KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

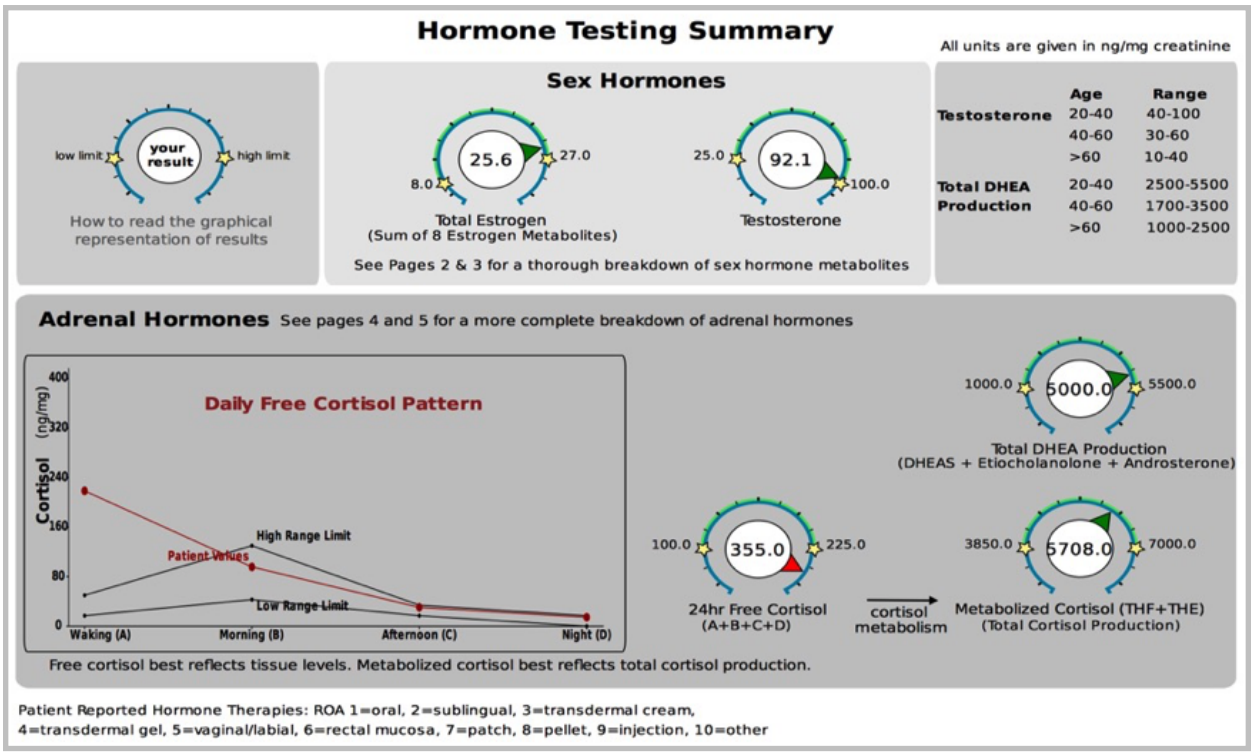
Hypoglycemia - Part Three

The common presentation of functional hypoglycemia I see in practice is postprandial. These patients typically have normal or low-normal, within the lab range at least, fasting glucose, but they exhibit telltale signs of hypoglycemia between meals. These include fatigue, lightheadedness, shakiness, blurred vision, palpitations, anxiety, brain fog, spaciness, extreme hunger where they feel like they are going to die if they don't eat, and intense sugar cravings.

Marker	Value	Functional Range	Lab Range
Glucose	72	75 - 90	65 - 99
Hemoglobin A1c	5.3	4.8 – 5.4	4.8 - 5.6
Uric Acid	5.8	3.7 – 6.0	3.7 - 8.6
BUN	18	13 – 18	6 - 20
Creatinine	0.89	0.85 – 1.1	0.76 - 1.27
BUN/Creatinine Ratio	20	8 – 19	8 - 19
Sodium	142	134 – 140	134 - 144
Potassium	4.1	4.0 – 4.5	3.5 - 5.2
Chloride	99	100 – 106	97 - 108
C02	22	25 – 30	18 - 29
Calcium	9.8	9.2 – 10.1	8.7 - 10.2
Phosphorus	3.0	3.5 – 4.0	2.5 - 4.5
Magnesium	2.2	2.0 – 2.6	1.6 - 2.3
Protein, total	7.6	6.9 – 7.4	6.0 - 8.5
Albumin	5.3	4.0 – 5.0	3.5 - 5.5
Globulin	2.3	2.4 – 2.8	1.5 - 4.5
A/G ratio	2.3	1.5 – 2.0	1.1 - 2.5
Bilirubin, total	1.0	0.1 – 1.2	0.0 - 1.2
Alkaline Phosphatase	82	42 – 107	39 - 117
LDH	176	140 - 180	121 - 224
AST	36	10 - 30	0 - 40
ALT	22	10 - 29	0 - 44
GGT	18	0 - 40	0 - 65
TIBC	327	250 – 350	250 - 450
UIBC	153	150 - 375	111 - 343
Iron	174	85 – 135	38 - 169
Iron saturation	53	15 – 45	15 - 55
Ferritin	199	30 - 150	30 - 400
Vitamin B-12	435	450 – 2000	211 - 946
Vitamin D, 25-hydroxy	17.1	35 - 60	30.0 - 100.0
Cholesterol, total	177	150 - 240	100 - 199
Triglycerides	63	50 – 100	0 - 149
HDL	69	55 – 85	> 39
LDL	95	0 - 175	0 - 99
T. Chol / HDL Ratio	2.6	< 3	0 - 5.0
Triglycerides / HDL Ratio	0.91	< 2	< 3.8
CRP-hs	0.26	< 1.0	0.00 - 3.00
Homocysteine	14.4	< 7.0	0.0 - 15.0

Here's an example of such a patient. It's a 33-year-old male with a chief complaint of a sensation of pressure in the upper left side of his abdomen. He also complained of severe irritability if meals are missed, fatigue relieved by eating, feeling shaky and jittery between meals, occasional blurred vision, and sleep disturbance. He had no problem falling asleep, but he wakes frequently

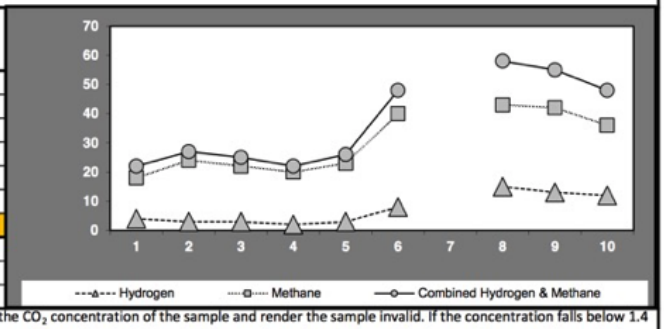
throughout the night. As you can see, his fasting glucose is only slightly below the functional range at 72. His A1c is normal at 5.3. He doesn't have any other markers specific for blood sugar dysregulation, but his vitamin D is quite low at 17, and he has iron overload, which as you know now affects metabolic function. He also has high homocysteine levels, which, as you'll learn later, are a marker for impaired methylation and are independently associated with cardiovascular disease. His BUN-to-creatinine ratio is elevated, which is often a marker of dehydration when it's only mildly elevated like this, and his AST is above the functional range. In fact, as we'll find later, many studies suggest that the lab reference ranges for both AST and ALT should be lower because they can be indicators of metabolic disease.



Data

H_2 = Hydrogen CH_4 = Methane CO_2 = Measured

	Sample	ppm H_2	ppm CH_4	Total H2 + CH4	CO_2 %*
1	Baseline	4	18	22	OK
2	20 min	3	24	27	OK
3	**46 min****	3	22	25	OK
4	**70 min****	2	20	22	OK
5	**91 min****	3	23	26	OK
6	**118 min****	8	40	48	OK
7					N/A
8	**139 min****	15	43	58	OK
9	**163 min****	13	42	55	OK
10	**185 min****	12	36	48	OK



*Dilutions of the sample may occur during the sampling procedure which may decrease the CO_2 concentration of the sample and render the sample invalid. If the concentration falls below 1.4 %, the entry for CO_2 will be marked as Quantity Not Sufficient (QNS) and the entries for H_2 and CH_4 will be highlighted. If the sample is otherwise unusable the entry for CO_2 will be marked as Not Available (N/A) and the entries for H_2 and CH_4 will be highlighted. See notes section for details if cells are highlighted and blank or highlighted and contain N/A or QNS.

Analysis

	Result	Flag	Normal
Combined baseline total =	22	H	≤20ppm
Greatest H_2 increase over the lowest preceding value within first 120 minutes =	6	-	≤20ppm
Greatest CH_4 increase over the lowest preceding value within first 120 minutes =	22	H	≤12ppm
Greatest combined H_2 & CH_4 increase over the lowest preceding value within first 120 minutes =	26	H	≤15ppm

Interpretation

SIBO Suspected - Elevated Hydrogen	Increases of hydrogen greater than 20ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**NEGATIVE**
SIBO Suspected - Elevated Methane	Increases of methane greater than 12ppm over the lowest preceding value within the first 120 minutes (+/- 5min deviation) are indicative of bacterial overgrowth.	**POSITIVE**
SIBO Suspected - Elevated Combined Hydrogen & Methane Gasses	Increases in combined hydrogen and methane gas values greater than 15ppm over the lowest preceding value are indicative of bacterial overgrowth.	**POSITIVE**

Hormone testing revealed high levels of free cortisol, especially at night and overnight with high-normal total cortisol. He was also positive for methane-predominant SIBO, which was likely causing his abdominal discomfort.

BACTERIOLOGY CULTURE

Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
4+ Bacteroides fragilis group	3+ Alpha hemolytic strep	
3+ Bifidobacterium spp.	1+ Beta strep, group B	
4+ Escherichia coli	3+ Gamma hemolytic strep	
NG Lactobacillus spp.	4+ Hemolytic Escherichia coli	
3+ Enterococcus spp.	1+ Klebsiella pneumoniae ssp pneumoniae	
2+ Clostridium spp.		

NG = No Growth

BACTERIA INFORMATION

Expected /Beneficial bacteria make up a significant portion of the total microflora in a healthy & balanced GI tract. These beneficial bacteria have many health-protecting effects in the GI tract including manufacturing vitamins, fermenting fibers, digesting proteins and carbohydrates, and propagating anti-tumor and anti-inflammatory factors.
Clostridia are prevalent flora in a healthy intestine. Clostridium spp. should be considered in the context of balance with other expected/beneficial flora. Absence of clostridia or over abundance relative to other expected/beneficial flora indicates bacterial imbalance. If *C. difficile* associated disease is suspected, a Comprehensive Clostridium culture or toxigenic *C. difficile* DNA test is recommended.
Commensal (Imbalanced) bacteria are usually neither pathogenic nor beneficial to the host GI tract. Imbalances can occur when there are insufficient levels of beneficial bacteria and increased levels of commensal bacteria. Certain commensal bacteria are reported as dysbiotic at higher levels.
Dysbiotic bacteria consist of known pathogenic bacteria and those that have the potential to cause disease in the GI tract. They can be present due to a number of factors including: consumption of contaminated water or food, exposure to chemicals that are toxic to beneficial bacteria; the use of antibiotics, oral contraceptives or other medications; poor fiber intake and high stress levels.

YEAST CULTURE

Normal flora	Dysbiotic flora
1+ Candida albicans	

MICROSCOPIC YEAST

Result:	Expected:
Few	None - Rare

The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.

YEAST INFORMATION

Yeast normally can be found in small quantities in the skin, mouth, intestine and mucocutaneous junctions. Overgrowth of yeast can infect virtually every organ system, leading to an extensive array of clinical manifestations. Fungal diarrhea is associated with broad-spectrum antibiotics or alterations of the patient's immune status. Symptoms may include abdominal pain, cramping and irritation. When investigating the presence of yeast, disparity may exist between culturing and microscopic examination. Yeast are not uniformly dispersed throughout the stool, this may lead to undetectable or low levels of yeast identified by microscopy, despite a cultured amount of yeast. Conversely, microscopic examination may reveal a significant amount of yeast present, but no yeast cultured. Yeast does not always survive transit through the intestines rendering it unvialble.

Comprehensive Parasitology,stool, x3

PARASITOLOGY/MICROSCOPY	
Sample 1	
Mod	Blastocystis hominis
Mod	Endolimax nana cysts
Few	Endolimax nana trophs
Few	Yeast
Sample 2	
Many	Blastocystis hominis
Mod	Endolimax nana cysts
Rare	Endolimax nana trophs
Few	Yeast
Sample 3	
Few	Blastocystis hominis
Few	Endolimax nana cysts
Rare	Endolimax nana trophs
Few	Yeast

PARASITOLOGY INFORMATION

Intestinal parasites are abnormal inhabitants of the gastrointestinal tract that have the potential to cause damage to their host. The presence of any parasite within the intestine generally confirms that the patient has acquired the organism through fecal-oral contamination. Damage to the host includes parasitic burden, migration, blockage and pressure. Immunologic inflammation, hypersensitivity reactions and cytotoxicity also play a large role in the morbidity of these diseases. The infective dose often relates to severity of the disease and repeat encounters can be additive.

There are two main classes of intestinal parasites, they include protozoa and helminths. The protozoa typically have two stages; the trophozoite stage that is the metabolically active, invasive stage and the cyst stage, which is the vegetative inactive form resistant to unfavorable environmental conditions outside the human host. Helminths are large, multicellular organisms. Like protozoa, helminths can be either free-living or parasitic in nature. In their adult form, helminths cannot multiply in humans.

In general, acute manifestations of parasitic infection may involve diarrhea with or without mucus and or blood, fever, nausea, or abdominal pain. However these symptoms do not always occur. Consequently, parasitic infections may not be diagnosed or eradicated. If left untreated, chronic parasitic infections can cause damage to the intestinal lining and can be an unsuspected cause of illness and fatigue. Chronic parasitic infections can also be associated with increased intestinal permeability, irritable bowel syndrome, irregular bowel movements, malabsorption, gastritis or indigestion, skin disorders, joint pain, allergic reactions, and decreased immune function.

In some instances, parasites may enter the circulation and travel to various organs causing severe organ diseases such as liver abscesses and cysticercosis. In addition, some larval migration can cause pneumonia and in rare cases hyper infection syndrome with large numbers of larvae being produced and found in every tissue of the body.

One negative parasitology x1 specimen does not rule out the possibility of parasitic disease, parasitology x3 is recommended. This test is not designed to detect Cyclospora cayetanensis or Microsproridia spp.

GIARDIA/CRYPTOSPORIDIUM IMMUNOASSAY

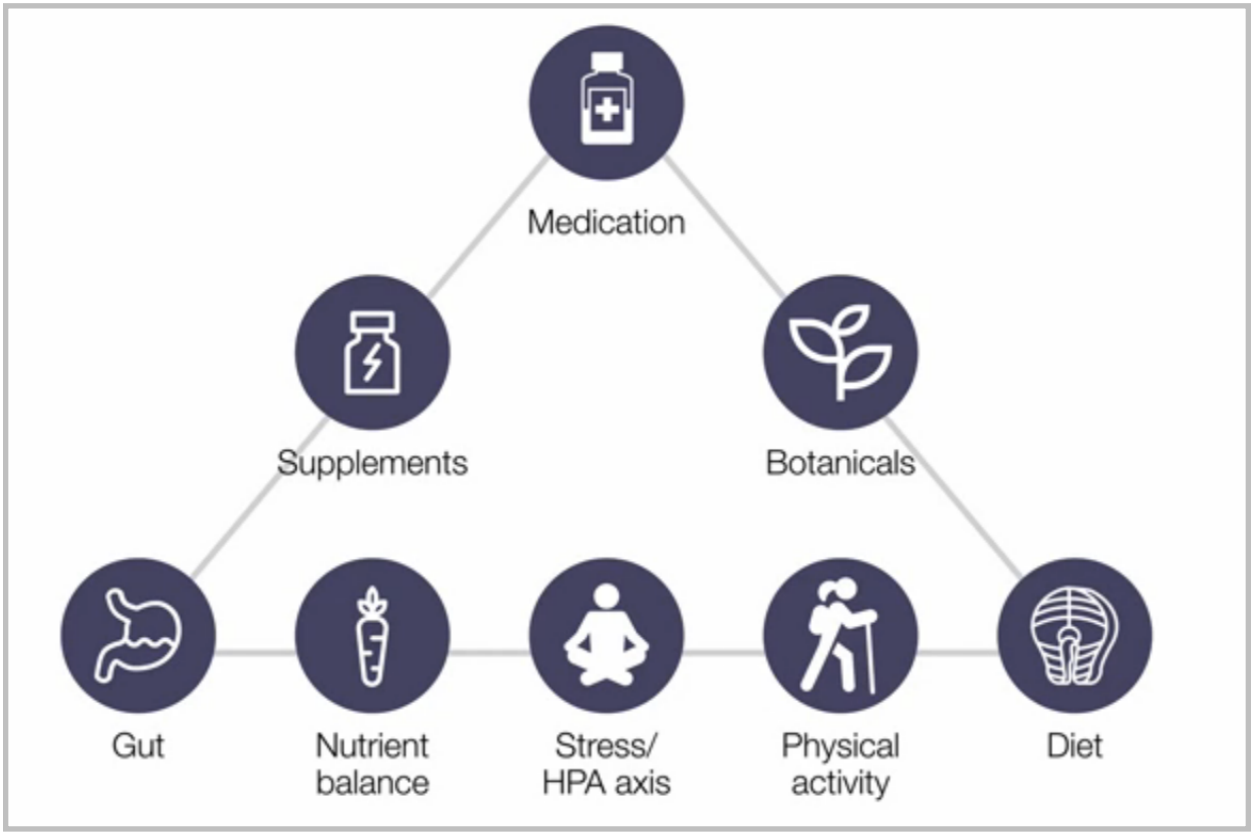
	Within	Outside	Reference Range
Giardia duodenalis	Neg		Neg
Cryptosporidium	Neg		Neg

Giardia duodenalis (AKA *intestinalis* and *lamblia*) is a protozoan that infects the small intestine and is passed in stool and spread by the fecal-oral route. Waterborne transmission is the major source of giardiasis.
Cryptosporidium is a coccidian protozoa that can be spread from direct person-to-person contact or waterborne transmission.

Stool testing revealed significant dysbiosis, mild fungal overgrowth, and Blastocystis hominis.

If we go back to the earlier diagram on the causes of hypoglycemia, we see that he has at least three of them, though in his intake history, he also mentions chronic stress, and that would make four. We haven't yet even tested for toxins such as metals or mold, so he could have more than four. So, this is what you'll typically see in patients with hypoglycemia, whether it's functional or conventional. When you address these issues, the hypoglycemia typically resolves on its own. In other words, hypoglycemia is most often a symptom of a deeper problem, just as most symptoms are.

Let's move on to talk about treatment of hypoglycemia. This discussion will focus on addressing hypoglycemia in patients without diabetes, in patients with prediabetes or diabetes that are relatively uncomplicated and not taking insulin, and in patients with functional hypoglycemia. If the patient is on insulin and/or several other blood sugar-regulating medications, it's probably best to refer out or at least work in conjunction with his endocrinologist unless you have experience managing patients on insulin and these other medications, which can get complicated.



Still, most of the interventions we'll discuss here apply to those patients and will help them. This diagram should look familiar. It's identical to the hyperglycemia interventions we talked about in the last presentation. The only differences are slight tweaks to diet, HPA axis management, and physical activity, so let's talk about those.

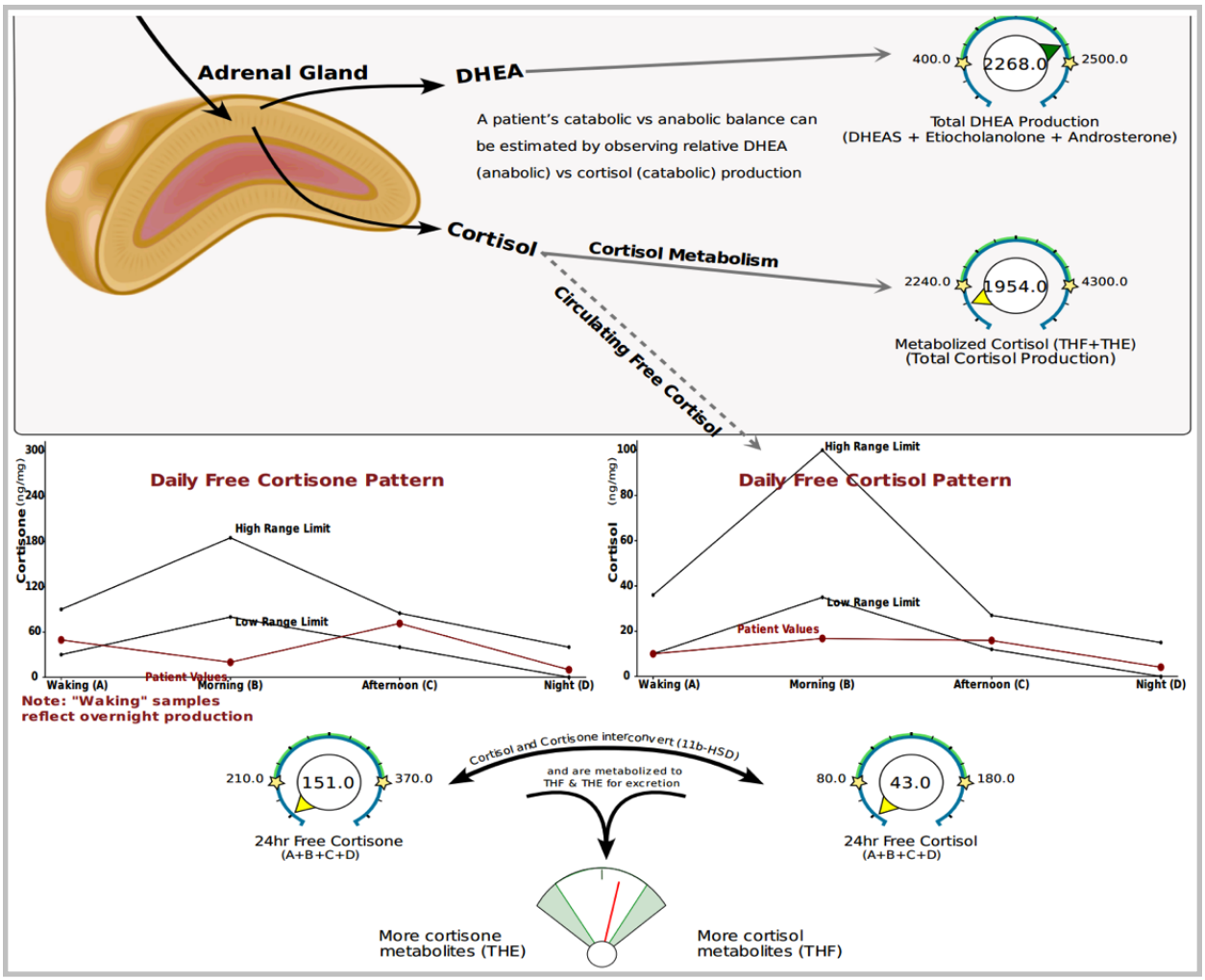
The first is diet. As with hyperglycemia, a Paleo template with a high-protein intake is a great starting place. With hypoglycemia, I've found that a high-protein breakfast is even more important, and we suggest patients eat at least 30 g of protein at breakfast. It's pretty hard to get this just by eating eggs. Eggs only have 6 to 7 g of protein per egg, so it's usually necessary to have some kind of animal protein or fish along with the eggs or instead of eggs. I've also found that protein powder while on paper does have a high level of protein, it doesn't seem to have the same stabilizing effect on blood sugar, unfortunately. So, a smoothie with 30 g of protein doesn't have the same impact as steak and eggs or a salmon breakfast with salad and potatoes, for example.

With the hyperglycemia recommendations, I suggested avoiding snacking, but with hypoglycemia, it depends somewhat on whether it is occurring in a context of hyperglycemia or by itself. If it is with diabetes and hyperglycemia, you can try those recommendations first—avoiding snacking in between meals—but you should be aware that fasting may exacerbate the hypoglycemic episodes, and you may need to try the hypoglycemia recommendations, which are to eat something every two to three hours. This could be eating three normal meals and then snacking between meals, or it could be having five or six small meals throughout the day. Snacks and meals should always

contain some protein and fat and never be carbohydrate alone because eating carbohydrate alone can exacerbate the symptoms of hypoglycemia.

What about carbohydrate intake? I've found that a moderate carb intake works best for most hypoglycemic patients, and a starting place is 20 to 30 percent of calories from carbohydrates, but these should always be real-food carbs such as sweet potatoes, taro, yuca, or plantains, particularly green plantains. Hypoglycemic patients do particularly poorly with refined carbohydrates and sugar. That said, some hypoglycemic patients do seem to do better with a lower-carb intake, maybe 15 percent of calories overall, and this is more common in patients who also have hyperglycemia and insulin resistance.

With physical activity, you have to be careful with overtraining or excessive activity in patients with hypoglycemia. Many patients with low blood sugar also have low cortisol or cortisol dysregulation. Too much physical activity can, of course, worsen this, and these patients usually do better with gentle activity and lightweight lifting. I've found that outdoor activity can be particularly beneficial in this population.



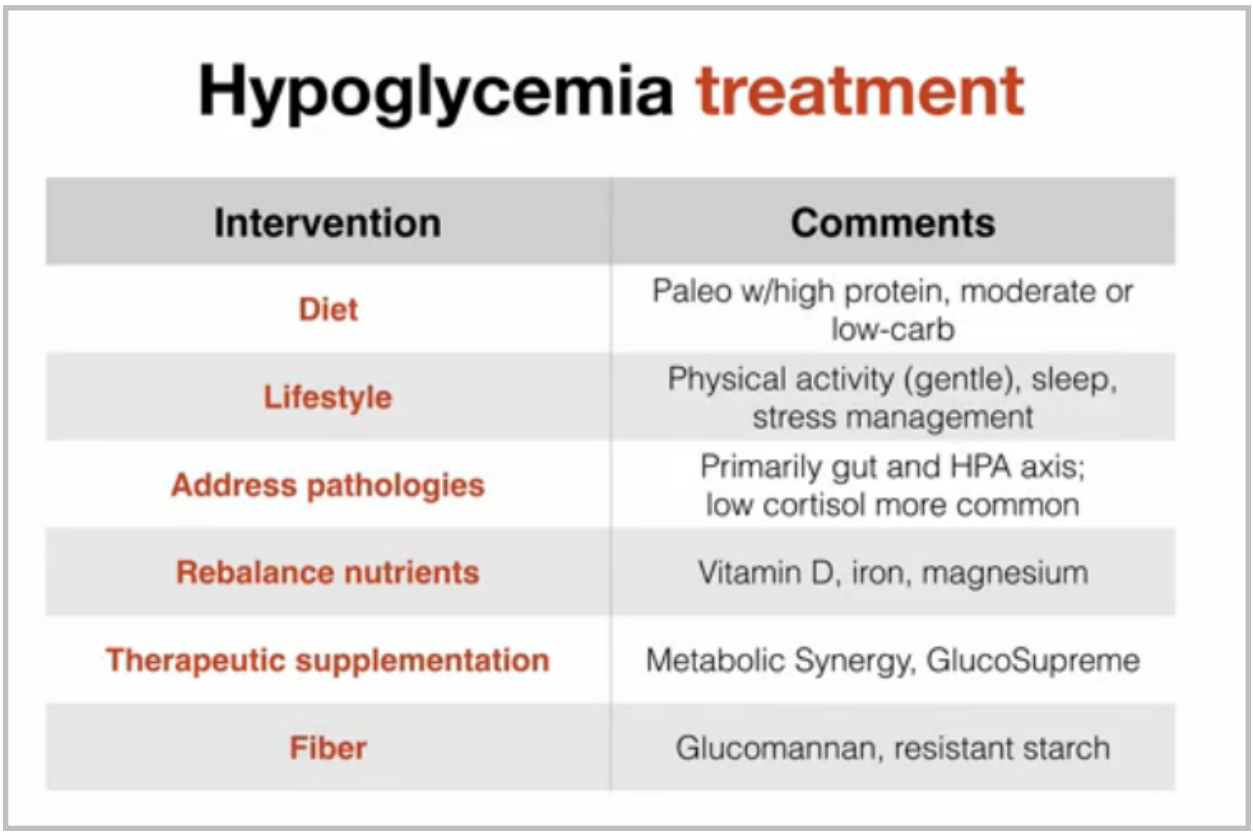
As with hyperglycemia, it's very important to address HPA axis dysfunction in these patients. The difference is that with hyperglycemia they often will have high cortisol. It's not a hard and fast rule, but it's just an anecdotal observation. With hypoglycemia, hypocortisolism is more common. Refer to the HPA axis unit for more info on managing low-cortisol conditions.

Nutrients for blood sugar regulation

Nutrient	Dose
Chromium	100-300 mcg/d
Alpha-lipoic acid	200-400 mg/d
Magnesium	300-500 mg/d
Biotin	200-500 mcg/d
Green tea extract	200-300 mcg/d

For supplements, the blood sugar regulating nutrients are the same as they are for hyperglycemia. These include chromium, alpha-lipoic acid, magnesium, biotin, and green tea extract, and these nutrients really have more of a regulatory than a suppressive effect, so they can be used in both conditions. The same is true for the botanicals such as berberine, gymnema, banaba, and fenugreek, so you can use the same combination of Metabolic Synergy and GlucoSupreme from Designs for Health in patients with hypoglycemia.

I also recommend the same types of fiber that we discussed in the hyperglycemia unit, glucomannan and resistant starch, and this can cause favorable changes in the gut microbiota that may improve blood sugar regulation.



Hypoglycemia treatment

Intervention	Comments
Diet	Paleo w/high protein, moderate or low-carb
Lifestyle	Physical activity (gentle), sleep, stress management
Address pathologies	Primarily gut and HPA axis; low cortisol more common
Rebalance nutrients	Vitamin D, iron, magnesium
Therapeutic supplementation	Metabolic Synergy, GlucoSupreme
Fiber	Glucomannan, resistant starch

So, finally, here's a summary of hypoglycemia treatment. We've got diet, a Paleo template with high protein or moderate or low carbohydrate; lifestyle with gentle physical activity with getting plenty of sleep, managing stress; addressing underlying pathologies, of course, primarily gut and HPA axis, but you have to think about environmental toxins such as mold and heavy metals that can affect mitochondrial function and energy production; rebalancing nutrients, so bringing vitamin D levels up if they are low, bringing iron down if it's high or up if it's low; ensuring adequate magnesium status. You have therapeutic supplementation with things such as Metabolic Synergy and GlucoSupreme and then fiber therapy with glucomannan, resistant starch, or other types of microbiota-accessible carbohydrates.

Okay, that's it for now. See you next time.