KRESSER INSTITUTE
FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Other Metabolic Patterns - Part One

Hey, everyone. In this presentation, we're going to talk about other metabolic patterns that show up on a functional blood chemistry panel. These are either less common patterns or less complex patterns, so we're not going to spend a lot of time on them.

The first pattern is gout. Gout is a type of inflammatory arthritis caused by elevated levels of uric acid in the blood, forming crystal deposits in the joints, tendons, and surrounding tissue. Gout typically affects the feet in general and the big toe joint specifically and causes severe pain and swelling. In the past, gout was referred to as "rich man's disease," as it typically affected the upper class and royalty who could afford rich foods such as meat, sugar, and alcohol.

Uric acid is a byproduct of the metabolism of purines, one of the two types of nitrogenous bases that form the basic structure of DNA and RNA. While purines are present in all foods, they are typically higher in many of the foods emphasized on a nutrient-dense Paleo diet, such as red meat, turkey, organ meats, and certain types of fish and seafood. Patients with gout are often advised to reduce or eliminate these purine-rich foods with the goal of preventing excess uric acid production and thereby reducing the symptoms of gout. Research has confirmed the association between high purine intake and acute gout attacks, suggesting that those diagnosed with gout would benefit from a reduction in purine-rich foods.

So, does this mean we need to change the dietary advice we offer patients with gout? Not so fast. While a high purine intake is associated with gout attacks in those who already have hyperuricemia, or high levels of uric acid in the blood, purine intake alone is not enough to trigger these attacks. In fact, uric acid levels are frequently decreased during gout attacks, sometimes to within the normal range.

Another factor associated with gout flares is an increase in C-reactive protein, CRP, and interleukin-6, cytokines that are produced during numerous inflammatory conditions. These inflammatory cytokines are increased in the joint fluid and serum of patients with acute gouty arthritis. Therefore, systemic inflammation is probably a key factor affecting the likelihood of developing gout flares, and as we know, diet, of course, plays a significant role in inflammation. While foods such as grass-fed beef, sardines, and mackerel are high in purines, they are also high in anti-inflammatory omega-3 fatty acids and low in other pro-inflammatory compounds.

Excess fructose intake is another potential trigger of gout. I don't believe, and research does not support, the idea that fructose in whole foods such as fruits contributes to metabolic disease. However, some studies suggest that excess fructose from sugar-sweetened beverages in a hypercaloric state may have harmful metabolic effects that are distinct from glucose, and gout may be one of them. For example, one study confirmed the uric acid-elevating potential of fructose both by producing excess uric acid and reducing its excretion in the urine.

While some uric acid in the blood is normal, providing a level of antioxidant protection, excess uric acid acts as a pro-oxidant, and it is the major causative factor for gout. Some researchers even suggest that this excess uric acid in the blood is a major factor for the development of insulin resistance and metabolic diseases, so if you're avoiding excess fructose consumption from high-fructose corn syrup and excess sucrose or table sugar, you'll be at lower risk for gout than someone who is washing their burger down with a can of Coke.

Whenever we consider a correlation between a dietary component such as meat and a disease such as gout, we have to remember that correlation does not equal causation. There is undoubtedly a correlation between the Western diet and gout, and researchers have assumed that meat was to blame, but the Western diet is also high in sugar, refined grains, industrial seed oils, and other processed foods. Given that inflammation is a necessary precondition of gout, it's more likely that these other factors in the Western diet are playing a role, especially since gout is rare in traditional hunter–gatherers. It's nearly impossible for epidemiologists to separate meat consumption from this general pattern of eating when studying modern cultures. After all, most so-called health-conscious eaters in our generation believe that meat is unhealthy and typically eat less of it. While most epidemiological studies attempt to control for these confounding factors, the truth is that most high consumers of meat are generally prone to other unhealthy habits such as smoking and drinking and are typically more overweight than low-meat consumers in these studies.

Of course, this doesn't tell us anything about the active health-conscious Paleo eater who avoids high-fructose corn syrup and excess omega-6 fatty acid intake, as well as other pro-inflammatory foods such as refined grains, and who doesn't drink heavily or smoke.

Insulin resistance is another factor in the pathogenesis of gout. This isn't surprising, since gout often appears in the context of metabolic disease. Elevated insulin levels reduce the excretion of uric acid, and gout patients often have diabetes, vascular disease, and poor glucose tolerance.

> Although **high-protein diets** contain large quantities of purines and are associated with an increased rate of endogenous purine production, such diets **often increase urinary urate excretion, and may even lower serum urate levels.**
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> **Fam AG. J Rheumatol.** 2002 Jul;29(7):1350-5

Another nail in the purine hypothesis coffin is the fact that studies have shown that purine restriction doesn't improve gout. It's also true that studies have shown that consumption of both dietary purines and protein increases the excretion of uric acid, suggesting that the body has a mechanism for regulating purine levels with varying levels of intake, which shouldn't be a surprise because we also see this mechanism with acid and calcium.

Some research has shown that dehydration may trigger or exacerbate gout. Vitamin C deficiency has also been implicated. For example, gout incidence is inversely associated with the intake of vitamin C, and vitamin C increases the excretion of uric acid. Studies have linked even moderate alcohol intake with gout. Finally, as you may recall from the iron overload presentation, phlebotomy significantly reduced the incidence of gout attacks, so iron overload may be a frequently missed cause of gout. That shouldn't be surprising because iron is pro-inflammatory.

Markers to consider for gout

Marker	Level
Uric acid	High
BUN	High
RBC	High
HGB	High
Glucose, A1c, insulin, leptin, etc.	High
Iron markers	High

These are the markers on the blood chemistry panel you should be aware of that can be out of range in gout. The primary marker to look at, of course, is uric acid, but BUN, RBC, and hemoglobin may be elevated if dehydration is present and related. You might also expect to see markers of insulin resistance, since that is often the underlying factor, as well as elevated iron levels. In many cases these markers will not be out of the lab range. They'll only be out of the functional range.