TO B OR NOT TOO B……..OR IS IT PROTEIN?

READERS SUMMARY:

1. WHY IS PALEO PROTEIN CRITICAL TO CARTILAGE AND TENDON REPAIR?
2. HOW DOES PROTEIN HELP REPAIR CARTILAGE IN INJURY AND DEGENERATION?
3. WHY ARE B VITAMINS CRITICAL TO THE PALEO TEMPLATE?
4. WHY A PALEO TEMPLATE IS BEST FOR A PREGNANT MOM OR A YOUNG CHILD?

Today, we are going to go back to the top ten Paleo supplement blog and begin to talk in depth about why protein and B Vitamins are critical components to a paleo template. This is covered in levee 14 and 24 of the QUILT. One of the facets of this lifestyle is becoming active again. To become active and remain active requires a person to have optimal functioning cartilage, tendons, and muscle. As most of you know, I make a living operating on these structures, so I think have a pretty good understanding of how to make them optimal both before and after I have to treat them. This topic is also near and dear to me, because a meniscus knee tear is what got me to adopt this new lifestyle. If you listened to my podcast with Jimmy Moore, you might remember that I would not have any surgery until I repaired the nutritional deficiencies I thought were at the root of the problem. I significantly increased my protein and fat intake to give my body its best chance to heal that meniscus tear. I never got this advice from my consultant orthopedic surgeons. I got it from reading myself about how one should regenerate cartilage. To do so requires a lot of dietary methionine. The principal source of methyl groups is from methionine found dietary protein. SAMe (S-adenosyl methionine) is a principle example. The B vitamins choline, inositol, and B12, are some others. These are provided for in

dietary abundance in most varieties of paleolithic diets. B Vitamins are used to transform the methionine to substance required to regenerate our cartilage. Methionine becomes SAMe using Vitamin B6 and Mg as cofactors. SAMe is the major source of methylation in our body. B Vitamins are involved in transmethylation, transsulfuration, and aminopropylation steps in the body. Most reactions involving B vitamins are characterized by being energy producing or anabolic, because they help in making us ATP. They also are vital for life and gene regulation. The B vitamins also are “the guardians” of our epigenetic switches that determine how our metabolisms respond to macronutrients. We have already seen how the new B vitamin PQQ is critical in exercise. Moreover, gene transcription is turned on and off by DNA methylation patterns. All the known DNA methyltransferases use SAMe as the methyl donor. So we will take a tour around our body’s systems to see what B Vitamins and protein do for us as we begin to optimize ourselves.

METHYLATION:

Methylation is not just one specific enzymatic reaction. There are hundreds of methylation reactions in all cells or the body. Methylation is simply the adding or removal of the methyl group (CH3) to a compound or other moiety. When some compounds receive a methyl group, this begins a reaction such as turning a gene on or activating an enzyme. When the methyl group is donated or removed, the reaction stops, or a gene or enzyme is turned deactivated. Some key methylation reactions would be:

1. Detoxification of dietary phenols from fruits
2. Methyl transfers turn on production of serotonin and melatonin
3. DNA methylation altering epigenetic signaling.
4. Cancer cells are characterized by a generalized disruption of the DNA methylation pattern involving an overall decrease in the level of 5-methylcytosine together with regional

hypermethylation of particular CpG (cytosine-phosphate-guanine sites) islands.

The extent of both DNA hypomethylation and hypermethylation in the tumor cell is likely to reflect distinctive biological and clinical features of the cancer in question.
Not all people or cancers have the same methylation rates. Humans can be hypermethylators or hypomethylators. Some genetic diseases even show a pattern of hyper or hypo methylation. An example of this is Autism Spectrum disorders where 50{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of people with it are hypomethylators and 10-15{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} are hypermethylators. Cancer is another example. Neoplasia is characterized by “methylation imbalance” where genome-wide hypomethylation is accompanied by localized hypermethylation and an increase in expression of DNA methyltransferase

EPIGENETICS:

Methylation contributing to epigenetic inheritance can occur through either DNA methylation or protein methylation. You have heard about epigenetics in some of my other blogs. I have also commented on how transgenerational epigenetic signaling is critical to initially setting a fetus hypothalamus for its life. What the baby eats from its diet from 0-6 years old will set the hypothalamic switches of how calories will be partitioned from macronutrients. Research in humans has shown that repeated high level activation of the body’s stress system, especially in early childhood, can alter methylation processes and lead to changes in the chemistry of the individual’s DNA. The chemical changes can disable genes and prevent the brain from properly regulating its response to any type of biologic stress. Researchers and clinicians have drawn a link between this neurochemical disregulation and the development of chronic health problems such as depression,

obesity, diabetes, hypertension, and coronary artery disease as the child ages.

DNA methylation in vertebrates typically occurs at CpG sites . CpG sites are cytosine-phosphate-guanine sites, where a cytosine is directly followed by a guanine in the DNA sequence. This methylation results in the conversion of the cytosine to 5-methylcytosine. The formation of Me-CpG is catalyzed by the enzyme DNA methyltransferase. Human DNA has about 80{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6}-90{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of CpG sites methylated, but there are certain areas, known as CpG islands, that are GC-rich (made up of about 65{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} CG residues), wherein none are methylated. These are associated with the promoters of 56{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of mammalian genes, including all ubiquitously expressed genes. One to two percent of the human genome are CpG clusters, and there is an inverse relationship between CpG methylation and transcriptional activity.
Protein methylation typically takes place on arginine or lysine amino acid residues in the protein sequence. Arginine can be methylated once or twice, with either both methyl groups on one terminal nitrogen or one on both nitrogens by peptidylarginine methyltransferases (PRMTs). Lysine can be methylated once, twice, or three times by lysine methyltransferases. Protein methylation has been most-studied in the histones. Histones directly control DNA/RNA binding sites for control of the epigenetic switches or for gene translation. The transfer of methyl groups from S-adenosyl methionine to histones is catalyzed by enzymes known as histone methyltransferases. Histones that are methylated on certain residues can act epigenetically to repress or activate gene expression. Protein methylation is an example of one type

of post-translational modification.

CARTILAGE OPTIMIZATION:

Chondroitin sulfate, glucosamine sulfate, N-acetyl glucosamine, hyaluronic acid, and mucopolysaccharides are all building blocks of cartilage, and they are all dependent upon sulfur groups for complete synthesis of healthy cartilage tissue. So you might be asking yourself where does the sulfur come from? It comes from methionine's break down to homocysteine. This releases a toxic sulfite molecule but it is immediately bound to Molybdenum and this liberates a non toxic sulfate molecule. The free sulfate group then is able to regenerate our cartilage and tendons. This is very important when you are lifting and squatting with heavy weights and running sprints.
This process uses SAMe (S-adenosyl methionine) as the methyl transfer moiety between methionine and homocysteine. The methyl donations from SAMe , which are also used for the synthesis of neurotransmitters, and essential cell components such as phosphatidylcholine and phosphatidylserine in myelin sheaths of nerves or in the adrenal cortex. SAMe has also been used by itself as a nutritional supplement, but when you look at the pathway's inner workings, unless you have all the necessary components available to optimize the efficiency of the whole pathway, SAMe can metabolize to homocysteine in just two more metabolic steps! This can lead to a large rise in homocysteine. I always ask if someone is supplementing with SAMe for this reason. To detox the high level of homocysteine, we need Vitamin B6 and Magnesium as a cofactors. If either one is deficient this will also lead to a build up of homocysteine on your lab values. This is why we use homocysteine levels as a clinical marker for problems in methyl transfer reactions. This is especially true in the cardiovascular system for poor energy utilization. It is also why I generally do not recommend supplementing with SAMe at all.

High levels of homocysteine clinically is a marker of disease

and poor energy utilization. Other conditions which have been linked to high homocysteine levels include: Cardiovascular disease, Multiple sclerosis rheumatoid arthritis, spontaneous abortion, placental abruption, renal failure, and type II diabetes.

HEAVY METAL CLEARANCE:

The same reaction occurs in the liver and excess sulfate is utilized for detoxification that bind heavy metals such as lead, mercury and cadmium. So if one is B Vitamin deficient, you may be more susceptible to heavy metal toxicity if your body or diet contains them.

DEPRESSION:

Homocysteine levels are related to depression in several ways. The methyl group metabolism provided for by the pathway of homocysteine (when correctly functioning) is necessary for the production of depression-relieving neurotransmitters such as serotonin and dopamine. The B vitamins are also crucial in the direct synthesis of the brain neurotransmitters. Aside from the fact that they are needed (especially B-6, B-12 and folate) for the homocysteine pathway to provide methylation, they are essential to the pathway of making these neurotransmitters . The neurotransmitter acetylcholine also is involved with homocysteine as well. High homocysteine levels have been linked to Alzheimer’s disease. This occurs due to poor energy utilization leading to protein folding problems that cause the development of the neurofibrillary tangles. The tangle appears to affect oxygen utilization in the neurons and renders them unable to produce acetylcholine, the brain neurotransmitter necessary for thought processes. Many times when one makes the switch to paleo, people will complain of “paleo flu”. Often this “flu” is poor methylation that causes a low energy state. Testing easily can pick this up.

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