Cold Thermogenesis 5: Biologic magnetism

Readers Summary

1. How can cold change human biochemistry, a real world example?
2. What are the major biochemical change induced by cold in mammals?
3. If humans have this adaptation in their blind spot, do other species use it?
4. Is there a ketosis training fallacy?
5. What is the ketogenic diet advantage in mammals?

My first encounter with thermoplasticity in human biology

I first became aware of this seeming paradox as a neurosurgical resident in my first year of training. We were doing a real “gnarly” brain surgery case. It was a young mother who had a massive basilar tip aneurysm. Back in the mid 90’s before endovascular coiling procedures we use today, this was the most risky operation that existed in all of medicine. I spent a month prepping for this case. We had to enlist the cardiovascular surgeons to come in and surgically open the patients chest wide open to stop her heart on purpose temporarily and place her on complete cardiopulmonary bypass to stop all the blood flow to her brain. We had less than 20 minutes to then place a clip across the aneurysm to save her life. To complete this herculean surgical task, we had to fill her entire chest cavity with ice to preserve her heart muscle and cool her core temperature so that we could have 20 minutes to complete the brain surgery. Simultaneously, we would open her skull and split the Sylvian fissure in the

brain and approach her basilar artery in the geographic center of her head and attempt to put a clip on it without disturbing any of her surrounding anatomy. The best mental image I can give you for this is the ultimate game of "Operation" you used to play as a kid. You must avoid hitting the sides or the nose lights up!!!! One problem in this case, in this game there was live bullets. This maneuver was deadly if not performed correctly the first time. This is one of the most delicate surgeries one can do on a human. Moreover, even if we were successful with the clip obliteration of the aneurysm, we had to restart her frozen heart, get her off cardio pulmonary bypass without an air embolus and awake. In this case everything went well until the last part and this taught me a lesson I would never forget. She died after the operation was a complete success. Her head was already closed up surgically and dressed, the intraoperative angiogram looked awesome, and we restarted her heart and got her off cardio pulmonary bypass without any evidence of a stroke and then she died suddenly.

She received two units of cooled banked blood because our surgical team felt she lost some ability to carry oxygen in her blood because several of the monitors showed she had a low oxygen carrying capacity of her hemoglobin. This concerned us because we were worried about her risk of having a stroke because of low oxygenation due to her loss of blood flow for 20 minutes when she was on full bypass.

So we did what any surgeon would do. We gave her blood to restore her oxygen carrying capacity and the oxygen monitors showed her oxygenation had totally returned to normal. We were all happy until I noticed her pupils were fixed and dilated when I was putting on her dressings. She also had blue fingers. And then all of a sudden she got a fatal heart rhythm, and she died right there in my arms. I was devastated. I will never forget talking to her family later that day.

What I found out 2 weeks later about why this happened was

more shocking. She died because of the combination of her cooled blood with her cooled heart allowed for a biologic change in how oxygen was released in her capillaries. In cold environments, oxygen is not released in the same fashion as it is normally in a warmed surgical environment. In capillary beds that feed cells for respiration, the oxygen is tightly bound and it is returned to the heart still oxygenated. This is why cold can make life survive in hypoxic environments for long periods of time. This highly oxygenated blood was sensed as normal by our oxygen monitors giving us the false belief that everything was fine. Her blood was fully oxygenated but the cold provided us with a major issue we were unaware of. If a anesthetized patients core temp is too cold red blood cells do not release the oxygen at the right time or in the right place in a capillary bed to allow for respiration. It does not matter if your blood is well oxygenated at all. She basically suffocated because the cold starved her tissues of oxygen. The cold cause increases the binding affinity of oxygen. It also causes protein transformations of the Hemoglobin molecule due to alterations in the cell's ability to sense magnetic fields. In fact, cold environments can have some rather shocking effects on human biochemistry due to magnetic effects, I learned after this case. One factor can change everything you think is true. I never forgot this lesson. If we had used slightly warmer blood, as we warmed up her core temperature she likely would have never died after this epic operative feat. We did all the crazy hard surgical things correctly but the physical and chemical effects of cold on the oxygen disassociation curve took our surgical victory to utter defeat in the matter of 5 minutes.

The reason this happened was from the paramagnetic effects of blood during a temperature cold while the patient was under a general anesthetic. When you are anesthetized you lose you magnetic sense. Super-paramagnetism is a form of magnetism, which appears in small ferromagnetic or ferrimagnetic nanoparticles. The hemoglobin molecule is one such particle.

In sufficiently small nanoparticles, magnetization can randomly flip direction under the influence of temperature alone! The typical time between two flips is called the Néel relaxation time. In the absence of an external magnetic field, when the time used to measure the magnetization of the nanoparticles is much longer than the Néel relaxation time, their magnetization appears to be in average zero: they are said to be in the superparamagnetic state. In this state, an external magnetic field is able to magnetize the nanoparticles, similarly to a paramagnet. However, their magnetic susceptibility is much larger than the one of paramagnets. Cold is directly linked to magnetic effects.

The moral of this story is that biochemistry acts differently at extremes. Most things published in a biochemistry book are about normothermic reactions. Do not forget this because everything you hear from a scientists mouth is based upon those conventions. Modern humans have two pathays they can operate on metabolically. One is just OK (mesophilic), and the other on is optimal (Psychrophilic) 99{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of the world does not know about the Ancient psychrophilic (cold) pathway in mammals. That is changing rapidly today. We are going to discuss this over the next few blogs as I slowly break down the biochemistry for you to digest.

The biochemistry of cold: Be prepared… It’s going to hurt your head

Non scientist: Cold adapted mammals can do things warm adapted ones can’t because at extremes chemistry, physics, and biology change when the temperature is colder.

Geek Alert: Our anthropocentric point of view has resulted in

the classification of cold-adapted organisms as extremophiles, even though environments of permanently cold temperatures (around 0°C) abound on Earth, especially when one considers that these include not only the polar and alpine regions but also deep-sea waters. **90{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of life** on this planet is cold adapated as we speak. Psychrophiles, both prokaryotic and eukaryotic, have successfully colonized these cold environments and are able to grow efficiently at sub-zero temperatures. This adaptation requires a vast array of structural and physiological adjustments in order to counteract the reduction in chemical reaction rates due to the low temperature of the habitat. Most scientists study human physiology in mesophilic environmental conditions. This is a big problem. The reason is that humans have completely different abilities in cold and the resultant physiologic changes are often 180 degrees opposite that one would expect. This fact has blinded many scientists and physicians to some deep realities about human biology.

Temperature is one of the most important environmental factors for life as it influences most biochemical reactions. Low temperatures slow down and strongly inhibit chemical reaction rates catalyzed by enzymes, the 'work- horses' of cell metabolism. The effect of temperature on chemical reactions is basically described by the Arrhenius equation: k = Ae -Ea/RT , where k is the rate constant, A is Ea is the so-called activation energy, R is the gas constant (8.31 kJ mol ~1) and T is the temperature in kelvins. Accordingly, any decrease in temperature will induce an exponential decrease of the reaction rate, the extent of which depends on the value of the activation energy. The thermodependence of the activity can be approximately expressed by the Q10 value that is normally close to 2- 3. This is the main factor preventing the growth, at low temperatures, of non-adapted organisms. So biochemistry of cold says we should have slow growth patterns based upon the biochemistry. I told you earlier that evolution

has sped up tremendously as time has gone on. So the question remains is, how did evolution overcome slower growth? Since the cell cycle was slowed by cold it sped up epigenetics to compensate for the slower growth. That is the basis of **Factor X**. It is the most important part of my theory because it is why the human brain was naturally selected for in a mismatched environment.

The low temperature challenge to life

For the non scientists: enzymes adapt at extremes to allow for ideal function and ideal signaling to improve metabolic efficiency

For the geeks: Biochemistry at extremes reveals three basic features…

1. Psychrophiles synthesize enzymes with higher specific activity (kcat) at low and moderate temperatures
2. The apparent maximal activity for cold-active enzymes is shifted towards low temperatures, reflecting their weak thermostability.
3. The adaptation is not apparently complete, as the specific activity displayed by psychrophilic enzymes around 0°C, although high, remains generally lower than that of the mesophilic enzymes at their own environmental temperature.

Kinetic optimization of enzymes: Biochemistry is thermoplastic too!

For the non scientists: the take home: If evolution faced this problem before it has a plan to adapt already built in. **Cold makes proteins and enzymes bend in different ways than occurs in warm states. Skip ahead to next one to make your head feel better.**

Geek view: A possible strategy to counteract the negative effect of cold on the activity of an enzyme could be to synthesize more enzyme, but it should be easily understood that this would be energetically expensive move. Energy sources in cold are scarce because food is not abundant therefore evolution had to come up with a plan B. Therefore, the common strategy used to maintain sustainable activity at a permanently low temperature is to produce a cold-adapted enzyme with enhanced catalytic efficiency kcat/Km (Feller & Gerday 1997). A compilation of available data (Smalas et al. 2000) indicates that cold-adapted enzymes optimize their catalytic efficiency by increasing kcat, decreasing Km or by changes in both parameters simultaneously. Mother Nature is a master of biochemistry at extremes. Too bad our species is not. She uses quantum effects to make this work.

As also expected in cold, all psychrophilic enzymes studied so far display much lower delta H# values, with the consequence that the temperature dependence of kcat is buffered and thus the deleterious effect of low temperatures on enzyme reaction rates is moderate in nature.

This feature leads to an antagonistic effect of the activation entropy so that the activation energy is not as low as would be expected from the decrease in activation enthalpy. It follows that the decrease of the activation enthalpy of a reaction catalyzed by a psychrophilic enzyme can be considered as the main adaptive character to low temperatures.

These interactions initially contribute to the stability of the protein folded conformation and, as a corollary, their alteration presumably gives rise to an increase in the flexibility of the structural domain of the enzyme involved in catalysis. This is a huge change in thermodynamics. As a consequence of active-site flexibility, the ground-state ES complex occupies a broader distribution of conformational states translated into an increased entropy of this state when compared with that of the mesophilic homologues, leading to a

negative value of delta (delta S #)p-m3.

Activity – Stability – Flexibility Relationships of the biochemistry

For the non scientist: cold shrinks proteins and alters their function to meet new demands. Cold affects the microgravity of enzymes in us to change their physiologic abilities. Cold requires that we add *certain* PUFA's to our cell membranes and alteration of protein folding to accomplish biochemical reactions.

Geek View: Low temperatures tend to improve the **compactness** of a proteins by limiting the 'breathing' of the structure corresponding to micro-unfolding processes. Cold affect local gravities and magnetic fields of small things in our cells. Therefore, at low temperatures, a mesophilic protein will lose the mobility required for its catalytic activity. What this means is that as it get colder we need to make the molecules more flexible to work in the cold. This means at extremes, physic laws (quantum things) do some strange things to our biochemistry. The current accepted hypothesis (Gerday et al. 1997; Zavodszky et al. 1998) suggests that psychrophilic enzymes have to increase their plasticity in order to perform catalysis at low temperatures. They do this by compliant design changes by the "addition or subtraction of packets of energy" to the protein back bone. The enhanced plasticity being generated by the generally **low stability of the protein structure**. This balance between flexibility and stability represents one of the crucial points in the adaptation of a protein to environmental temperature swings. **We now know in 2012 that cell membrane signaling is the single most important feature of cold adaptation. The colder it is the more omega 3's are need for cell membrane signaling. The warmer it is the less omega three we need in cells to signal. This implies that in warm adapted mammals**

omega 3's (DHA) might have deleterious effects at excess. They actually do if they are used incorrectly.

It has been shown that the psychrophilic alpha-amylase from Pseudoalteromonas haloplanktis has reached the lowest possible stability of its native state (Feller et al. 1999). This has been notably demonstrated by DSC, which is a powerful tool to investigate the thermal unfolding of proteins. Differential Scanning Calorimetry (DSC) is unsurpassed for understanding the stability of biological systems. DSC directly measures heat changes that occur in biomolecules during controlled increase or decrease in temperature, making it possible to study materials in their native state. I also saw this some remnant effects in my example that opened this blog. Not only was oxygen binding tighter than normal but there had to be changes in the hemoglobin molecules to make this physical chemistry happen. It appears that there are some unusual effects in the chemical bonds and in atoms on a sub atomic level that allow biochemistry to adapt. These adaptations are also present in humans when they are cold adapted. I mentioned earlier in the CT series that mammals have a unique way of altering their own cell membrane structures in anticipation of cold. My theory had predicted that because of the physics of the chemistry at cold I am describing to you here. It is clear **certain PUFA additions** make the cell membranes more fluid in cold so their signaling can work well with a different environmental signal. This in effect makes the cell membrane looser or more fluid. This has bigger implications for the optimal fuel for mammals in cold. The more extreme the environment the more flexibility the cell membrane needs. This is why omega three fats would be favored over omega six fats in mammals who live in the coldest environments on Earth. The reason is that omega three fats have more unsaturated bonds that allow for more fluidity in the cell membranes for ideal signaling. There are also electrical reasons for this as well. DHA can select for certain phospholipids to work in a more optimal electric manner. Take a guess where the omega three

sources come from? The deep ocean. It appears evolution is using form for function ideally, once again. The best natural source is krill and other fish that support huge ecosystems in our polar seas for these mammals. Seafood is always the right choice, but the use of krill oil use makes a lot more sense for warm adapted mammals than fish oil does because of its stability in warm temperatures. DHA is also not optically stable outside of fish. This is a major down side to fish oils.

Non scientist and geek unite: The best food source then for a cold adapted mammals biochemistry would be a ketogenic Epi-paleo diet that has a high omega 3 content.

For the non scientists: This is similar to all the paleo 1.0 books we have in print today. They have come to the same conclusion however from a different route than I have. I did not come to this life template via paleo 1.0/2.0, as I mentioned in my podcast with Jimmy Moore in May 2011. I came to it by following evolutionary medicine and where it took me. We did, however, meet here. This is no coincidence either. This is precisely why I believe the optimal diet for all eutherian mammals is a ketogenic seafood laden paleolithic diet when they are cold adapted.

I think some will say here , "Doc are you totally forgeting that we have had to time to adapt to a different diet and do well"? I have not forgotten at all. People have forgotten our environment today is radically different too. I think this is precisely what the evolution of the leptin receptor has allowed for over time in land based mammals and especially in modern primates and hominids.

Radical Rule Number 8: The leptin receptor is primordially a cold based electron counter. I think it evolved the ability to function in warm environments as mammals evolved onto land and took the planet over. **They began in the cold seas**.

My point is that while we can tolerate other diets and thrive on them, they are not optimal because they are not using the leptin-melanocortin pathway for optimal living. That is the distinction I am making here. I think the modern paleo template is great in comparison to a SAD, but the best design for all mammals is to use this fuel source while one is in this pathway for optimal functioning.

Non scientists pay attention here: Let us use A new Ferrari as an analogy to explain this. If you spend $250,000 on this car, would you put cheap gas in it to drive around or will you put super octane in it? Most car enthusiasts would not think twice about those options After all if you can afford this type of car what is the point of saving 20 cents a gallon on gas? If you buy a new laptop, do you put bad software in it? If you do, what do you get? You get bad performance. For tangible things we get this point implicitly. Where our neolithic thoughts trip us up is in our own "Ferrari engines" from evolutionary design. Modern humans are facing the same choice. What are they putting in their engines? They are choosing cheap gas constantly, and not the best gas at the correct time of the season. And what do they get? Mediocrity as a species is that answer. More biochemistry coming… Geek alert.

Non Scientist take home: there is a lot of life (90{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6}) that is cold adapted on earth. There is plenty of proof that biochemistry at extremes is common and exists.

Geek Alert: Do we have proof of this from real life on our planet now? Yes, in cold adapted Antarctic fishes. The molecular flexibility I mentioned above, should possibly be accompanied by a weaker substrate binding strength and consequently by an "evolutionary pressure on Km" in order to maximize the overall reaction rate. Psychrophilic enzymes, however, display identical substrate binding site and active site architecture when compared with their mesophilic

homologues, as illustrated in the case of A4-LDHs (lactate dehydrogenase) from South American and Antarctic notothenoid fishes (Holland et al. 1997; Fields & Somero 1998) and chloride-dependent alpha amylases from Antarctic bacteria and pig pancreas (Qian et al. 1994; Aghajari et al. 1998a; D'Amico et al. 2000). An experimental demon- stration of the relationship between kcat and Km was recently provided using cold-adapted and mesophilic alpha-amylases (D'Amico et al. 2001). Stabilizing weak interactions found in the porcine alpha-amylase, but absent in the cold-active alpha-amylase, were reintroduced by site-directed mutagenesis in the psychrophilic enzyme.

Normal mammalian biochemistry

Non scientist and geeks unite: Mammals have special cold adaptors on their skin that wire to the gut and to the central nervous system. This system is not well studied but it is clear that they are involved in readying the animal for cold adaptation quickly and eventually hibernation. Mammals add PUFA's from their tissue stores directly to their cell membranes by a process that we know exists because chemistry says it has to for life to live at the ocean floor. I discussed them in Cold Thermogenesis two blog. We do not know the precise molecular mechanisms yet, but we do know that **it is not dietary dependent**. It appears construction the cell is the key to life's success. This is how mammalian biology is designed to work normally. It is actually initially signaled for by excessive dietary carbohydrate loads in the diet during summer and fall that occur prior to hibernation. Since This is why diabetes, AD, and most other neolithic diseases of aging seem to be associated with high omega 6 tissue content. When humans never face a winter to rid themselves of the omega 6 levels in their tissues they concentrate slowly over time. When this occurs we see higher tissue omega six levels and our 06/3 ratios become unfavorable for health. Diabetics have the highest levels. **People with chronic neuropathy and**

chronic pain have higher levels. The work of Chris Ramsden has been very helpful to me as a neurosurgeon in treating these people.

It is not that the omega six content itself is pathologic, because we need to use them for life daily in the proper ratios. Where it becomes a problem is when we do not rid our cell membranes of excessive PUFA content once winter ends. The reason is because we never face winters any longer because of our brain has created warm clothing and housing for us to use. This is a mismatch. this allows us to concentrate omega sixes slowly over time. We see this in excessive 06/3 ratios in younger people and it eventually increases their HS CRP. It will further cause other hormonal decay with time. I am no longer surprised that I rarely see normal hormone panels in my patients. Modern human behavior is built upon these mismatches because our neolithic thoughts are not congruent to any circadian cycle. **Normal mammalian biochemistry is based upon timing from circadian cycles and food signals.** As I said in the Leptin Rx and the FAQ's blog timing is as important to us as what we eat. This is why. to regain control you first have to know how fast your chemical clocks are running in you. This gives you insight to how much your modern life is hurting your cellular biology.

When dietary carbs show up in our diet normally, we begin to normally upload our PUFA's to our cell membranes because our cell membrane need to be more flexible in the cold of winter. For modern humans winter never comes because we cover our bodies in modern life. The other mismatch is our diet. We eat a 24/7 diet of carbohydrates and PUFA's while winter never comes. We eat this because we "feel" better doing this. That "feeling" might be slowly killing you. Wild mammals might have feelings, but they can not act upon them because their are no supermarkets in the middle of Yellowstone park catering to their needs and wants year round. Our brain created all of modern life. This creates huge problems for our cells. Our

cells get over run with omega 6's and become pro inflammatory over time as our cells are recycled in sleep with autophagy. This is where the cytokine storms and leptin resistance comes from that shorten our telomeres and age us faster. These cytokines are the fuels that speed our chemical clocks up and shorten our telomeres. We remain unaware of this when we are young and have a large supply of stem cells to replace the ones we are destroying, but it catches up to us eventually. It is clear that there is a mechanism to replenish stem cells but it appears it does not work optimally when our chemical clocks are working too fast. We deplete more than we make. It is also clear that organ have their own individual chemical clocks so we see differential aging in organs because of this.

The only known way to reverse this process is cold thermogenesis while eating a diet that optimizes our Ferrari engines given to us by Mother Nature. What else do we do to keep ourselves in the dark about mismatches? Humans protect themselves from the cold by clothing and heating. We no longer hibernate because our brain extinguished that need. We do not have a lot of surface hair either to warm ourselves because we no longer needed it when we evolved into a warm environment and began able to control it with clothing. Mammals became able to compensate for a slowed growth rate in cold, by speeding up epigenetic expression of our genome to eventually create our species whose brain power far outstrips its somatic genes. We are still prisoners to many parts of our mammalian biochemistry and we seem blind to this as well. The brain is so advanced that it puts our genes constantly at risk, while we remain blind to it as we deplete our life force within us slowly. We, as a species have not realized this until we found out about telomere biology and what it means.

We can now see if this theory is correct for ourselves by checking our cellular age against our real age. So far, not one person I have checked has a lower biologic age then a

chronologic age on telomere assays. This implies that much of modern life is a mismatch. It also implies we need to question every aspect of our behavior to understand the mismatch and how it might harms us. This is how an optimal human thinks. This is also how thoughts can change our DNA. This is why I gave you the banana analogy in the Paleo Summit talk. It is an easy way to show you how blind you really are to this situation. Most people found it fascinating because they never thought about it before I said it. I can not stop thinking about this since I realized it was true for our species 6.5 years ago. When I saw my own mismatch for the first time it was sobering. Much like the video I showed you in the Holy Trinity blog. I have been studying human mismatches, and the inflammation cascades they cause for the last 6.5 years. I spend many days and nights thinking about ways to use this evolutionary medicine to help treat and often reversing disease in my family and in my patients. It is critical to a healthy lifespan.

Mammalian life uses this evolutionary blueprint. We are mammals. Mammalian biochemistry is thermoplastic in vivo. NASA andAthletes have found it first. Their application and the applications by NASA have opened my eyes. We need to apply this information to modern healthcare. Sleep and longevity researchers are “waking” up to this new reality today. Sadly, the human researchers do not understand that all their current studies are not controlling for this mammalian ability. This throws many of their results up in the air. That is a tough reality to swallow. I had to eat my own dogma 6.5 years ago and adapt my own practice. It was difficult. I sat down with a some friends who are biochemist in academia in Nashville and this news was sobering to them too. This reality has made them think differently as well about many aspects of science.

So what other things might cold do to us?

Studies done on the Sherpa's and NASA astronauts clearly show a major metabolic benefit that has not been well explored by modern science and medicine. These ancient programs can allow humans to not only survive on low calorie diets, but they can actually make us superhuman in some respects. Sherpa's and astronauts can sustain themselves well on a lowered caloric intake yet with superior ability to handle their climates when they are cold adapted. The same has been found true of the native Inuit on their native diet as well. This ability is no longer found in the modern Inuit because most now eat a Western diet. We also found out since the Cold War ended that the Russians have also stumbled onto this science in their research. Their athletes and cosmonauts have been using this data for years to dominate at alpine sports in Olympic games. It appears the U.S. Olympic swim team and Lance Armstrong got the message too before any of their competition here in the US or in Europe. It completely explains why they were able to do things some humans previously could not accomplish. It maybe why people still accuse them of cheating. We all heard about Michael Phelps eating escapades by being able to eat larger amounts of calories daily routinely in his training for the Olympics! Most scientists at the time said the NBC report of Phelps feat was not possible. Ray Cronise was one of those scientists. Well, by conventional calorimetry studies it is impossible. This is why many scientists were lost. They forgot to look under the right rock for the reason it might be true. I can assure you Phelps and Lance Armstrong learned what I learned about leptin and about cold. They used this knowledge to become world class athletes, and I used it to reverse my obesity.

The reason modern science believe this to be impossible is because their studies fail to account for the thermal

coefficient of the environments that they trained in. Phelps works out in a pool at 50 to 60 degrees for an extended amount in a day. His training regimen is closely guarded. His competitors have publicly commented that they know what is published in his books are smoke screens because he wont even train with his own teammates. Armstrong still has never said precisely what he did but there are many leaks that he worked out in freezers installed in his house with stationary bikes built in to them. He also guards his training regimen. This regimen shredded their body fat to the small single digits, and it allowed them to gorge on calories that they became able to just burn off as free heat, while increasing their ability to perform work at superhuman levels. This was possible because they found out that in cold, the leptin receptor allows for unbelievable adaptability in resting RER. In Phelps and Armstrong's case, they were both able to expand their native VO2 max ranges north of 70 according to their former trainers! This is truly super human ability territory and explains their fabulous athletic feats. There are other humans who can induce this biochemistry too.

The Sherpa's have the ability naturally because of where they live. In the cold and high altitude of the Himalaya's. They cold adapt in a few days when they take a climber to the summit of Everest. They lose an unreal amount of weight when they climb, so they eat pure butter and lard the last 2000 ft of the ascent. NASA studied them closely and used this information to help maintain the weight of the astronauts who also lost tremendous weight during space walks in the 1960's and 1970's.

Many believe that humans are best adapted to use carbohydrates to burn for fuel using endurance exercise. Take a look at the following link from 1994 about the use of fat burning on its effects on VO2 max testing that is of prime importance in any high performance athletes. The Buffalo Bills of the NFL are the first team to institute this change because they were made

aware of this study done in 1994 in runners. It is one of the few studies that give a "glimpse" of what a cold adapted runners can do eating fat. Ironically, these runners were all from Buffalo, NY where it happens to be cold. This is the only reason this VO2 max expansion was found. When the NASA data came out over the last ten years the NFL took notice finally when it was brought to their attention by a the agent of a hockey player. The Bills have been the NFL team most ready to adapt because of what happened to Kevin Everett their TE in 2007. That story is for a later blog on Factor X.

Conventional wisdom and Paleo dogma state that you can increase your carb load as you exercise. When you use carbs to fuel your Vo2 max flattens. When you are fat adapted your V02max expands. No one seems to correlate it with their performance VO2 max to see how dietary fat helps or hurts their exercise in a thermoplastic environment. We have all seen and heard that those thoughts all over many blogs about how performance suffers on ketosis. The real problem is they have no idea that it soars when your biochemistry is cold adapted. Well this article shows that assumption may not be true at all. In fact, the opposite might be true. Both used cold training techniques to raise their level of performance. Can fat loading be a better choice than carb loading for performance? Could this be true? Why might be this be the case? Question everything is my response.

Training Fiction: Ketosis is most efficient mammalian fuel in the cold not carb loading.

Modern hominids think this is reversed because all the research is done on warm adapted humans eating the wrong diet. The elite athletes are now finding out that is not true thanks to NASA.

Burning fat (FFA) actually increases our VO2max when the ancient pathway is induced. I test VO2 max routinely in some of my patients, and I will tell you those people who are

interested in long term performance and longevity use a ketogenic version of the paleolithic diet show huge gains in their VO2 max over 24-36 months of adaptation. Being adapted to fat is better for performance too. It increases strength and power because the cold increases the steroid receptor affinity for steroid binding. This means your Growth Hormone and testosterone levels surge as you cold adapt over 2-3 years. No one studies it that long but it does occur. Modern elite athletes are now using it routinely. It just does not happen as quick as most athletes want in modern training, therefore they mistakenly believe that carbs are better for their performance in the short term. The reason is that they only measure their performance over a few months at most. Few cold adapt. The elite athletes are all beginning to cold adapt these days. The NASA data and Russian data is no longer a secret. Believing that carbs are better for performance might be also be a big mistake that might subjugate your paleolithic genes.

When humans are warm adapted carb provide great fuel but they also increase our ROS as we do this and we deplete our stem cells. Ironically, this methodology shows no measurable loss in performance to the person in the short term, it actually improves it in the short run. This falsely gives the person a false sense of security that they are improving their body. The look at their facade as proof. The real problem presents but it does when the get past their 45th birthday. These athletes are depleting their stem cells. It can be measured in their telomere lengths. Why does this happen? Carb training increases ROS at the first cytochrome of mitochondria when we make ATP from glucose.

So what happens to athletes who are cold adapted who use fat to train? Why is ketogenic diet more energy efficient at a Krebs cycle level? The reason is that mammals generate very little ROS comparatively to the warm adapted carb burners mammals at their mitochondria. Why?

Non scientict read here: when you eat fat your mitochondria are less leaky so you age slower. When you eat carbs you leak more and shorten your telomeres.

Geek alert: During oxidative phosphorylation, almost all of the reducing equivalents produced by glucose metabolism in the Krebs cycle are in the form of NADH (cytochrome 1/where carbs enter) with the exception of the succinate dehydrogenase step, which takes place in mitochondrial complex II and makes FADH2. Metabolism of one molecule of glucose produces an NADH:FADH2 ratio of 5:1 whereas fatty acid metabolism in beta oxidation and the Krebs cycle will produce a ratio of â‰¤3:1 depending on the length of the fatty acid. This implies that fat burning is reducing to the interior of the cell compared to glucose burning. Carbohydrates create more oxidation inside the cell. If you do this over a life time you are just throwing gasoline on your stem cell population as you age. The toll is seen in your telomere length.

This effect is more pronounced in organs that use tremendous energy like the brain. Over a life time this can results in serious disease of aging that occur sooner than expected. This is what we see in our modern world. Our species is mediocre because this has remained in our blind spot. This is commonly seen in retired NFL football players who have substantially reduced life spans. The NFL is the best example of my theory in practice today. They train hard and carb load while building amazing bodies that just wither away quickly as they hit their 5^{th} decades. If you train and eat like this, you burn out fast instead of fading away slowly. When you look at the NFL data on longevity it is eye opening. In modern humans, aging is a biologic novelty.

NADH is oxidized only in mitochondrial complex I whereas FADH2 is oxidized only in complex II. Complex I produces more reactive oxygen species than complex II. This means that carbohydrate metabolism increases “mitochondrial leakiness”

compared to fat burning does. The more leakiness a cell metabolism exhibits the shorter are its telomere lengths. Short telomere lengths correlate with disease and shortened lifespan. Fats metabolism by contrast is a less leaky process. Moreover, oxidation of fats reduces mitochondrial leakiness and decreases intracellular oxidation that depletes stem cells and shortens our telomeres over a life time. This is why telomere lengths are a great way to see what your lifestyle choice are doing to you as a gross measure of effectiveness.

The production of a specific number of ATP molecules from glucose/carbs has the potential to generate more reactive oxygen species compared to the generation of the same number of ATP molecules from fatty acids.

The trainer blind spot

They key question then should be why are these benefits not perceived by athletes or trainers today? The reason is quite simple. Modern life is fast and we want results yesterday. This is another example of how our neolithic beliefs subjugate our paleolithic genes. Once again, time is relative for most performance athletes and trainers. This fact is axiomatic in physics, chemistry and biology. This is a neolithic thought that can hurt you over a lifetime without you realizing it if you do not look for the evidence in your cells. None of them have realized that the thermal coefficient of their environment makes this biochemistry work against their telomere lengths in this fashion. It is all relative to the time of the adaptation. If they changed the environment to cold and used the same diet things would be dramatically different because ROS would be low and the stem cells protected. If the diet was adapted to a ketogenic version over 24-36 months they would see amazing expansion of performance. **At extremes, biochemistry changes in nature for our benefit. Evolution has a plan for this because it tapped**

it many times before. REALIZE THAT modern trainers are oblivious to this therefore they regurgitate what is best from the literature that is based upon mammals who are warm adapted eating a warm adapted diet! Can you say major mismatch!

Can you prove me wrong or right on this training assertion? Yes you can. We can follow this with VO2 max progression in training or with a quantified self platform of testing. You could also check your telomere lengths over a fat burning and carb burning training periods. Many professional teams are realizing just how bad warm adapted training on a carb loaded diet is. Since VASPER was studied in space in the 1980's and 90's, the world of training has been inverted over night. **It promises 2 hours of exercise in 20 minutes using cold technology licensed from NASA.** You will not find this reflected in the modern day literature yet because its been in exercise physiology's blind spot. It takes 15-25 years for bench top research to hit the clinical shores. You will find that when you fat burn 100{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} of the time your VO2 max goes higher than at any time when you are training using carbohydrates. You can do this yourself in your own gym without any Rx. It is the ultimate challenge to our community. You owe it to yourself to question your own dogma and find out what I already know to be true. The ketogenic version of the paleo diet is what mammals are best adapted to because it increases our VO2max, REE and RER. This is how all mammals are designed to function best. We seem to forget we are mammals too. NFL teams are now introducing this type of training over the last few years because of NASA technology and findings. Moreover, they are trying desperately to make their game safer for the players. This was recently licensed to a company called VASPER in California. It appears humans are awakening that their might be a new way to train to live that they have never pondered before.

Individual difference in humans who cold adapt

Special forces training has been at the fore front of this type of information. I have a few friends who are former Seals and Rangers. I spent a lot of time talking to them picking their brains about their training. Most of what they were taught and trained for is not published for obvious reasons. Here is what I found. Cold tolerance is increased by large body size (small surface area – body mass ratio), abundant subcutaneous fat, good physical fitness (good ability for heat production, good circulation), male gender (predominantly due to larger body size), young age (via muscle mass and circulation), cold adaptation and good health. Recently it has been shown that also personality affects thermal responses, especially the levels of extrovertion and neuroticism. Increased level of neuroticism dampens or slows the autonomic thermoregulatory responses whereas increased extrovertion has an opposite effect.

Cold acclimatization and acclimation

Why has this escaped your awareness? Your brain is far advanced in design than your genes are because of epigenetics. This is a mismatch you remain blind too for your whole life. This was the basis of my Paleo Summit talk. I am going to continue to make you aware of how many modern humans face. They are vast because of our amazing brain. Each mismatch that does not favor our genes shortens your telomeres right under our nose’s. That is a reality you better get very comfortable with because it is why our species is now mediocre. It is why old age happens in the 50’s now and why neolithic disease is accelerating in younger generations. It is why children now have heart and carotid disease below ten

years old. It is why heart failure is the number one reason for admission and death in all humans. It is why Alzheimers is now common when 100 years ago no one knew what it was. It is why colon cancer went from 37th to 2nd in death from cancer. It is why ADD and ADHD are common today and were not in decades past. It is why the NHANES curves for obesity have shifted. Yes, fructose is playing a role, but it is not the major cause. There is not a disease we face that is not accelerating as time marches on. It is because our modern world is speeding up our biological chemical clocks because our brain is expert at creating biologic mismatches for our genome.

There is a reason these things are happening. These diseases did not just show up out of the blue. These mismatches speed up our chemical clocks. It means the young become older faster so the diseases of aging will show up in us as young people. This has happened in just 8 generations from the Industrial revolution. It is a situation where a "progeria-like state" has become our modern day primordial condition.

The cold and a ketogenic diet can slow and often reverse that process. Thermal adaptation, either natural acclimatization or artificially produced acclimation, to cold takes 2 weeks. After the development of adaptation, the physiological responses to cold are usually attenuated and cold environment is subjectively considered less stressful than before adaptation. Cold adaptation of hands diminishes the local vasoconstriction which allows higher circulation and skin temperatures in hands (fisherman's hands). The classical forms of physiological cold acclimatization are insulative (increased skin vasoconstriction or subcutaneous fat), hypothermic (decreased core temperature), insulative hypothermic (most common type of cold acclimatization) and metabolic (increased energy consumption).

Why have we not seen this in modern humans?

Behavioral adaptation is most important for the survival of human species. It includes e.g., well heated houses, good thermal insulation of clothing, warm vehicles and short exposures to cold. In fact, behavioural adaptation can work so well, that no physiological adaptation is developed in winter, as shown in young urban residents. These neolithic creations are why we do not see the metabolic benefits of this pathway in modern humans often. When modern humans become aware of them and their benefits they may consider building a small part of their current environment for cold thermogenesis. Modern humans may find that when they cold adapt it will help treat diseases due to mismatches in circadian biology.

Warm clothes and buildings are neolithic creations that kept us in the dark about the ancient pathways benefits. Wild mammals can't do what our brain allows us too. Mismatches are not just not good for humans in our modern world where it constantly seems like it is summer time due to artificial light and 24/7 access to carbohydrates.

Neolithic disease of aging is total chaos. Health is perfect order, in between is mediocrity. We are searching for optimal.

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- Cold Thermogensis 2
- Cold Thermogenesis 4: The Holy Trinity
- The Paleo Summit: Is The Paleo Diet The Answer?
- My Leptin Prescription
- The Leptin Rx: FAQs

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