Lesson #5 – The FBCA Thinking Process

In yesterday's lesson I covered the "***Functional Hierarchy***", which is my way of organizing the Functional Blood Chemistry Analysis. In today's lesson I am going to cover the ***FBCA Thinking Process***, which is a way you can think about each and every biomarker on a blood test.

So here's where we are in the process:

1. You've decided to order a comprehensive blood test on your patient
2. You're sure you want to do a Functional Analysis because "Normal is Not Optimal"
3. You know what biomarkers you want to order and have ordered the test
4. The results have come back and now you're looking at the individual biomarkers themselves.

It's really important to have a way to not only connect the biomarkers together, but also to really think about what physiologically in the body is causing these biomarkers to be elevated or decreased. So here's the thinking process I want you to be conversant with for each and every biomarker on a test.

So you have to think about the following:

1. Where does this biomarker come from?
2. What are some of the reasons that it might be elevated?
3. What are some of the reasons why it might be decreased?

So, rather than going through each and every biomarker, I'm going to use BUN (Blood Urea Nitrogen or Urea) as our example.

BUN is a very common biomarker. It's probably going to be on every single blood test you do unless you're only running a CBC. I'm going to answer the above questions using BUN as our example. You can then take this thinking process and apply it to other biomarkers on blood tests.

Let's get started with question number one:

1. **Where does BUN come from?**

Before we answer this question we need to know what BUN stands for. As you know, many of the biomarkers on a blood test are listed using initials rather than their full names, for instance BUN, MCV, MCH, MCHC, ALT, SGOT, etc. This can be confusing for the patient so you have to know what each and every biomarker that is listed in this way stands for. BUN stands for Blood Urea Nitrogen.

Even just saying that kind of gives you a clue of what BUN is and some clues about why it might be elevated or decreased: it's found in the blood, it's associated with urea and nitrogen. What's the main source of nitrogen in the body? Answer: amino acids. And if we think back to our basic biochemistry, what does every amino acid have that makes it an amino acid? A nitrogen atom in its chemical structure. When our bodies take amino acids in and we break them down, the body has to do something with that nitrogen and that's where the urea cycle comes in.

What about urea? Here's where having a background in biochemistry is really helpful. If you can cast your mind back to the urea cycle you will remember that urea is formed in the liver and is the final product in protein catabolism or protein breakdown. So now we're getting somewhere, right? Blood Urea Nitrogen: found in the blood, urea involved with protein breakdown and the liver because the nitrogen from the amino acid gets fixed into the urea molecule in the liver.

BUN is formed almost entirely by the liver from both protein metabolism and protein digestion. What do we have to consider with protein digestion? Yes, primary digestion in the stomach and the presence of adequate hydrochloric acid. This is the very first thing I list on my Functional Hierarchy, the gastrointestinal system. So BUN is also associated with the GI, which is why it is one of those biomarkers that I look at for evidence of hypochlorhydria or low stomach acid. Hypochlorhydria impairs protein digestion, and poor protein digestion can cause a shift in the BUN.

Let's continue on with question number two:

2. **What are some of the reasons why BUN might be elevated?**

Now that we have an idea of where BUN comes from, let's now think about some of the reasons why it might be elevated. Here are three factors you should consider when it comes to an increased level of any biomarker in the body:

- Is an elevation of this biomarker due to too much being consumed from the outside (i.e., exogenously)
- Is an elevation of this biomarker due to too much being synthesized or created internally (endogenously)?
- Is the excretion of this biomarker somehow compromised so that less is being excreted and thus levels rise in the blood?

The exogenous question can be really important for things that are typically consumed: calcium, phosphorous, vitamin D, vitamin B12, iron, etc. In the terms of BUN, excessive protein intake can cause an increased BUN because BUN levels are associated with dietary protein intake. The protein gets broken down into the constituent amino acids, the body has to deal with the nitrogen in the amino acid, which goes into the urea cycle, and the way the body gets rid of urea is through Blood Urea Nitrogen.

Probably the most important consideration for BUN is the endogenous production because there are a number of factors that can increase BUN endogenously. For instance, an increased BUN level is often associated with a decreased production of hydrochloric acid in the stomach, hypochlorhydria. This leads to increased levels of undigested protein in the intestines and greatly predisposes one towards the development of a dysbiotic bowel with an overgrowth of bacteria. Putrefactive action of this bacterial overgrowth on the excess nitrogenous waste releases significant quantities of ammonia. Some of this ammonia will be converted into urea by the liver causing an increase in BUN and increased bacteria in the colon will also metabolize urea often leading to an increased BUN.

The third factor above has to do with how the body gets rid of a particular biomarker. So in terms of the BUN, the first thing you should think of is the kidney. An elevated BUN can mean that it's not being excreted properly so levels are building up in the body. BUN is removed primarily by the kidneys. So any dysfunction or disease in the kidney will cause its levels to rise

which is why BUN is primarily a kidney marker. Renal conditions happen on a spectrum all the way from dysfunction of the kidneys on one end through to overt kidney disease on the other end. I look at dysfunction of the kidneys in terms of a dysfunction called renal insufficiency, which is a condition where the kidneys are not just functioning properly. They're not broken, they're just not working properly and BUN levels start to creep up outside of the optimum range. They have not yet crossed above the normal or pathological range. We are still dealing with a functional issue here. Another thing to consider is that the creatinine might also be doing the same thing. So renal insufficiency or decreased renal function often occurs before one sees overt renal disease. We start to think of renal insufficiency when the BUN gets over 16 milligrams per deciliter in the States or over 5.71 millimoles per liter in the standard international units that are used outside of the States.

At the other end of the spectrum we have overt kidney disease. Significant impaired kidney function can lead to renal disease. In this case the BUN is typically above the normal or pathological range. Above 25 milligrams per deciliter or above 8.93 millimoles per liter for standard international units.

So let's take a look at our third and final question.

3. **What are some of the reasons why BUN might be elevated?**

So what are some of the reasons why BUN might be decreased? The answer is almost opposite of the questions that we just asked. We need to look at these 3 factors:

- There's not enough exogenously
- There's not enough endogenously
- Too much is being excreted

So when thinking about a decreased level of any biomarker, the first thing you have to ask yourself whether there is a lack of this biomarker being consumed from the outside (exogenously) or if the lack of this biomarker is due to it not being synthesized or created internally (endogenously).

Let's take a look at the BUN example. When it comes to BUN we should quickly go to protein intake, which is why BUN is a great marker for protein intake in the body. A decreased BUN level is associated with a diet that is low in protein, protein deficiency, etc. As we mentioned above, the amount of urea excreted as BUN varies with the amount of dietary protein intake. Low protein diets may show up with a decreased BUN level, below 10 or 3.57 millimoles per liter.

We should also think about the GI tract and the possibility of malabsorption. Decreased BUN is associated with a chronic intestinal malabsorption, which is an inability of nutrients to be absorbed through the intestinal wall. Malabsorption can lead to a functional protein deficit (along with a lot of other things), which in turn can lead to lower levels of protein catabolism and low BUN levels.

Continuing with our GI theme, we should also consider how proteins are digested further down the GI tract. A decreased BUN is associated with pancreatic insufficiency or lack of enzymes that are being secreted from the pancreas. Decreased levels of digestive enzymes, especially proteases, can lead to a functional protein deficit. This in turn will lead to lower levels of protein catabolism and lower BUN levels.

Given that BUN is synthesized in the liver, and the liver is one of the key organs in the body to become dysfunctional, it is not a stretch of the imagination to think that liver dysfunction can cause a decreased BUN. Dysfunction of the liver will have an impact on protein synthesis, which will affect the availability of protein for catabolism resulting in low BUN levels. This is not just limited to liver dysfunction because liver disease and liver failure can cause this too.

Finally, we have to look at ways in which there might be excess BUN excretion. In terms of the kidney, we know that renal disease actually causes BUN levels to increase because it cannot be excreted properly. So what could possibly cause the opposite? Again, we have to take a look back at renal physiology to see that the kidney is under the influence of a hormone called ADH or antidiuretic hormone. ADH is produced in the posterior pituitary and its job is to stop the kidney from releasing too much water. A posterior pituitary dysfunction can affect ADH output. Too little ADH and the kidneys release too much water, which can cause the kidney to excrete too much BUN. So, a decreased BUN is associated with an ADH secretion issue. If you're suspecting an ADH issue, check the urine specific gravity because it will be decreased and you'll see a BUN:Creatinine ratio that's below 10. These findings are supportive of a dysfunction in the posterior pituitary. This is not super common but worth considering.

I hope you have found this helpful and can apply this information to all the biomarkers on a blood chemistry and CBC panel. In our next lesson I'm going to cover an important document that shows you all of the biomarkers and their associated clinical dysfunctions. This is not to be missed!

Until next time,

All the best,
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