KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Blood Chemistry Case Assignments (Answers)

CASE #1: HYPERGLYCEMIA

Answer: Given the known impaired fasting blood glucose, this is a good patient to run a THD* panel to include additional markers of glucose regulation, beta cell function and insulin sensitivity. This was done and the panel is shown below.

* **Note:** *True Health Diagnostics (THD) is no longer in business. See* **this post** *for the latest updates.*

Glycemic Control	Glucose (mg/dL)			118		> 125	100-125	70 - 99	
	HbA1c (%)				5.5	≥ 6.5	5.7 - 6.4	≤ 5.6	
	Estimated Average Glucose (mg/dL) (calculated)				111.2	≥ 139.9	116.9 - 139.8	≤ 116.8	
	Fructosamine (µmol/L)				299	> 346	302 - 346	< 302	
	Glycation Gap				-1.30	> 0.77	0.45 - 0.77	< 0.45	
	Postprandial Glucose Index		8.2			> 7.9	6.0 - 7.9	< 6.0	
Insulin Resistance	Leptin (ng/mL)				4	> 43	20 - 43	< 20	
	Leptin:BMI Ratio				0.19	> 1.17	0.66 - 1.17	< 0.66	
	Adiponectin (µg/mL)		7			< 10	10 - 14	> 14	
	Free Fatty Acid (mmol/L)				0.31	> 0.70	0.60 - 0.70	< 0.60	
	Ferritin (ng/mL) *				131	> 252	147 - 252	< 147	
	α-hydroxybutyrate (µg/mL)§				2.8	> 5.7	4.5 - 5.7	< 4.5	
	Oleic Acid (µg/mL)§				21	> 79	60 - 79	< 60	
	Linoleoyl-GPC (µg/mL)§				19.3	< 10.5	10.5 - 13.0	> 13.0	
	IR_i Score (calculated)				19.0	< 8.0	8.0 - 10.0	> 10.0	
	HOMA-IR (calculated)				1.2	> 4.2	2.6 - 4.2	< 2.6	
Beta Cell Function	Insulin (µU/mL)				4	≥ 12	10 - 11	3 - 9	
	Proinsulin (pmol/L)			8		> 16	8 - 16	< 8	
	C-peptide (ng/mL)				1.6	> 4.6	3.1 - 4.6	1.0 - 3.0	
	Proinsulin:C-peptide Ratio		5.1			> 4.9	3.6 - 4.9	< 3.6	
	Anti-GAD (IU/mL)				< 5	> 5 Positive		≤ 5 Negative	

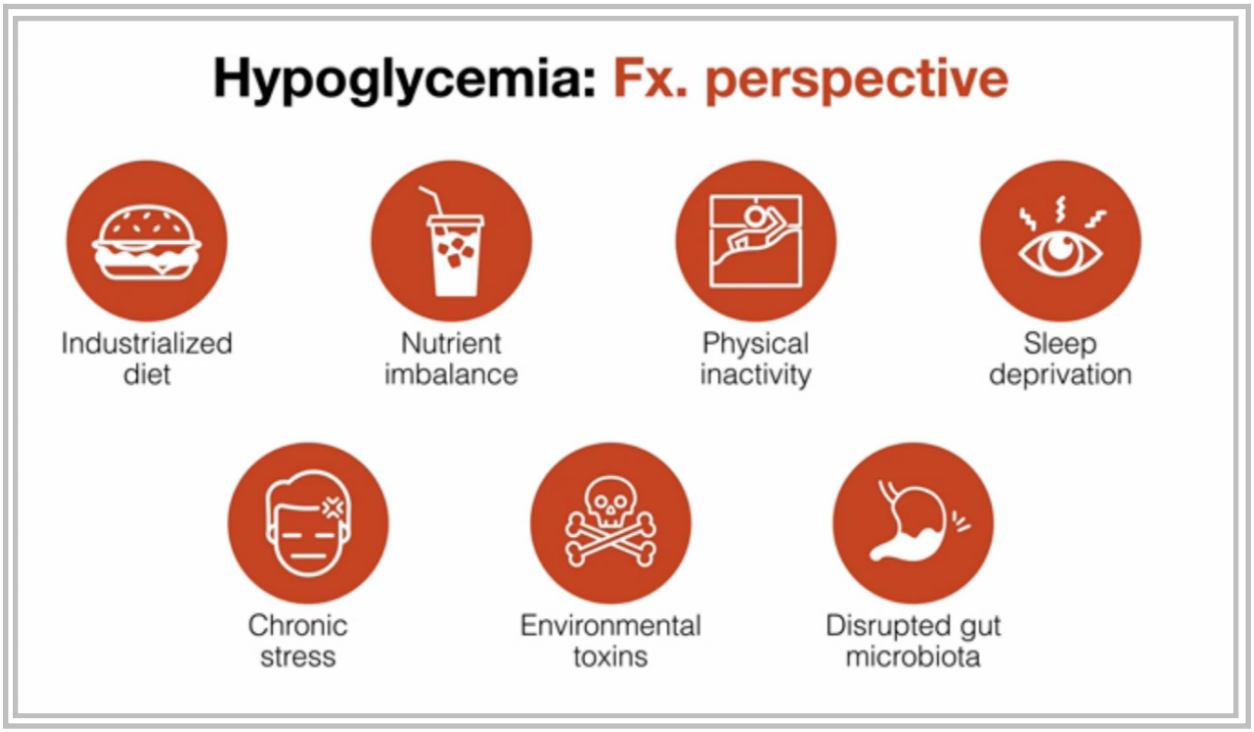
As reported by the patient, his fasting blood glucose is high, but hemoglobin A1c is only mildly elevated above the preferred upper limit of 5.4 and fructosamine is normal at 299. The postprandial glucose index doesn't seem too reliable, so I often disregard that value. His markers for insulin sensitivity and beta cell function look good. Overall, it looks like the primary concern is the fasting blood glucose but that average blood sugar throughout the day is likely well controlled.

As we discussed in the hyperglycemia section, in a small number of cases, and most frequently in men as with this case, fasting blood sugar is high, but A1c and post-meal glucose are normal. It is still unclear what causes this, but researchers speculate that these people may have a defect in basal insulin secretion that should take place during a fasted state and sleep. The second-phase insulin response is still functional, which keeps post-meal blood sugars normal, but their basal or fasting insulin secretion is impaired, which leads to high fasting blood sugar.

I tested him for LADA to ensure this wasn't an early presentation, but all antibody levels were normal. Based on all the findings, we're using a glucometer to adjust the quantity and timing of carbohydrates to lower the morning glucose and ensure the postprandial glucose never goes above 140.

CASE #2: HYPOGLYCEMIA

Answer: Lifestyle and HPA axis are the driving factors here. The significant hypocortisolism is certainly playing a role in his hypoglycemia, and if we go back to the diagram looking at causes of hypoglycemia, we can see that he has at least five contributing factors including chronic stress and sleep deprivation (possibly resulting in his current hypocortisol state), physical inactivity, nutrient imbalances and SIBO (i.e., disrupted GI microbial environment).



Given his job, it's difficult for him to change much about his work day, but he did decide to move closer to work to decrease the 2-3 hours spent commuting in favor of exercise and cooking at least one of his meals at home. We started him on antimicrobial protocol to treat SIBO and both cod liver oil and vitamin D drops to increase his vitamin D levels, and magnesium based on his low serum magnesium. He went for one blood donation and results of the follow up iron panel and CBC will determine if additional blood donation should be considered. Additionally, we had a discussion about sleep hygiene and started adrenal support including adrenal glandulars, Vital Adapt, Acetyl-CH, and melatonin.

CASE #3: IRON DEFICIENCY

Answer: This boy has notable dysbiosis, iron deficiency with associated anemia (consistent with the MCV of 75), borderline low vitamin D and a mild elevation in TSH at 2.6. With a ferritin of 10 and findings of iron deficiency anemia, this is consistent with Stage 3 iron deficiency. In further discussion with his mother, it was revealed that at around 16 months of age he developed an apparent aversion to meat, and only very recently had again started eating meat, though mostly chicken with red meat up to twice per week. Additionally, the notable dysbiosis and fungal overgrowth shown on GI testing also predisposes him to iron deficiency. As mentioned above, his TSH is high-normal out of the functional range. Iron deficiency has been shown to impair thyroid function in numerous ways. It reduces T4 to T3 conversion. It reduces thyroid hormone synthesis, and it reduces thyroid peroxidase activity. Thrombocytosis is also a common outcome of iron deficiency anemia, which explains his high platelet count.

We started him on liposomal iron (IronSmart) and cod liver oil, and will repeat markers in five weeks, including an iron panel with ferritin and CBC.

CASE #4: IRON OVERLOAD

Answer Case #4: This panel may look familiar from the iron overload presentation. His panel is fairly normal, until you look at ferritin. We repeated the iron panel to confirm and similar results were obtained. Blood donation was recommended, but he needed a prescription for therapeutic phlebotomy and the hospital requested confirmation of hemochromatosis.

23andMe Name	Other Name(s)	DNA Change	Genotype	Result
rs1800562	C282Y	G to A	AG	Has one mutation in the HFE gene linked to hemochromatosis. A person with one of these mutations is not typically prone to higher levels of iron in the body, but can pass the mutation to offspring. May have other mutations in the HFE gene (not reported here). Variants detected: C282Y
rs1799945	H63D	C to G	CC	
i3002468	S65C	A to T	AA	

Interestingly, he only had the one SNP associated with HFE. As we discussed in the iron overload presentation, there is evidence suggesting that heterozygous carriers of HFE SNPs are at increased risk of iron overload, but unfortunately most physicians are not aware of this.

An MRI obtained for the specific purpose of measuring iron deposition in the organs reported moderate hepatic iron overload with the estimated hepatic iron concentration of 190 micromol per gram (normal < 36 micromoles).

Over the past seven months, he's donated blood approximately six times with the resultant iron panel:

TESTS	RESULT	FLAG	UNITS
Fe+TIBC+Fer			
Iron Bind.Cap.(TIBC)	292		ug/dL
UIBC	220		ug/dL
Iron, Serum	72		ug/dL
Iron Saturation	25		%
Ferritin, Serum	**556**	**High**	ng/mL
Hemoglobin			
Hemoglobin	14.6		g/dL

Given his good tolerance of blood donation and normal hemoglobin, we'll continue blood donation about once monthly until reaching a target ferritin of <100 and iron sat <40 and then maintain ferritin <150 and iron sat <45.

CASE #5: B12 DEFICIENCY

Answer: Several findings are consistent with low B12, including (most obviously) her low serum B12, high serum methylmalonic acid, and high homocysteine. Of note, the large MCV would also be expected with low B12 and/or folate, and may be seen with macrocytic anemia (her hemoglobin and hematocrit are just above the cut off for functional anemia), though her low RBC does suggest borderline functional anemia. Her diet in Chile was very limited, so she was encouraged to increase

variety and was also started on Trifolamin. Her known metal toxicities will increase her need for B vitamins given the heavy burden this places on her detoxification pathways, so B12 supplementation was recommended throughout metal detox.

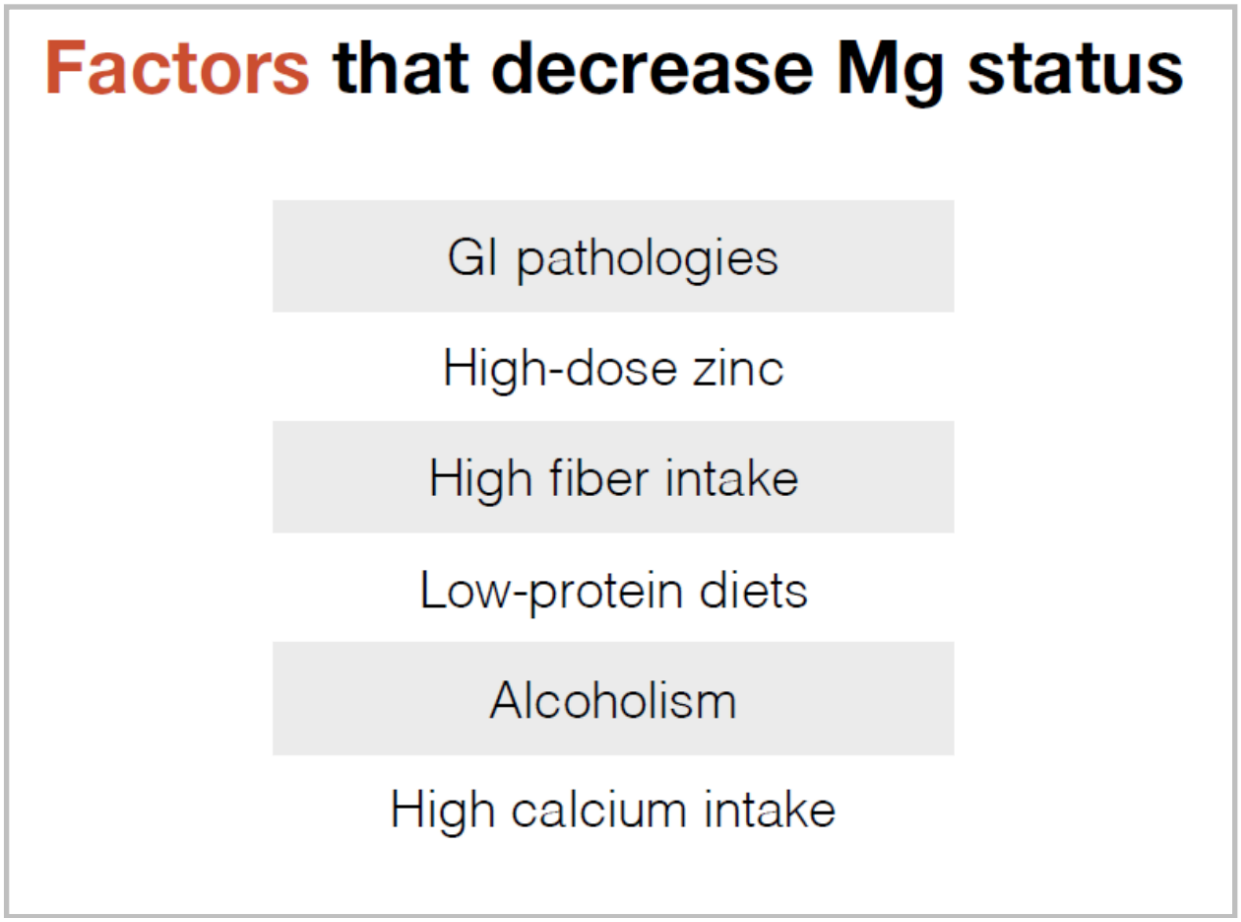
She has several other markers needing correction here including the iron overload and low vitamin D. Note also that her zinc to copper ratio is out of balance and her reverse T3 is elevated, both of these potentially indicating inflammation and likely related to her known metal toxicity.

CASE #6: ZINC-COPPER IMBALANCE

Answer: Comprehensive testing identified moderate yeast overgrowth and elevated mercury levels. Her blood panel showed markers consistent with inflammation, namely a high copper-to-zinc ratio and elevated hs-CRP. She was started on a metal detox protocol and once mercury levels are lowered, we'll address the yeast overgrowth, then repeat the comprehensive blood panel.

CASE #7: MAGNESIUM DEFICIENCY

Answer: Further testing identified SIBO. So, she now has at least three factors that decrease magnesium status: 1) GI pathology (SIBO), 2) long-term zinc intake, and 3) high calcium intake through supplements.



Remember also that those with a serum magnesium below 1.95 have a 50% increased risk of developing diabetes. She was started on the herbal antimicrobial protocol, started on magnesium glycinate 400 mg daily, GlucoSupreme and Metabolic Synergy for better blood sugar control and advised to stop both calcium and zinc supplementation.

CASE #8: VITAMIN D IMBALANCE

Answer: Now, this is a pretty involved case just to illustrate vitamin D deficiency, because there's a lot going on with this patient and it's so difficult to know what the main driving factors are for each person. So of course, he has a really low vitamin D level at 16.2, but it's also really interesting that his PTH is 24, which we would normally think of as adequately suppressed, and his calcium is actually in the normal functional range, albeit low normal. Despite the PTH and calcium values, a vitamin D of 16.2 is still too low.

Remember that vitamin D plays a role in our immune response and modulating inflammation. His body is clearly struggling with chronic GI microbial imbalances including both SIBO and multiple parasites. Additionally, look at all the markers of inflammation present on his blood panel: CRP 6.09, high copper to zinc ratio, and a relatively high ferritin given the low iron (note that he is on the border of iron deficiency and functional anemia with an MCV at the low range of normal). His homocysteine is also elevated to 11.4, suggesting his methylation and therefore his detox capacity are likely compromised.

CASE #9: THYROID HYPOFUNCTION

Answer: These findings are consistent with hypothyroidism. Note that the Free T4 is just above the normal range, and reverse T3 is also slightly high, suggesting impaired T3 conversion. At this time, we didn't routinely screen everyone for TPO and thyroglobulin antibodies, so a follow up thyroid panel was ordered to include thyroid antibodies and she was found to have TPO antibodies of 98 and thyroglobulin antibodies were < 1.0. We also ran a Cyrex Array #3 which showed several antibodies for wheat and gluten out of range. Sometimes patients find these panels helpful in being more committed to a gluten free diet, and this seemed to be what she needed to follow a strict gluten free diet. She was started on Nature-Throid. She was also started on liposomal glutathione and curcumin for immune support and decreasing inflammation.

CASE #10: THYROID HYPERFUNCTION

Answer: This is a case of Graves disease, and remember that up to 25% of Graves' disease cases remit spontaneously. Since only her TSH is low, and both free T4 and free T3 are normal, the decision was made to address the SIBO, then address metal toxicity while providing immune support without direct treatment of the hyperthyroidism. We continued to monitor her thyroid function throughout treatment with the agreement that were we to see an increase in the thyroid hormones, then she would see an endocrinologist for specific treatment.

CASE #11: IMPAIRED KIDNEY FUNCTION

Answer: Upon further discussion, he reported eating about 1-2 pounds of meat per day in an effort to gain weight. We decreased his protein intake to about 100 grams daily, increased his hydration for a couple weeks, and then repeated the metabolic pain and saw normalization of the BUN, creatinine and uric acid.

Although studies suggest that, on average, even very high protein intakes do not cause kidney problems in people without pre-existing kidney disease, that doesn't mean it never happens. Remember, we treat individuals—not averages—so it's important not to invest too much faith in population-based studies.

CASE #12: IMPAIRED LIVER FUNCTION

Answer: Her AST and ALT are not quite at a 2:1 ratio as is often described in alcoholic liver disease, but certainly approaching that ratio. Her high glucose, hemoglobin A1c and high triglycerides suggest insulin resistance. Low vitamin D may also contribute to her blood glucose dysregulation. She was able to follow a Paleo diet after we developed some strategies for preparing meals ahead of time and discussed better options for her to choose at Whole Foods. We also started her on Theanine Serene with Relora and Acetyl-CH to help with sleep and she was able to stop drinking. Given the degree of elevation of AST and ALT, she was also started on NAC and Milk Thistle for additional support.

CASE #13: IMPAIRED GALLBLADDER FUNCTION

Answer: These findings are suggestive of biliary tree dysfunction. Note that bilirubin is mildly elevated and the most common cause is Gilbert's syndrome, which is completely benign and does not require treatment. To confirm, we measured direct and indirect bilirubin.

Bilirubin, Total/Direct, Serum			
Bilirubin, Total	**1.5**	**High**	mg/dL
Bilirubin, Direct	0.32		mg/dL
Bilirubin, Indirect	**1.18**	**High**	mg/dL

The high indirect bilirubin here is consistent with Gilbert's.

Since he's eating a standard American diet, we ran a Cyrex Array #3 panel and found several markers of wheat and gluten intolerance. He was started on a Paleo diet and started digestive bitters to improve bile flow.

CASE #14: ANEMIA IRON DEFICIENCY

Answer: Her heavy menstrual bleeding is a clear cause for her iron deficiency anemia. Interestingly her MCV is 90, larger than expected for pure iron deficiency anemia, but notice that her homocysteine is elevated and serum MMA is borderline high, both suggesting there may also be a component of functional B12 and folate deficiency, which may also be contributing.

We ran a DUTCH complete hormone profile which showed estrogen dominance. We also ran GI testing which showed severe methane predominant SIBO. We started her on liposomal iron, Trifolamin (for B12 and folate), antimicrobial protocol to treat SIBO and DIM Detox to help lower estrogens. She should also be referred to a gynecologist for an exam to evaluate for fibroids and polyps.

CASE #15: ANEMIA (B12 DEFICIENCY)

Answer: This is a case of functional anemia, meaning that the RBC, hemoglobin and hematocrit are in the conventional lab range but out of the functional lab range. She is supplementing with iron, but wasn't aware of the lack of B12 in a vegetarian diet. The high MCV is pretty strongly suggestive of anemia due to B12 and/or folate deficiency. She should be started on B vitamin supplementation and the CBC should be followed up in about four weeks and monitored until its normalization.

Her iron is also way too high. But of course in this case you can't recommend blood donation because she already has functional anemia. She needs to stop her iron supplementation but this would also be a case to consider using lactoferrin to help remove some of the iron. Check the iron panel in about six to eight weeks and continue to monitor because in vegetarians and vegans, I've seen the iron levels drop pretty quickly once they're off iron supplements, so be sure to follow this closely.

CASE #16: ANEMIA (CHRONIC DISEASE)

Answer: This is a case of anemia, but the cause is less clear. Her iron panel is normal and markers for B12 and folate are normal. Looking at the MCV it is on the low-normal side of the spectrum. So you could start to think about this as a microcytic anemia, even though, technically, the MCV is in the normal range. Since iron is normal, and in light of the long history of prolonged illness, this is consistent with anemia of chronic disease.

CASE #17: DYSLIPIDEMIA

Answer: In this case, his SIBO and yeast overgrowth may be contributing to his dyslipidemia. He was started on herbal antimicrobials to address both the SIBO and yeast overgrowth. He was also started on Annatto Tocotrienols and pantethine to address the dyslipidemia more aggressively. After successful treatment of the GI dysbiosis then we'll follow up with a repeat THD* panel. Remember that pantethine and tocotrienols can take up to 9 months to have their maximal effect on lowering LDL (with the bulk of that effect typically observed within the first 4 months), so we'll want to wait at least four months for the follow up panel.

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CASE #18: CHRONIC INFECTION AND IMMUNE DYSREGULATION

Answer: Unfortunately there's a lot going on with this child and he does need to see a Lyme Literate Practitioner for his elevated Borrelia antibodies. In addition to the Borrelia, we're also seeing gut dysbiosis though it's often difficult to know if the Blastocystis is really pathogenic given that it's found on so many PCR studies (more than 80% based on some recent studies). The yeast overgrowth is worth addressing and could be a reasonable starting place for him.

Notice also that his ferritin is significantly elevated which may represent his body sequestering iron into ferritin to effectively keep it from pathogens. Platelets are high so this needs to be repeated to confirm the degree of abnormality. AST is also high, so will need to be monitored. The low glucose may be associated with impaired mitochondrial function, so additional testing for mitochondrial function should be considered, and it could be related to Chronic Inflammatory Response

Syndrome (CIRS) due to the effects of biotoxins on the mitochondria (especially since his mother notes that mold is one of his most identifiable and strongest triggers).

CASE #19: IMPAIRED METHYLATION

Answer: Her low serum B12, high homocysteine and functional macrocytic anemia are all consistent with a B12 and/or folate insufficiency. The high homocysteine suggests that this low B vitamin status is also associated with impaired methylation. She has a number of inflammatory markers including a high CRP, high reverse T3, and low zinc-to-copper ratio. We ordered an HDRI Functional Methylation Panel to evaluate methylation more completely. We also started her on curcumin and liposomal glutathione for antioxidant and immune support. Her initial Doctor's Data stool test and SIBO breath test were essentially normal, but given her GI symptoms and high eosinophils, we were particularly concerned about parasites, so we ordered a stool test from Parawellness to look further for possible parasites. Her high LDL also raises concern for chronic infection, leading us to test further.