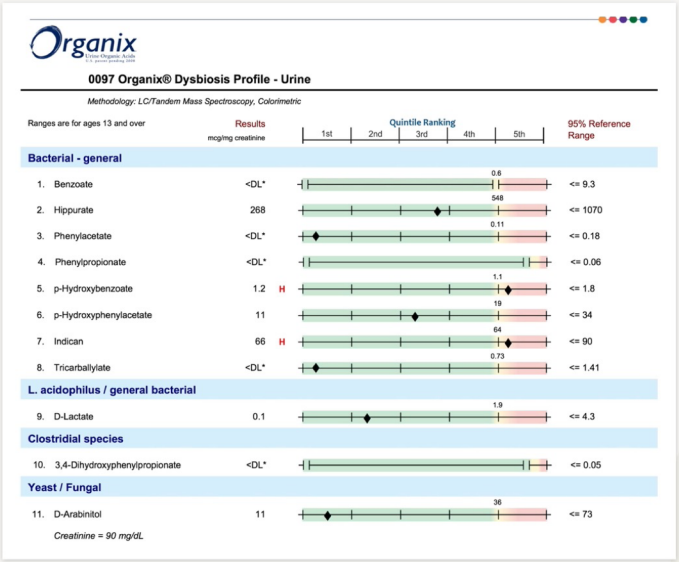


It should only be present in low concentrations in healthy people, but it may accumulate in significant amounts in phenylketonuria, or PKU, which is an inherited disorder which increases phenylalanine levels in the blood, which can cause neurotoxicity and brain damage. Infants with the classic presentation of PKU develop normally until a few months old, then they start to have seizures, delayed development, behavioral problems, and psychiatric disorders and can develop permanent intellectual disability if not treated. There are less severe forms of PKU that present with milder cognitive, behavioral, or neurological problems, but in the vast majority where you see elevations in phenylacetate, they'll be mild and they'll be indicators of microbial overgrowth, not PKU. If you do see very high levels of PKU in a young child, especially if they have cognitive, behavioral, or neurological problems, I would suggest referring out to a specialist in inherited diseases.

The lab results on this slide are from a 61-year-old patient with migraines, eczema, and mild gastrointestinal distress. As you can see, there are several markers that are out of range, and she was also positive for SIBO on a breath test. After treating her for SIBO and microbial overgrowth here, she improved significantly and her labs improved.

Next marker is phenylpropionate, and I couldn't actually find a lab test result that was out of range for this marker, despite running this test for over five years consistently. So that maybe should tell

you something about how common it is for this marker to be out of range. It is another byproduct of intestinal action on polyphenols and phenylalanine. It's metabolized by a medium-chain Acyl-CoA dehydrogenase, so that's MCAD, and it's generally not present in the urine, which may explain why I haven't seen it very often. Very high levels can indicate MCAD deficiency, which is a genetic condition that prevents the body from converting fat to energy, particularly during fasting. So you might see this in young kids with mitochondrial disorder presentation. Signs and symptoms typically appear during early childhood, so you might see vomiting, lethargy, hypoglycemia; they're at higher risk for seizures, breathing difficulties, liver problems, and even brain damage. But similar to the previous marker, if you see mild elevations here, they likely do not indicate MCAD deficiency. They would be a sign of microbial overgrowth, and again, if you see very high levels, particularly with some of the symptoms we just mentioned, you'd want to refer out to a specialist in inherited disorders.



Organix

0097 Organix® Dysbiosis Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

Ranges are for ages 13 and over		Results mcg/mg creatinine		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
Bacterial - general					
1.	Benzoate	<DL*		0.6	<= 9.3
2.	Hippurate	268		548	<= 1070
3.	Phenylacetate	<DL*		0.11	<= 0.18
4.	Phenylpropionate	<DL*			<= 0.06
5.	p-Hydroxybenzoate	1.2	H	1.1	<= 1.8
6.	p-Hydroxyphenylacetate	11		19	<= 34
7.	Indican	66	H	64	<= 90
8.	Tricarballylate	<DL*		0.73	<= 1.41
L. acidophilus / general bacterial					
9.	D-Lactate	0.1		1.9	<= 4.3
Clostridial species					
10.	3,4-Dihydroxyphenylpropionate	<DL*			<= 0.05
Yeast / Fungal					
11.	D-Arabinitol	11		36	<= 73

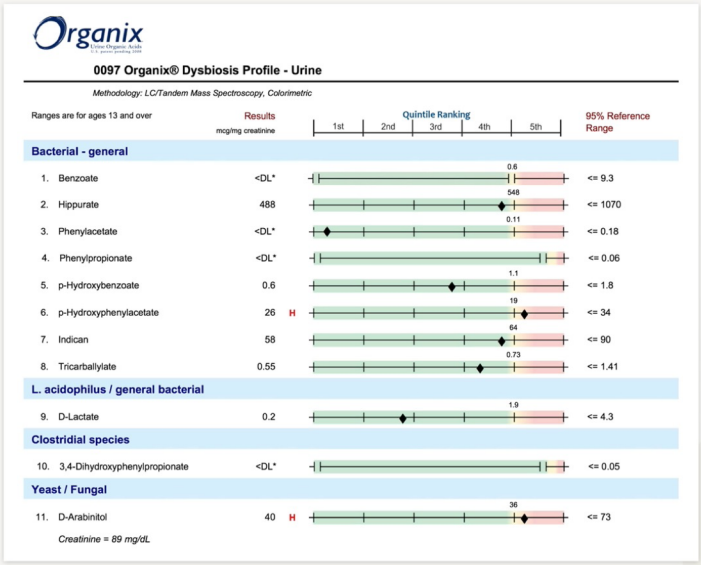
Creatinine = 90 mg/dL

P-Hydroxybenzoate

Next marker is P-hydroxybenzoate. This is derived from the bacterial metabolism of polyphenols and tyrosine. It's not a significant product of normal human cellular metabolism, so you wouldn't expect to see it at high levels in the urine of healthy people. Elevations indicate microbial overgrowth, especially of E. coli. E. coli creates P-hydroxybenzoate from the metabolism of glucose. So, here we see it in the high-normal range along with high-normal indican.

This patient was a 36-year-old female with ulcerative colitis and also significant dysbiosis with Citrobacter and Klebsiella, which are pathogenic at higher levels. She had elevated levels of lactoferrin, calprotectin, and lysozyme, which are the inflammatory markers on the Doctor's Data panel. So though her markers were only high-normal here and I wouldn't treat her just on the basis of these results alone, because of the rest of her presentation, we did treat and she experienced some significant improvements. For this particular patient, there was more work to be done, even

after addressing the dysbiosis, because of the autoimmune nature of ulcerative colitis, but she did experience some significant improvement.



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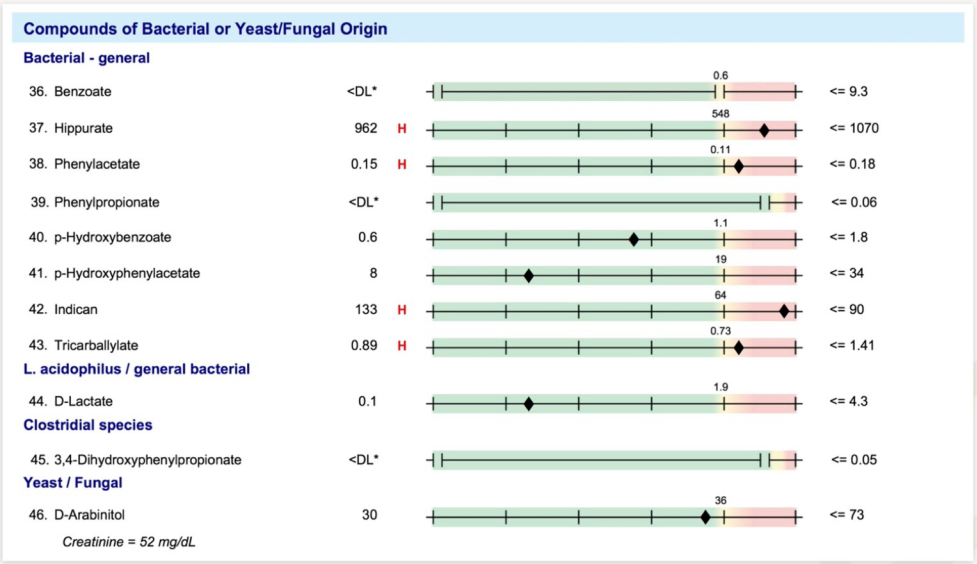
1. Benzoate	<DL*		0.6	<= 9.3
2. Hippurate	488		548	<= 1070
3. Phenylacetate	<DL*		0.11	<= 0.18
4. Phenylpropionate	<DL*			<= 0.06
5. p-Hydroxybenzoate	0.6		1.1	<= 1.8
6. p-Hydroxyphenylacetate	26	H	19	<= 34
7. Indican	58		64	<= 90
8. Tricarballylate	0.55		0.73	<= 1.41
L. acidophilus / general bacterial				
9. D-Lactate	0.2		1.9	<= 4.3
Clostridial species				
10. 3,4-Dihydroxyphenylpropionate	<DL*			<= 0.05
Yeast / Fungal				
11. D-Arabinitol	40	H	36	<= 73

Creatinine = 89 mg/dL

P-Hydroxyphenylacetate (HPA)

Next marker is P-hydroxyphenylacetate, or HPA. This is derived from the bacterial metabolism of tyrosine. It's been found to be useful in detecting small bowel disease that's associated with giardia, ileal resection, and other conditions caused by overgrowth, anaerobic bacteria, in particular in the small bowel. It can be very high in patients with cystic fibrosis or other conditions that impair amino acid absorption. Since tyrosine is released from protein, it's rapidly absorbed in most people, so you won't see this marker elevated as a sign of dysbiosis very often.

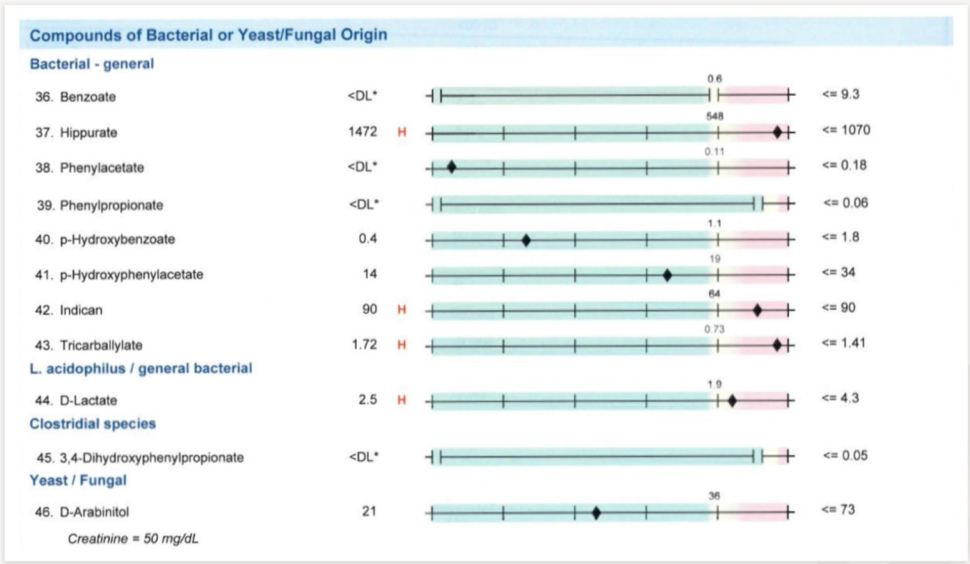
This particular patient was a 49-year-old female with high cholesterol and migraines. Her other gut markers were normal, she didn't have any gut symptoms, and the P-hydroxyphenylacetate here, along with the D-arabinitol, were only slightly out of the normal range, so I decided not to treat her with a gut protocol.



Indican

Indican is the next marker. It's derived from the bacterial metabolism of tryptophan. Elevated indican is an indication of bacterial overgrowth in the upper small bowel. It's one of the few markers that tells you where the overgrowth is occurring, and I've seen two or three studies recently that are investigating indican as a marker for SIBO because of this specificity. Patients with celiac disease are at higher risk for having elevated indican levels. Indican can also help differentiate between pancreatic insufficiency and biliary stasis as a cause of fat in the stool, steatorrhea. If indican is high, it would suggest pancreatic insufficiency, whereas if it's normal, it would suggest biliary stasis as the cause of excess fat in the stool. Incomplete protein digestion can cause elevations in indican, so it can be a marker for low stomach acid rather than bacterial overgrowth, though they often go together, as you now know.

The patient whose results are on this slide is a 51-year-old male whose chief complaint was accumulation of belly fat, low libido, brain fog, gas, bloating, and muscle aches. All of the markers here are in the high-normal range except for indican, which is actually out of the lab range. In this case, he did not have SIBO according to the breath test, but he did have dysbiosis and fungal overgrowth on the stool test, so we went ahead and treated with antimicrobial protocol, and his brain fog, gas and bloating, and muscle aches did improve. The belly fat and low libido had to be addressed separately.



Tricarballylate

The next marker is tricarballylate. This is produced by aerobic bacteria. The important thing to know about this marker is that it has an extremely high affinity for magnesium, which prevents its absorption, so in ruminants, they develop severe magnesium deficiency and a condition called grass tetany from overgrowth of specific strains of bacteria that produce tricarballylate, and the disease in ruminants is caused by overfeeding of high carbohydrate herbage, interestingly enough, and so it's thought that high levels of tricarballylate may result from diets high in processed and refined carbohydrates in humans, like the classic Standard American Diet. So if it's elevated, the patient will need magnesium in addition to gut treatment because they're poorly absorbing magnesium.

This patient is a 43-year-old female with microscopic colitis, lupus, hemorrhoids, hypothyroidism, and a rash on her lower legs. She also had fungal overgrowth on the stool test and high baseline methane on the breath test. So, she responded well to gut treatment and to a liposomal form of magnesium, which is better absorbed than some of the oral forms.