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VIRTUAL LAF CONFERENCE

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SUBJECT: *Potassium/Sodium Ratio in Atrial Fibrillation*

Sodium and potassium! Biophysicist Richard D. Moore explains:

"For purely *physical* reasons (connected with the law of osmotic equilibrium), inside the cell the sum of sodium and potassium *must* be constant. This means that... sodium and potassium are unalterably linked together like two children on a teeter totter. You can't change one without changing the other.

"Thus, in the perspective of biophysics, it makes no sense to talk about either sodium or potassium alone - these two substances *always* affect each other in a reciprocal relation. Hence their *ratio*... reflects the state of the living cell more completely than either sodium or potassium alone... It is not only a simplifying concept, but a much more scientifically valid measure of the state of health of the living cell.

"Reflecting the action in the cell, potassium and sodium always work in a reciprocal manner in the whole body... This means that increased consumption of potassium will drive sodium out of the body through the kidneys. Thus, potassium has been called "nature's diuretic"... This is an example of the fact that elevation of sodium inside our body cells must always be accompanied by a decrease in the potassium level." [1, 11]

From the article Paleolithic Nutrition Revisited: A twelve-year retrospective on its nature and implications: [2]

"The nutritional needs of today's humans arose through a multimillion year evolutionary process during nearly all of which genetic change reflected the life circumstances of our ancestral species. But, since the appearance of agriculture 10,000 years ago and especially since the Industrial Revolution, genetic adaptation has been unable to keep pace with cultural progress. Natural selection has produced only minor alterations during the past 10,000 years, so we remain nearly identical to our late Paleolithic ancestors and, accordingly, their nutritional pattern has continuing relevance. The pre-agricultural diet might be considered a possible paradigm or standard for contemporary human nutrition."

Sodium (Na) and potassium (K) are critical nutrients, but today's typical diet might supply 5 times the amount of Na, and only 1/4th the amount of K that we evolved with. In our evolutionary past the kidneys became configured to optimize the body's cellular Na and K levels by conserving the sodium available and by discarding excessive potassium. Our kidneys have essentially not changed since then, but the typical diet is now upside down, with disease-causing consequences for all cells and systems.

Our bodies are 'The Body Electric'. [3] Each of the body's cells is like a battery (10, 20 trillion?), charged to their functional voltage by the enzyme Na/K-ATPase, commonly called 'Na/K pump', or 'sodium pump'. "Depending on cell type, there are between 800,000 and 30 million [Na/K] pumps on the surface of cells. They may be distributed fairly evenly, or clustered in certain membrane domains, as in the basolateral membranes of polarized epithelial cells in the

kidney and intestine".[4]

Na/K pumps span the cell membrane, and generate the electrical voltage (potential) to charge the cell/battery by continuously pumping ~3 Na⁺ ions out of the cell in exchange for ~2 K⁺ ions pumped in.[5, 6] In cardiac muscle a 'trans-membrane potential' of about 90 millivolts (mV) is generated (negative inside), which provides for the cell's electrical requirements: voltage-gated ion channels, calcium pumps, etc. To attain this functional voltage requires the intracellular K/Na ratio to be at least 20 to 1 [7], which in turn requires the dietary K/Na ratio to be at least 4 to 1.[1] The kidneys ideally maintain serum K and Na at the levels they were evolved to maintain, but the high intracellular K/Na ratio can not be attained if intracellular Na is too high (as Dr. Moore explains, above).

Na/K pumps are proteins, synthesized within the cells, each consisting of many hundreds of the 20 different amino acids in chain-like linkage, assembled in accordance with nuclear DNA codes, then folded and configured for their specific function. Code errors (genetic or by damage) or lack of required amino acids (genetic or dietary) can result in dysfunctional Na/K pumps (channelopathies) possibly resulting in low cell voltage. Having sufficient cellular amino acids available for protein synthesis is essential.[9] There are excellent computer-generated images of the Na/K pump protein structure at the Protein Data Base website.[5]

Na/K pumps are powered by the energy molecule adenosine-triphosphate (ATP), which for function requires an attached magnesium ion (Mg-ATP). ATP is synthesized from oxygen and food molecules in a process requiring Coenzyme Q10, carnitine, magnesium, ribose, phosphate, and many co-factors. In body cells the continuous pumping of K and Na consumes about 25% of the ATP produced, while in high energy-demand heart, brain, and neurons the consumption is as much as 70%.[4] Therefore, if ATP and magnesium are deficient, and if the intracellular ratio of K to Na is low, the cells' voltage will be low. Low cell voltage may express as abnormalities in cells and systems throughout, as in blood pressure, kidney function, electrically excitable tissues of the heart and brain.

In heart muscle cells the resting membrane potential (phase 4 of the cardiac cycle)[8] is the voltage of the cell while resting before being excited to de-polarize (discharge) and contract. Low resting voltage can trigger AF, and can be an explanation for the cyclical nature of paroxysmal AF. From the web page Cardiac Action Potential: [10]

"Phase 0 is the rapid depolarization phase. The slope of phase 0 represents the maximum rate of depolarization of the cell and is known as dV/dt max. This phase is due to the opening of the fast Na⁺ channels causing a rapid increase in the membrane conductance to Na⁺ (G_{Na}) and thus a rapid influx of Na⁺ ions (I_{Na}) into the cell - a Na⁺ current. The ability of the cell to open the fast Na⁺ channels during phase 0 is related to the membrane potential at the moment of excitation. If the membrane potential is at its baseline (about -85 mV), all the fast Na⁺ channels are closed, and excitation will open them all, causing a large influx of Na⁺ ions. If, however, the membrane potential is less negative [lower voltage], some of the fast Na⁺ channels will be in an inactivated state, insensitive to opening, thus causing a lesser response to excitation of the cell membrane and a lower V_{max}. For this reason, if the resting membrane potential becomes too positive [lower voltage], the cell may not be excitable, and conduction through the heart may be delayed, increasing the risk for arrhythmias."

This means that a slower depolarization (discharging) of the atrial muscle cells' voltage results in shortening of phase 2 of the action potential and the cells' refractory period (the time period during which cells are at zero volts and can't be excited), which increases the risk for AF.

Therefore, if atrial cell voltage is generally low, for reasons above, NSR might be on a proverbial razor's edge. If voltage drops just a bit lower AF might result, especially if there are other predisposing conditions, such as fibrosis [12] or electrical remodeling. AF induced release of sodium-lowering hormones such as ANP and BNP results in increasing the intracellular K/Na ratio, thus the cells' voltage, and NSR might return. In this case all body cells will have higher voltage, and one's body-mind might well experience well-being until the next cycle, as all cells and functions will have benefited by having higher voltage.

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Erling

Erling,

This is a wonderful post. My questions are the following: We understand that the uptake of potassium is difficult without a sufficient level of inter-cellular magnesium, but do the same set of conditions apply to ATP and potassium? Without a high enough level of ATP, will potassium levels always remain low, and the potential for an AF event high? Might this set of circumstances also explain vagal afib? After a period of exercise and/or stress during the resting period, are ATP levels likely to drop to a level that would reduce the capacity of the NA/K pump and, thus, induce an afib episode? In automobile parlance, the car is not going to run without enough gas in the tank. Mechanics figure these things out, why can't so many doctors?

Steve

Thanks, Steve - it's good to know that the information is understandable.

You've asked some good questions:

1. "We understand that the uptake of potassium is difficult without a sufficient level of inter-cellular magnesium, but do the same set of conditions apply to ATP and potassium?"

A reason that intracellular uptake of potassium can be difficult is a low intracellular level of Mg-ATP fuel for the Na/K pumps. Since Mg must be pumped into the cells by special Mg pumps, indirectly using the energy of Mg-ATP, if IC Mg is insufficient, Mg can't be pumped in, because ATP can't do it without Mg: a vicious circle. And if Mg can't be pumped in because of low Mg-ATP, neither can K be pumped in by the Na/K pumps: another vicious circle. This is a reason why a deficiency of IC Mg might be 'intractable' (refractory) and might require IV or IM infusions of Mg to 'break the circle' of IC Mg and IC K deficiency. See <http://www.mgwater.com/inmgdef.shtml> for good comments on this.

2. "Without a high enough level of ATP, will potassium levels always remain low, and the potential for an AF event high?"

The answer would seem to be yes, because if Mg-ATP fuel is not at a high enough level, the Na/K pumps will be slowed, the IC K/Na ratio will be lowered, resulting in the cell voltage being low. From the first post, above: "...if the resting membrane potential [voltage] becomes too positive [lower voltage], the cell may not be excitable, and conduction through the heart may be delayed, increasing the risk for arrhythmias."

3. "Might this set of circumstances also explain vagal afib?"

If I understand correctly, vagal afib is 'mediated' via increased neurotransmitter acetylcholine (ACh) at vagus nerve connections to the atrial muscles. ACh increase effectively shortens the atrial muscle cells' refractory period (ARP), increasing the risk for Afib. From <http://courses.washington.edu/chat543/cvans/sfp/acetylch.html>: "The effect on action potential duration shortens the atrial refractory period. This is critical in patients who may have atrial flutter or fibrillation."

I would think that this effect adds to the effect of slowed Na/K pumps, decreasing cell voltage even more, and increasing further the potential for Afib

4. "After a period of exercise and/or stress during the resting period, are ATP levels likely to drop to a level that would reduce the capacity of the NA/K pump and, thus, induce an afib episode?"

Quite possibly. This would have a lot to do with the production rate of ATP in the mitochondria, which depends upon the state of the mitochondria and their unique DNA, and the IC levels of the required substances, such as Dr. Sinatra's 'awesome foursome': Mg, CoQ10, carnitine, ribose, and cofactor vitamins, taurine, etc.

5. "In automobile parlance, the car is not going to run without enough gas in the tank. Mechanics figure these things out, why can't so many doctors?"

Oh man! The best short answer I know is by biochemist Alan Gaby MD, in his book Preventing and Reversing Osteoporosis: "The Medical Profession: A Dysfunctional Family", which is part of chapter 25, "Natural Remedies: The Orphans of the Medical Industry". Not by any means a rant, this is a factual analysis of the situation by a great physician who knows.

Erling

Erling - enlightening responses to Steve, thanks.

Steve - Regarding your ATP question, I'd like to add the following about d-ribose and ATP:

Consider that a heart experiencing regular bouts of AF is akin to significant exertional exercise. In that regard, d-ribose is an excellent adjunct to the Essential Trio protocol because it assists in the synthesis of ATP. As stated in one of the earlier ribose posts, studies to show the ATP recovery rate in skeletal muscle following exercise to be greater than 3 days. So in cardiac muscle tissue (not skeletal) that may also be lacking magnesium and potassium, and in the case of frequent afib, that heart muscle is going to need some interventional boosts of the key nutrients in order to function as it should.

As stated in various articles on d-ribose:

D-ribose, a building block of ATP, is a carbohydrate molecule found in every living organism, facilitates and assists in the synthesis of ATP. Ribose restores intracellular energy levels in the cardiac muscle tissue and helps maintain healthy heart function.

The primary source of energy for all cellular processes is a molecule known as ATP (adenosine triphosphate). Healthy, active cells constantly replenish their supply of ATP to produce vital cellular energy. However, under conditions of stress, injury, or aging, critical body tissues such as heart and skeletal muscles cannot produce ATP quickly enough to perform optimally.

Check out this link: <http://www.medicalpublications.org/dribose.htm>

Dr. Sinatra is fond of stating, "It's all about ATP"... and this important potassium post clearly emphasizes the need to make sure we have all the critical nutrients available for ATP production. Most importantly, evaluating our daily intake of sodium (salt) to prevent suppression of potassium, is the absolute key to optimal potassium levels.

Jackie

Thanks Erling and Jackie for answering my questions. Your follow-up posts are very informative. Does the following make sense? Given the likelihood of low magnesium in the onset of afib, if oral magnesium does not work why not go straight (without hesitation) to intra-muscular shots. Maybe one of the problems is that individuals are overwhelmed by the number of afib episodes they experience and thus, don't take the time to get those IC mag levels up. As both of you have pointed out for many of us afibbers, the RDA for minerals etc. are way below what is potentially therapeutic. In this regard, afib is the end of the line of some bad habits and one must attempt to eliminate it with a certain fearlessness, a willingness to supplement in a major way. As you said Jackie ATP levels are plummeting during constant episodes and fixing that problem may require 10-20 grams of ribose, 1500 of carnitine, 200 of CoQ10, 6-7000 mgs of Taurine, for me 4-600 mgs. of L-theanine has been a great help. Potassium is the only component part that one might have to hold back on. Our motto should be "find new limits!"

Steve

Steve - Yes, of course. Going right for IM injections of magnesium would be very useful. In one of the recent posts, Erling was enthusiastically encouraging that course of action; however, some individuals may find a problem with accessing a practitioner who is willing or qualified to provide that service.

As for the high-dose carnitine and from my own experience prior to ablation, I was unable to use any carnitine without provoking AF; post-ablation, no problem.... so just be aware that it may not be totally benign. I also don't think it's necessary to use the high dose taurine.

But... holding back on potassium may not be smart, especially if it means limiting food sources of potassium to manage a certain level... somehow a 4500mg figure keeps being mentioned. I have not read of any strict vegetarians 'overdosing' on potassium from food sources. As Erling referenced - the Paleolithic Era of eating estimates that potassium intakes are estimated in studies to be between 10,000 and 15,000 mg daily. But- once again, it's really that Na/K ratio that's critical.

When estimating food sources of potassium from various charts found online, just keep in mind that very often, those charts were done in the '40's and 50's and since then, the natural mineral content of soil has been depleted. Potassium, typically, is not added back into the soil by AgriBusiness. Therefore, using an online chart for nutrient content may be misleading and people thinking they are getting close to 4500 mg a day potassium from food may not be getting anything even close to that.

And the most important thing...which is the topic of this thread... is that potassium is easily overshadowed by sodium content when eating away from home, eating packaged or commercially prepared foods and by not reading labels of anything that is packaged and used in home cooking. Until afibbers deal with the Sodium/Potassium ratio, afib can persist.

Of course the key issue speaks to low IC magnesium and is supported by studies... ie, when IC magnesium is low,

potassium leaves the cell and cannot re-enter, which creates a risk of arrhythmia.
(This is covered and referenced in The Strategy)

Since Super Bowl Sunday's coming up, the stores are filled with snack items, so I decided to do some label reading of the types of foods offered for these parties. Absolutely astounding - the amounts of sodium found on labels - and; of course, items like chicken nuggets and wings didn't have labels to indicate sodium, but you can be sure they are also just loaded with salt and other chemicals.

Jackie

Jackie,

A bowl of soup and a ham sandwich is probably 1200-1500 mgs of sodium.
Yikes!

Steve

Yes - Yikes indeed! Impossible to maintain that important ratio if we ate like that all day, every day.

I'm always shocked at labels... I also checked a box of cereal... and snack crackers..... amazing amount of sodium/serving.

People are addicted to the taste of both salt and sugar, for sure.

Awareness is critically important if we expect to improve our AF odds.

Jackie

Hi Jackie –

Thanks for your good comments. This was an attempt to amplify the essence of your The Strategy - What Metabolic Cardiology Means to Afibbers - which assembles the wisdom of top scientist/physicians into an encompassing whole, namely the health and functioning of cells as relevant to heart rhythm. In the course of delving into facts and figures and images, I again became amazed and awed by the mystery of creation, of such wonders as the sodium-potassium pump – and the minds that can decipher it all – and then present it to us through their created internet phenomenon. And then to realize that not only Paleolithic kidneys, but brains too have not changed much since then
<http://www.afibbers.org/resources/strategy.pdf>

Thanks for highlighting to Steve the importance of ribose in generation of new ATP. You won't mind if I expand on that?- from your Strategy, Dr. Sinatra's book on Metabolic Cardiology, where Chapter 3 is devoted to ATP. Figure 3.1 diagrams its chemical structure: a ribose molecule as "backbone" joining the adenine molecule to three phosphate molecules (hence 'adenosine tri-phosphate'). The vast majority of ATP is recycled (in the mitochondria) from 'spent' ADP (adenosine di-phosphate) and does not require new ribose. But some ATP is always lost, requiring new ("de novo") synthesis of replacement ATP, the amount depending on many factors, such as level and duration of exertion/ATP expenditure, state of health of the mitochondria, etc. Further on, Table 3.3 shows the extremely slow rate of synthesis of new ATP, due to the very slow rate of internal synthesis of ribose. So, supplementary ribose markedly speeds the process of new ATP synthesis.

Erling

My hope is for good challenges to all this, to show flaws, or unsupportable 'leaps to conclusions' that are in there -- it's just a beginning for further clarification, I hope. And here is the most amazing thing I learned, in the paper from Colorado State University http://www.vivo.colostate.edu/hbooks/molecules/sodium_pump.html:

"Depending on cell type, there are between 800,000 and 30 million pumps on the surface of cells." That's per cell,

average ~10 million, maybe? What does that mean?

~10 million Na/K pumps per cell, multiplied by ~15 trillion cells (batteries) per body = ~150 quintillion (I looked it up) Na/K pumps per body -- spelled:

~150,000 Na/K pumps per body (is that right?). That's just a rough estimate, of course, so don't quote me.

Can we think of ourselves as vast collections of.... batteries with lots of built-in battery chargers?

Erling

Great posts!

Made me think about phosphates as in three of them to each adenine. Had a look at my Jan 10 Exa and noted that my phosphorus level was above range at 19.0 (range 14.2 to 17.0). leads me to wonder whether maybe my high phosphorus is because there aren't enough adenines around to mop them up as it were! probably over-simplified by me as usual, but just maybe worth a mention??

Maybe just as well I'm back on 15mg of Ribose per day again! (Since last week after reading threads here - I did use it for a few months a couple of years ago but let it lapse as I sometimes look at the raft of supps I take and wonder if I'm to some extent overdoing things and throwing my money away....)

Phase 0 is the rapid depolarization phase. The slope of phase 0 represents the maximum rate of depolarization of the cell and is known as dV/dt max. This phase is due to the opening of the fast Na^+ channels causing a rapid increase in the membrane conductance to Na^+ (G_{Na}) and thus a rapid influx of Na^+ ions (I_{Na}) into the cell - a Na^+ current. The ability of the cell to open the fast Na^+ channels during phase 0 is related to the membrane potential at the moment of excitation. If the membrane potential is at its baseline (about -85 mV), all the fast Na^+ channels are closed, and excitation will open them all, causing a large influx of Na^+ ions. If, however, the membrane potential is less negative [lower voltage], some of the fast Na^+ channels will be in an inactivated state, insensitive to opening, thus causing a lesser response to excitation of the cell membrane and a lower V_{max} . For this reason, if the resting membrane potential becomes too positive [lower voltage], the cell may not be excitable, and conduction through the heart may be delayed, increasing the risk for arrhythmias."

As someone for whom Flecainide works well (so far) both as small daily dose and larger PiP dose, and knowing that Flecainide is a class 1C anti-arrhythmic agent that acts by blocking the fast inward sodium channel during phase 0 of the action potential, I'm now figuring that Flec makes the membrane potential less negative and less excitable (to an ectopic focus?) with the lower V_{max} resulting in lower EF?? But then the lowered negativity of the membrane potential increases membrane potential positivity which delays conduction maybe leading to increased arrhythmia risk??!! What the Lord giveth, the Lord taketh away?! Or am I getting a totally wrong handle on all of this? ERLING?? (-;

(And that ignoring the fact that Flecainide not only blocks sodium, but also works on the ATP sensitive potassium channel (KATP channel) current AND also blocks potassium currents via the voltage-gated rapid delayed rectifying potassium channel (I-Kr) (eg see <http://www.ncbi.nlm.nih.gov/pubmed/8019764> which suggests that in rabbits Flec increased the mean open time of the inward rectifier potassium channel) AND blocks the extrusion of calcium ions (and I am high in Ca)!!)

Head cramp indeed! I wish I had more time free outside of work and family (and building a new house) to spend a good amount of hours trying to help everyone else here - and our wonderful Erling in particular - unravel all of this.....

Here's a bit of a head cramp on why Flec likely converts AF to NSR, but it doesn't - to me at least - explain how Flec keeps a lot of (usually vagal) folks out of AF in the first place:

<http://europace.oxfordjournals.org/content/early/2010/02/18/europace.euq011.full>

Right, back to the building site.....

Mike (brain-cramped and more than happy to be simply doing some first fix joinery!)

Hi Mike!

Many thanks for your comments. I'm delighted to know that you're building your house! That is my most enjoyable occupation. I wish you all possible delights and success!

Deciphering the description of the Cardiac Action Potential is almost comical http://en.wikipedia.org/wiki/Cardiac_action_potential. For awhile it seemed I'd followed Alice down the rabbit hole and nothing was as it seemed -- up was down, positive was negative... But I did finally get it straight -- I think. Your comment is classic: What the Lord giveth, the Lord taketh away?! Or am I getting a totally wrong handle on all of this?

I need to start at the beginning to see if I can even explain it clearly to myself. Looking at 'Phases of the cardiac action potential' graph about halfway down the page, it does not seem intuitively obvious that it is a graph of changes in a cell's voltage as time advances from left to right, for one complete pulse-beat. The 'action' begins at the bottom of the near-vertical phase 0 line, with the voltage decreasing (less negative) as the line rises from the phase 4 'resting membrane potential' negative voltage to a slight positive voltage at the top (phase1). Then the cell voltage increases (more negative) to (essentially) zero at phase 2 and the cells are discharged. This phase is the 'absolute refractory period' (ARP), when cells absolutely can't be excited to contract. As time advances down phase 3, the cells gradually recharge, ARP becomes ERP (effective refractory period) which terminates when cells are ~1/2 charged. At phase 4 cells are fully charged and resting, ready for the next 'action' at phase 0.

The steepness (slope) of the phase 0 line represents the rate of change of the voltage (dV/dt in math speak). The text explains that if the resting membrane voltage (phase 4) is lower (more positive) than is ideal, the phase 0 line will be less steep, making the phase 2 line shorter (shorter ARP). At http://en.wikipedia.org/wiki/Antiarrhythmic_agent, about halfway down, the ARP shortening effect of Class 1c antiarrhythmics is diagrammed. How can that be? We think that a shortened RP will *provoke* Afib. But lessened steepness also means slower depolarization (dV/dt). Might this account for flecainide's reported slowing of conduction velocity through the cells?

You say that flecainide "acts by blocking the fast inward sodium channel during phase 0 of the action potential", which is the same channel that is blocked (inhibited) by low 'resting membrane potential (phase 4) voltage. Does flecainide do this without affecting the voltage?

As an aside, I recall occasional Afib ECG's during my AF years ('95 - '02) where the rhythm printout said "low voltage". Nobody explained, and I didn't know enough to ask. That now seems significant. I'm hoping that someone will explain what 'low' means to an ECG computer?

I will study the article you linked to. Good luck with the construction!

Erling

Erling,

Great work.

I've not had time to study this with care as am busy with other, non-afib, projects. However I did spend some time with my 1993 version of Moore's book.

The participation of insulin in the sodium potassium relationship is worth exploring. One item of note is that increased insulin increases endogenous digitalis like substance (EDLS). EDLS inhibits the sodium potassium pump.

Also, insulin causes the kidney to retain Na.

Insulin also has effects on Ca and Mg in the cell.

Don't have time to work all this out, but it might be interesting to follow up on.

I've puzzled about why paleo diet can be effective for afib. There are several possible reasons - eliminating food additives, such as MSG; eliminating potential food allergens, such as gluten, gliadin and dairy; and lastly paleo diet can be ketogenic, depending upon how implemented or in any case reducing insulin spikes. This insulin reduction may lead to changes because of some of the properties listed above.

Regards,

George

Interesting, George... the insulin aspect. Initially, I felt the Paleo diet connection to success was the reduction of inflammation caused by grains... still do, but obviously, that may not be the only factor involved in why Paleo eating helps afibbers. This is an ongoing investigation so whatever you find as a contribution will be most welcome. Thanks!

Jackie

Thanks George!

And thanks for your good comments. Extending the understanding of the K/Na relationship effects will be important in furthering the understanding of AF causation. The contribution of insulin to this harmonizes with Dr. Rosedale's 'Insulin and Its Metabolic Effects' http://www.afibbers.net/forum/read.php?f=10&i=1&t=1#reply_1

PS. Regarding EDLS's, there's this interesting bit in 'The Salt Solution' (ref. 2 in the first post, p.13):

"What does your diet have to do with how well these little but ever-so-important Na/K pumps work? Plenty, as it turns out. As you'll recall, our bodies are designed to hang on to sodium, which was scarce in the prehistoric human diet. Thus, the Na/K pumps in your kidneys, which are somewhat different from your body's other Na/K pumps, have a special job: to save sodium that otherwise would be washed away in the urine by causing it to be transported back into the bloodstream.

Clearly, if you're eating too *much* salt [sodium], you don't want this to happen. Your problem is too much salt, not too little! So your body releases compounds, called natriuretic substances, or "ouabain", that slow down the Na/K pumps in your kidneys, allowing your kidneys to excrete more sodium into your urine. That's good in the short run because your body is getting rid of excess salt.

The problem is that if you continually overload your body with salt, these natriuretic substances begin to inhibit *all* of the Na/K pumps in your body, not just the pumps in your kidneys. So if you chronically eat too much salt, the natriuretic hormones your body secretes to defend itself against a sodium overload will chronically suppress the Na/K pumps in every cell of your body. This leads to an imbalance of potassium and sodium in every cell -- an imbalance that's much more extreme if there's too little potassium in your diet."

Erling

Hi Erling,

I haven't posted on afibbers for a while (started posting on this website in late 2002) Congratulations to you on your excellent research that I find very informative and interesting.

First a brief history-

I started with SVT attacks that eventually turned into LAF in late 1990's. 3 trips to the ER. Had only 5 afib attacks back

then but plagued by ectopics and SVT. I have now been afib free for 8 years. I did undergo an attempted ablation in 2003 but EP after inducing afib 4 times did not ablate because of "too many hotspots" (I think back then they lacked experience and confidence, especially in Australia). The only med I have taken is omeprazole (Losec) to reduce stomach acid because of reflux and loose LES. I was taking omeprazole daily for 9 years. I tried supplements but they all disagreed with me. I have never taken any antiarrhythmic heart meds.

In early 2005 I started eating natto food (the food and NOT the supplement nattokinase) on a regular basis no less than 4 times a week. I continued eating natto food religiously for the next five and half years. The natto food together with the omeprazole to reduce stomach acid and to let more of the *Bacillus Subtilis* bacteria in the natto food survive in the gut greatly reduced my ectopics and completely eliminated the SVT. The natto food also kept my blood pressure in the normal zone (its a natural ACE inhibitor) and I had a great feeling of calmness within myself for these five and half years.

In August 2009 I stopped eating natto food altogether as I was gradually losing my strength with also a small noticeable reduction in muscle mass. Even my family and friends made an occasional comment when I was lifting furniture etc. I put this lose of strength down to the phytoestrogens and particularly Genistein in the natto food. Six months later I also stopped taking the omeprazole as well. Since then my strength has returned to normal. I now take no drugs, supplements or eat natto food.

The most amazing thing is that for last 6 months all ectopics have disappeared. I can't even stimulate them with coffee, alcohol, exercising etc. So far, I have for all intents and purposes a normal heart again which brings me to the reason why I am posting under your subject heading.

Is the phytoestrogen and Tyrosine kinase inhibitor, Genistein, in the natto food the reason ? Has the Genistein altered the cardiac ion channels in my heart?

Quite a lot of research has been done by cardiac arrhythmia research institutions on Genistein and the way Genistein affects and alters the cardiac ion channels. The research has been aimed at finding a way Genistein can be used as a possible drug for cardiac arrhythmias. Most of this research has been on rats so I guess I have to be a human guinea pig after eating natto food loaded with Genistein for five and half years!

Erling, as this Genistein research is so technical and beyond me will you have a look at some of the research papers and comment in layman's terms what it means? I think you will find it very interesting with regards to your theory on potassium/sodium ratio and the effects Genistein may play. I have documented some research papers below

Thanks and Regards

Dean

Some of the research on Genistein:

This link below lists some broad topics on Genistein research:

<http://www.ionchannels.org/showcitationlist.php?keyword=genistein>

Direct block of voltage-sensitive sodium channels by genistein, a tyrosine kinase

C Paillart, E Carlier, D Guedin, B Dargent, F Couraud

<http://www.ionchannels.org/showabstract.php?pmid=9023259>

Genistein, an isoflavone inhibitor of tyrosine-specific protein kinases, was shown to specifically block the $^{22}\text{Na}^+$ influx through voltage-sensitive Na^+ channels in cultured rat brain neurons, whereas other tyrosine kinase antagonists such as lavendustin A, compound 5, tyrphostin A47 and an erbstatin analog were inactive at concentrations known to block kinase activity in other neuronal systems. Dose-response curves for genistein indicated a half-maximum effect at 60 μM . Daidzein, an inactive analog of genistein, had a similar inhibitory effect on the $^{22}\text{Na}^+$ influx with a half-

maximum effect at 195 microM. The time course of genistein action was rapid, because maximum effect on $^{22}\text{Na}^+$ influx was obtained in less than 20 s at 100 microM. Analysis of Na^+ currents by the whole-cell recording technique showed that 20 microM genistein reduced the sodium current and shifted the voltage dependence of both activation and inactivation curves. No competition with $[^3\text{H}]\text{saxitoxin}$ binding was observed, whereas the binding of $[^3\text{H}]\text{batrachotoxinin A 20-}\alpha\text{-benzoate}$ to rat brain synaptosomal membranes was partially inhibited, which suggested a direct or allosteric interaction with neurotoxin binding site 2. These data taken together clearly indicate that the inhibition of voltage-sensitive sodium channels by genistein is not mediated by tyrosine kinase inhibition.

Dietary soy exerts an antihypertensive effect in spontaneously hypertensive female rats

<http://ajpregu.physiology.org/content/281/2/R553.full>

There is a number of other potential mechanisms, which were beyond the scope of this study, that may contribute to the antihypertensive effect of soy isoflavones. Genistein may inhibit influx of calcium through voltage-gated calcium channels (1, 12, 15, 46). Genistein also reportedly enhances flux through calcium-activated potassium (47). Alternatively, genistein has been reported to increase renal excretion of sodium and water (14, 30) and also caused vasodilation in an isolated perfused kidney preparation (14, 30), suggesting that a diuretic effect may contribute to the long-term BP effects of soy isoflavones. Finally, considerable evidence supports the involvement of the renin-angiotensin system in the development and maintenance of high BP in several forms of hypertension. It has been reported that soy-derived foods contain angiotensin-converting enzyme inhibitory activity (25, 37,38). Thus there are several potential mechanisms that may underlie the antihypertensive effect of soy and that need to be addressed in future studies.

In summary, the present study demonstrated that dietary soy, producing plasma genistein concentrations in the micromolar range, reduced the development of hypertension in OVX SHR. This effect did not appear to involve the NO system but may be related to an effect on the autonomic nervous system.

Genistein increases the sensitivity of cardiac ion channels to beta-adrenergic

LC Hool, LM Middleton, RD Harvey

<http://www.ionchannels.org/showabstract.php?pmid=9670916>

The whole-cell patch-clamp technique was used to monitor the effects of genistein, a tyrosine kinase inhibitor, on membrane currents recorded from isolated guinea pig ventricular myocytes. Under control conditions, genistein (50 micromol/L) did not activate the latent cAMP-regulated Cl^- current (ICI). However, in the presence of a subthreshold concentration (1 nmol/L) of the beta-adrenergic agonist isoproterenol (Iso), genistein caused a near-maximal activation of this current. In the absence of genistein, Iso activated ICI with an EC_{50} of 5 nmol/L. In the presence of genistein, Iso activated ICI with an EC_{50} of 0.3 nmol/L. This facilitatory effect was not observed in the presence of daidzein (50 micromol/L), an analogue of genistein that only weakly inhibits tyrosine kinase activity. Furthermore, peroxovanadate, a potent inhibitor of phosphotyrosine phosphatase activity, inhibited ICI activated by Iso alone, and it blocked the stimulatory effect of genistein in the presence of Iso. To determine whether the stimulatory effect of genistein was specific for ICI, we also studied its action on the cAMP-regulated delayed rectifier K^+ current (IK) and L-type Ca^{2+} current (ICa-L) present in these cells. Basal IK and ICa-L were partially (approximately 30% to 40%) inhibited by genistein. However, this inhibitory effect was mimicked by daidzein, suggesting that inhibition of tyrosine kinase activity is not involved. In addition to the nonspecific inhibitory effect, genistein also caused a significant increase in the beta-adrenergic sensitivity of the unblocked cationic currents. In the absence of genistein, 1 nmol/L Iso had no effect on either IK or ICa-L. However, in the presence of genistein, 1 nmol/L Iso significantly increased the magnitude of both currents. These results suggest that tyrosine kinase activity may play an important role in regulating beta-adrenergic responsiveness of the heart

Genistein sensitivity of calcium transport pathways in serotonin-activated vascu

SR Nelson, T Chien, J Di Salvo

<http://www.ionchannels.org/showabstract.php?pmid=9281312>

Recent studies showed that serotonin-activated increases in intracellular Ca²⁺ in vascular smooth muscle cells are associated with enhanced protein tyrosine phosphorylation. These responses were blocked by inhibition of tyrosine kinase activity with genistein, suggesting that the increases in Ca²⁺ and tyrosine phosphorylation are functionally coupled. Therefore, we sought to characterize genistein-sensitive Ca²⁺ transport pathways in rat aortic A10 cells loaded with fura-2. In the presence of extracellular Ca²⁺, serotonin evoked a transient increase in [Ca²⁺]_i that was followed by a smaller sustained increase. The transient was inhibited 25-40% by L-type Ca²⁺ channel antagonists and inhibited 90-95% by genistein. The sustained response was unaffected by L-channel antagonists and only slightly inhibited by genistein. In the absence of extracellular Ca²⁺, the transient was reduced by 50%, while the sustained component was virtually abolished. These results suggest that influx and release pathways are major contributors to the transient component, whereas the lower sustained component is largely limited to influx pathways. The influx pathway during the transient probably involves an L-type Ca²⁺ channel that is regulated by tyrosine kinase activity. The pathways that participate in the sustained response are different because they are insensitive to L-channel antagonists and only slightly inhibited by genistein. The transient evoked in Ca²⁺-free media was blocked by genistein, inhibited by caffeine, and prevented by thapsigargin. Ionomycin-induced release of Ca²⁺ was unaffected by genistein, reduced by caffeine, and essentially eliminated by thapsigargin. Therefore, thapsigargin-mediated suppression of serotonin-activated release probably reflects depletion of Ca²⁺ from the sarcoplasmic reticulum, whereas genistein-mediated suppression probably reflects inhibition of tyrosine kinase linked release. Caffeine-mediated suppression appears to involve both partial depletion of Ca²⁺ and interference with release. Each A10 cell expressed at least two different ryanodine receptors and two different receptors for inositol 1,4,5-trisphosphate.

Dean:

Yes I recall reading your posts about eating natto---genistein is found in soybeans which people with thyroid problems are supposed to stay away from as it interferes with thyroid hormone uptake.

Liz

Hello Dean!

It's great to be 'speaking' with you again! Thanks for the really good news about freedom from arrhythmias at long last! -- also stomach and BP issues?

'Genistein' is a new word for me, and its effect on ion channels will be interesting and important to learn about. The cutting-edge ionchannels.org website will be a good place to focus this, so thanks for the briefs. Your highlights are helpful. At a quick look, the key subjects are at the core of this theory of arrhythmia causation -- "theory" because it is solidly based on facts, whereas "hypothesis" would imply educated guesswork. All that is needed is to tie the proven facts together, so this will be another step in that direction.

Take care, Dean, and stay in touch! This will be fun.

Erling

Hi Erling,

Its good to 'speak' to you again too and especially without the word "magnesium" taking over the conversation!!!! I'm sure you will have plenty of fun researching Genistein and ion channels.

Just remember that studying ion channels can bring on madness.....

I will be watching your research with great interest.

Dean

PS. The Japanese consumed 7.5 BILLION packets of natto food last year!

Hey Dean,

7.5 billion!! Just think: the "brilliant" military occupiers of Japan banned natto because to them it smelled bad...

Yes!- magnesium has taken its rightful place as background for all the rest - shhh...

As said to Mike, I'm down the rabbit hole with Alice here -- mad as he is, the Hatter seems kinda happy...

Being anchored on the cellular K/Na ratio, this theory develops on the facts of cellular voltage, the functioning of electrolyte channels, including voltage-dependent ion channels (VDICs), the effects of lower-than-ideal voltage being generated by the Na/K pumps on voltage changes vs. time during the 'cardiac action potential', and specific effects on electrolyte control.

It became clear that low-voltage inhibition of inward-flowing Na⁺ ion channels at the onset of depolarization (phase 0) can set the stage for arrhythmias by shortening the myocytes' refractory period (RP). Another thread presented information on the control of calcium release from the 'sarcoplasmic reticulum' (SR) in initiating depolarization. Voltage-dependent Na/Ca exchange pumps are involved.

The following post will provide links to useful background information.

Erling

Useful reference materials:

-- Donald M. Bers Ph.D. <http://www.ucdmc.ucdavis.edu/pharmacology/Faculty/bers/index.html>

"Dr. Bers research program focuses on cellular and molecular factors involved in the control of cardiac muscle contraction, particularly as modulated by intracellular calcium [Ca]. Cellular Ca regulates contraction and is in a dynamic, yet delicate balance in cardiac muscle cells.

Variations in this Ca balance are crucial to physiological and pharmacological mechanisms that increase cardiac contraction (i.e., with inotropic agents such as digitalis). Disturbance of this balance also can be responsible for pathological states (e.g. incomplete relaxation between beats and the generation of cardiac arrhythmias). Thus, detailed study of cellular Ca regulation is central to understanding cardiac muscle contraction.

At each beat, Ca enters the cell via Ca channels (ICa) and via Na/Ca exchange. Some of the Ca that enters the cell triggers the release of additional Ca from the sarcoplasmic reticulum (SR). Ca from these sources binds to the myofilaments (MF) activating contraction.

During relaxation, Ca is removed from the cytoplasm by: (1) the SR Ca-ATPase (pumping Ca back into the SR), (2) the sarcolemmal Na/Ca exchange, (3) the sarcolemmal Ca-ATPase pump (pumping Ca back out of the cell), and (4) transport into mitochondria (where it modifies ATP production). Donald Bers' research involves the cellular Ca that regulates contraction and is in a dynamic, yet delicate balance in cardiac muscle cells."

-- http://en.wikipedia.org/wiki/Voltage-dependent_calcium_channel (VDCCs). "In cardiac muscle, opening of the L-type calcium channel permits influx of calcium into the cell. The calcium binds to the calcium release channels (RYRs) in the SR, opening them; this phenomenon is called "calcium-induced calcium release," or CICR. However the RYRs are opened, either through mechanical-gating or CICR, Ca²⁺ is released from the SR and is able to bind to troponin C on the actin filaments. The muscles then contract through the sliding filament mechanism, causing shortening of sarcomeres and muscle contraction."

-- Dr. Richard D. Moore's website: http://www.thehbpsolution.com/Home_Page.html

-- 'The high Blood Pressure Solution' by Richard D. Moore, MD, PhD: http://www.amazon.com/High-Blood-Pressure-Solution-Scientifically/dp/0892819758/ref=sr_1_1?s=books&ie=UTF8&qid=1297740758&sr=1-1

-- 'The Salt Solution' http://www.amazon.com/Salt-Solution-Increase-Potassium-Dramatically/dp/1583330852/ref=sr_1_1?s=books&ie=UTF8&qid=1297738971&sr=1-1 "Some 50 million Americans suffer from high blood pressure, the leading cause of heart attacks and stroke. Our high salt diet is a major contributor to not only high blood pressure, but also a host of other life-threatening diseases, including osteoporosis and asthma. The simple program outlined in this book can help anyone reverse the ravages of salt addiction. The Sodium Solution offers convincing evidence that lowering salt intake and increasing potassium may be the key nutritional step one can take to protect health and reverse disease."

-- Richard Passwater, PhD: website and articles index: <http://www.drpasswater.com/>

Dr. Passwater's interviews with the authors of The salt Solution:

Herb Boynton: http://www.drpasswater.com/nutrition_library/potassium_sodium.html

Richard D. Moore, MD, PhD: http://www.drpasswater.com/nutrition_library/Potassium%20to%20Sodium_Ratio.html

Mark McCarty: http://www.drpasswater.com/nutrition_library/potassium-sodium4.html

-- 'Healing is Voltage' by Jerry Tennant, MD: http://www.amazon.com/Healing-Voltage-NDM-Jerry-Tennant/dp/1453649166/ref=pd_luc_sim_00_02_t_lh "Every cell in the body is designed to run at -20 to -25 millivolts. To heal, we must make new cells. To make a new cell requires -50 millivolts. Chronic disease occurs when voltage drops below -20 and/or you cannot achieve -50 millivolts to make new cells. Thus chronic disease is always defined by having low voltage. This book tells you how to measure your voltage in each organ, how to correct it, and how to determine why your voltage dropped enough to allow you to get sick."

-- 'The Body Electric' by Robert Becker and Gary Selden: http://www.amazon.com/Body-Electric-Electromagnetism-Foundation-Life/dp/0688069711/ref=sr_1_1?s=books&ie=UTF8&qid=1297735312&sr=1-1 "In this landmark book, Robert O. Becker, M.D., a pioneer in the field of bioelectric science, presents a fascinating look at the role electricity plays in healing, challenging the traditional mechanistic model of the body. Colorful and controversial, this is a tale of engrossing research, scientific and medical politics, and breakthrough discoveries that offer new possibilities for fighting disease and harnessing the body's healing powers."

-- The History of Atrial Fibrillation: The Last 100 Years: <http://www.medscape.com/viewarticle/578021> "Atrial fibrillation (AF) has had a rich history that has touched the careers of many of the great clinicians and investigators of the 20th century.... In a study by Yater[11] in 1929, 145 patients underwent autopsy. The most common etiologies of these patients with atrial fibrillation were chronic endocarditis (19%), exophthalmic goiter (25%), adenomatous goiter (19%), and hypertension (8%). Note that these etiologies from this early pathology study on atrial fibrillation are in marked contrast to the main cause of atrial fibrillation today, namely, hypertension. Yater further stated that no distinctive lesion for atrial fibrillation was found and that the lesions themselves were not considered of sufficient importance to explain the arrhythmia."

Magnesium. There, I said it! It must be mentioned because without magnesium, the Na/K pumps can't function properly, and then it's all downhill from there.

:) Jackie

Hi Erling,

As ever, I only seem to have time to glance through your posts and pick up on certain interesting - to me at least - bits

such as:

"Disturbance of this balance also can be responsible for pathological states (e.g. incomplete relaxation between beats and the generation of cardiac arrhythmias"

I seem to recall that my last Exa in Jan 2010 showed that my IC Ca was way over range (3.2 - 5.0) at 7.0. As such, I maybe shouldn't be so surprised that I get so much ectopy - especially combined with low IC Mg (30.7 as against range 34-41). Question is; how can I get my IC Ca down?? I don't consume ANY dairy at all.

And to confound it all; why does the sodium (inward) channel blocker Flecainide appear to work so well for me if on the face of it the problem IC-wise is too low Mg and too high Ca??!! Especially given that my IC Na was, in fact, below range (3.8 - 5.8) at 3.2!! Go figure indeed!! Thinks..... if Mg and Ca compete; then I've got the worst and most excitatory worlds with low IC Mg and high IC Ca. But Na and K-wise; I'm LOW in Na and spot on K-wise... mmmm.... that still doesn't help me see how Flecainide works well for me in both more or less keeping AF at bay as a daily med and at converting the occasional episode so quickly when I do get one..... I guess that the whole thing is so finely balanced and complex that my looking for simple answers as I do is just too plain simplistic and naive.

The only thing that WAS IN RANGE in my Exa was K at bang-middle of range. ALL of the aforementioned assuming, of course, that the Exa figures from Jan 2010 were accurate/reliable.....

Keep up the good work Erling (-:

Kind regards,

Mike

Hi Mike, thanks for your note!

Apologies for not having yet replied on the important flecainide puzzle that you presented - it has me stumped for now. Gradually other puzzle pieces are coming together, and that piece will no doubt fit in when there's sufficient clarity about the workings of the electrolyte channels.

I'm really pleased that you read the article on Dr. Donald Bers and his research. Copyright 2011, he's asking and answering the same questions. Actually we're ahead, because biophysicist Dr. Richard Moore tied high IC calcium back to low functioning of the Na/K pumps and consequent low cell membrane voltage, which is the focus here. Quoting from Dr. Moore's 2001 *The High Blood Pressure Solution*:

"Remember, the electrochemical potential [voltage] of the "sodium battery" [cell] comes from the stored energy of all that sodium pushed outside the cell by the Na/K pump, but "wanting" to come back in because of its natural electrical tendency. One type of calcium pump acts by letting some of the sodium back into the cell; the energy that is released thereby drives calcium out of the cell. This type of calcium pump is called a sodium-calcium (or Na⁺/Ca⁺⁺) exchanger."

"The dissolved calcium inside a healthy living cell should be kept more than 10,000 times lower than outside. Keeping the calcium low is especially important in a muscle cell, because even a small rise in the calcium inside will cause the muscle to contract." [think depolarize - phase 0 of the cardiac action potential]. Also: "...there are atom-sized holes in the cell membrane, through which calcium can leak [in]. But these holes close when the membrane voltage is high enough, that is, when the "sodium battery" [cell] is fully charged. When the membrane voltage is slightly discharged these holes open, letting in calcium... Moreover, a decreased level of Mg⁺⁺ inside cells may lead to a further decrease in the activity of the Na/K pumps, which will lower the charge on the [cell membrane voltage], leading to decreased activity of the Na/Ca exchange pump and thus compounding the problem."

"A diet with a low [K/Na ratio] should result in an increase in EDLS [endogenous digitalis-like substance] in the blood plasma. The... increase will decrease activity of the Na/K pumps... Inhibition of the Na/K pump by elevated EDLS and low serum K levels would increase the level of sodium within the cell and decrease the voltage across the cell membrane. ...as little as a 5% increase in sodium within the cell would be sufficient to elevate the level of calcium by at least 15% to 20%. ...the increase in calcium within the cell could possibly reach as much as 200%, although almost

certainly it would be somewhat less."

Some thoughts about IC magnesium: we want to know the mechanism by which Mg is brought into the cell against its "concentration gradient", which requires energy. A strong suspicion is that it is inhibited by low Na/K pump functioning, in which case "refractory Mg deficiency" might be shown to result from a low IC K/Na ratio.

Best wishes, Mike! We'll continue with this.

Erling

Thanks Erling (-:

Although I'm still stumped as to my own electrolyte profile as abovementioned ie below range IC Na, mid range K, way high Ca and low Mg. Only the mid-range K looks any good - the others are clearly a mess, and obviously explain my own arrhythmia issues. But what to do?? And why does Flec work when my IC Na is BELOW range to start with? And what do I do to try and lower the Ca?? I suppose I can just keep upping the Mg, but when I do that I get increased ectopy. I'm OK at 6-800mg/day of glycinate; but if I add WW, it seems to do more harm than good ectopy-wise. Added to which I have for the last few months - including now as I write - been plagued with on-and-off bigeminy between 6am and 10am. I tried a drink of K in juice at 5am this morning and no difference. Very confusing all around.... always way more questions than coherent answers... maybe some of us are just destined to be plagued by such problems whatever we do or don't do!

Kind regards,

Mike

Mike – have you tried assessing, on paper, the daily amount of sodium you take in? (compared to potassium intake...food and supplements)

As mentioned in one of the earlier posts, we can't discuss potassium without also considering sodium in the same breath. What the Exatest showed back then may be not be the same balance now.

What's finally sinking in for me by repeat reading of Moore's work (which Erling just reiterated in his latest post). Moore says it's a common mistake to think about dietary sodium or potassium separately since they are inextricably linked in a reciprocal manner.

Moore notes Drs. Dahl and Kempner working with hypertensive patients learned that the minimum requirement of sodium is probably not more than 100 – 300 milligrams. Moore allows a recommended 500 mg sodium as a minimum which is the same minimum daily intake recommended by the National Academy of Sciences. Yet, the FDA sets a "daily value" of 2500 mg which Moore thinks is much too high.

The average American consumes about 4000 mg of sodium daily. Moore points out that the US dietary sodium intake is probably at least 8 to 10 times what it should be because of commercially prepared and processed food.

By comparison, Moore says we eat only about 2500 mg potassium daily which is not much more than half of what we should consume. The National Academy of Sciences recommends a minimum daily intake of 2000 mg potassium and the FDA sets a daily value of potassium at 3500 mg. Moore states that "if a person has normal kidney function, up to 175 meq/day or 6800 mg/day of potassium has been reported as not being dangerous for an adult. Dr. David Young, Dept Physiology and Biophysics (U of Mississippi School of Medicine) has been a pioneer in studying the regulation of potassium within the body. Dr. Young reports that healthy adults consumed as much as 10,000 mg/day of potassium without ill effects.

The summary Dr. Moore offers is that "We are Way out of Balance... emphasis on "WAY"

Dietary sodium is too high. At the same time, potassium intake is too low and since it is the balance between the

sodium and potassium that counts...we are way out of whack.

He says, our present dietary potassium- to sodium ratio is only about 1:1.6 or about 0.6 and that of our ancestors was about 16 which means by comparison, we are out of balance by a factor of almost twenty-five fold.

Compared to the minimum K/Na ratio, four or five, required to guarantee good health, we are out of balance by about eight times. He says, "our bodies are simply not designed to withstand such an extreme dietary imbalance, especially when it is maintained over years and years."

"To achieve maximum prospects for health, most Americans have a long way to go: from an average dietary K/Na ratio of between 0.38 and 0.6 to a recommended value at least ten times that.

(Moore) Further advice:

Always increase dietary K/Na ratios slowly.

A body deficient in potassium takes more time to adapt to increased dietary potassium.

Paradoxically, the presence of potassium deficiency means that when your body needs it most, restoration of body potassium must be done even more slowly.

The presence of hypertension, diabetes, kidney disease and some drugs can slow the body's adaptation to increase dietary potassium. Under these circumstances, changes in potassium-to-sodium balance may require the advice of a physician.

Some salt substitutes are recommended.

Natural, unprocessed food is the best source of potassium.

Jackie

References

The Salt Solution
Boynton, McCartney, Moore
Penguin Putnam Inc
© 2001

The High Blood Pressure Solution
Richard D. Moore, MD, PhD
© 1993, 2001
Healing Arts Press

http://www.drpasswater.com/nutrition_library/Potassium%20to%20Sodium_Ratio.html

Thanks Jackie,

It's important that you emphasized magnesium's fundamental role at the center of synthesis and utilization of Mg-ATP fuel for the Na/K pumps. Magnesium's concentration in the cells is second only to that of potassium; both are pumped into the cell from the serum against a much higher internal concentration. Potassium is pumped in by the Mg-ATP dependent Na/K pumps, while magnesium is pumped in how?? It is clear that an IC deficiency of Mg inhibits functioning of the Na/K pumps, and as you say, then it's all downhill from there.

In the above reply to Mike, Dr. Moore explains the process by which IC calcium levels are controlled by voltage derived from the Na/K pumps, and how a lower voltage results in higher IC calcium. This is one way in which low IC magnesium will provoke cardiac dysrhythmia -- via inhibition of the Na/K pumps and lowering of voltage.

Erling

Effect of potassium-enriched salt on cardiovascular mortality and medical expenses of elderly men:

<http://www.ajcn.org/content/83/6/1289.full.pdf>

Dr. Moore's website: http://www.thehbpsolution.com/Home_Page.html

http://www.thehbpsolution.com/Potassium_and_Sodium.html

http://www.thehbpsolution.com/New_Developments.html

Mike,

I was looking in Moore's 1993 book last night. Like the Na/K cycle, there is one for Na/Ca. It was 5 minutes before bed, so not time to do detailed analysis.

Also, insulin plays a role, too. I also looked into the insulin, Na & Mg relationships as described by Rosedale <http://www.drrosedale.com/> in his book. Suggest you read Dr. Rosedale's book as well as Dr. Moore's most recent (2001) book. Another suggestion is to have your fasting insulin tested. Rosedale has a cutoff of 10 (don't remember the units). You can get a glucometer and see where the offending parts of your diet are. Important times to measure are 1) fasting and 2) 45 minutes after a particular meal. Glucose should be between 60-85 mg/dL (3.33-4.72 mmol/L) at all times. You obviously don't have to sample all the time, just as data gathering. Note what you ate and what the glucose reading is. Pretty soon, you'll know foods that spike your blood sugar. If you keep blood sugar low & even, insulin will be likewise.

I'm convinced that elevated insulin plays a significant role in all of this Na/K cellular chemistry.

Cheers,

George

From the journal Hypertension (1996):

Activation of the Sodium-Potassium Pump Contributes to Insulin-Induced Vasodilation in Humans

Cees J.J. Tack; Jos A. Lutterman; Gerald Vervoort; Theo Thien; Paul Smits

<http://hyper.ahajournals.org/cgi/content/full/28/3/426>

Erling

Food for thought:

P-207: Insulin regulates human erythrocyte Na⁺/Mg²⁺ exchange

<http://www.nature.com/ajh/journal/v15/n3s/abs/ajh2002497a.html>

"Therefore, we speculate that insulin's effect on Na/Mg exchange may in part explain the low cellular magnesium levels observed in vivo under hyperinsulinemic conditions."

<http://clinicaltrials.gov/ct2/show/NCT00549536>

"Increased levels of intracellular calcium are thought to diminish maximal cellular response to insulin and induce insulin resistance"

http://www.vivo.colostate.edu/hbooks/molecules/sodium_pump.html

"Insulin is a major regulator of potassium homeostasis and has multiple effects on sodium pump activity. Within minutes of elevated insulin secretion, pumps containing alpha-1 and 2 isoforms have increased affinity for sodium and increased turnover rate. Sustained elevations in insulin causes upregulation of alpha-2 synthesis. In skeletal muscle, insulin may also recruit pumps stored in the cytoplasm or activate latent pumps already present in the membrane."

<http://ndt.oxfordjournals.org/content/14/10/2357.abstract>

"Insulin induces sodium retention by increasing distal tubular sodium reabsorption."

<http://www.ncbi.nlm.nih.gov/pubmed/8498495>

"These data suggest that 1) high sodium intake may exacerbate insulin resistance by increasing circulating free fatty acids, and 2) differences in sodium intake may influence measures of insulin sensitivity in other disease states."

<http://ndt.oxfordjournals.org/content/10/8/1286.full.pdf>

"The ability of insulin to reduce urinary sodium excretion has been recognized for at least 40 years. Conversely, recent data suggest that a high sodium intake may exacerbate insulin resistance"

http://en.wikipedia.org/wiki/Sodium-calcium_exchanger

"The sodium-calcium exchanger (often denoted Na⁺/Ca²⁺ exchanger, NCX, or exchange protein) is an antiporter membrane protein that removes calcium from cells. It uses the energy that is stored in the electrochemical gradient of sodium (Na⁺) by allowing Na⁺ to flow down its gradient across the plasma membrane in exchange for the countertransport of calcium ions (Ca²⁺). The NCX removes a single calcium ion in exchange for the import of three sodium ions.[1] The exchanger exists in many different cell types and animal species.[2] The NCX is considered one of the most important cellular mechanisms for removing Ca²⁺.[2]"

George

I'm going to bring up magnesium again. In an all-day seminar in insulin resistance by Metagenics, the main takeaway was this:

Magnesium inside all cells is what allows all of the other functions, pumps and exchanges to work.

The main cause of insulin resistance comes from the fact that magnesium in the blood can't access the inside of the cell because the outerlayer of the cell membrane is damaged, distorted, stiffened or hard. This means the magnesium receptor sites in that outer layer are also damaged so magnesium can't get in. This occurred from diet... bad fats, trans fats, hydrogenated oils.

To rectify that, (besides changing dietary choices) large amounts 4 - 6 grams daily of a high-quality Omega 3 fish oil changes or normalizes the phospholipid layer of each and every cell... remember how many trillions we have... and when repaired, this outer layer that holds the receptor sites for every nutrient required by the body (it's not just magnesium) are once again fully functional. Insulin resistance becomes a thing of the past.

Following a diet as suggested in George's post to facilitate the reversal of insulin resistance is also important... but until the receptor sites are fully functional and magnesium has free access to inside the cells, not much is going to change.... but when it does, all the other exchanges can function as well.

It's well known that diabetics are magnesium deficient and insulin resistance is the precursor to diabetes.

Jackie

Hi Mike,

Don't give up! Things are clarifying, and the solution to your puzzle might be found within the big puzzle. I'm taking the liberty of re-posting your Exatest results, as they are relevant to this discussion. You'll recall that the reported ratios

were incorrectly calculated - the corrected ratios are in brackets. We'll have to assume that the reported individual levels and the reference ranges are valid. The potassium/sodium ratio is out of range high - is that perhaps significant? Please check to see that these numbers are correct.

Erling

Intracellular levels, mEq/L:

(reference ranges in parentheses)

MAGNESIUM:.. 30.7 (33.9 - 41.9)
CALCIUM:..... 7.0 (3.2 - 5.0)
POTASSIUM:.. 160.8 (80.0 - 240.0)
SODIUM:..... 3.6 (3.8 - 5.8)
CHLORIDE:..... 4.6 (3.4 - 6.0)
PHOSPHOROUS: 19.0 (14.2 - 17.0)

Intracellular elemental ratios:

(reference ranges in parentheses,
corrected ratios in brackets)

PHOSPHOROUS / CALCIUM:... 3.3 [2.7] (3.5 - 4.3)
MAGNESIUM / CALCIUM:..... 7.0 [4.4] (6.1 - 12.2)
MAGNESIUM / PHOSPHOROUS:.. 1.6 [1.6] (1.8 - 3.0)
POTASSIUM / CALCIUM:..... 16.1 [23.0] (19.1 - 38.0)
POTASSIUM / MAGNESIUM:... 4.5 [5.2] (2.4 - 4.8)
POTASSIUM / SODIUM:..... 33.5 [44.7] (19.4 - 38.9)

Erling, George & Jackie,

Many thanks for your posts.

George; my last fasting blood glucose was 4.9 so not too bad.

Erling; it is indeed interesting and confusing that my K:Na ratio is ABOVE range when the inward Na-blocking Flecainide works so well for me in preventing and terminating AF (daily and PiP respectively).

Anyway, I've just devised myself a new protocol in an effort to greatly simplify things supplement-wise, as I seem to have got to the point where I simply don't know whether I'm coming or going with it all what with adding more and more things and not really having much idea as to what is helping or hindering/being synergistic or otherwise. I also concur with the view that one really ought to try and get what one's body needs from good food rather than a bunch of tablets. So; I started today to simplify things as follows. 1 litre of WW with 750mg elemental Mg with 2 heaped teaspoons ribose added along with lemon juice to neutralise. LOTS of fruit and veg and minimal carb - just a handful of nuts and a few crackers if I get low! That's it really for now, so I'll see where I go from here.

I have this last 4-5 months been taking a raft of Hc-fighting supplements and just got a battery of bloodwork done the day before yesterday the results of which I should get back next week - will be interesting to see what my Hc level is now. AND what the rest of my bloodwork is like too. I'll post the results in due course.

Kind regards,

Mike

Jackie, and all -

This is apparently the current state in understanding Mg transport into cells:

<http://physiologyonline.physiology.org/content/23/5/275.full.pdf+html>

The Unique Nature of Mg²⁺ Channels

"Considering the biological abundance and importance of Mg²⁺, there is a surprising lack of information regarding the proteins that transport Mg²⁺, the mechanisms by which they do so, and their physiological roles within the cell...."

Journal PHYSIOLOGY 23: 275–285, 2008

Andrea S. Moomaw and Michael E. Maguire
Department of Pharmacology, School of Medicine,
Case Western Reserve University, Cleveland, Ohio

Erling

My wife is battling Rheumatoid Arthritis, we are trying to maximise her water retention in an effort to eliminate chronic dehydration as a possible cause.

As adequate salt intake is critical to retaining sufficient amounts of water, I have the following questions.

Is there a difference between common "table salt" and "sea salt" in the above processes? Does all salt have the same effect? Would changing the type of salt we consume help? Is the following information correct?

<http://www.livingwithrheumatoidarthritis.com/Table-Salt.html>

Today's table and cooking salts are void of vital trace minerals naturally occurring in salt.

Common table salt is poison that has nothing in common with natural salt. "Chemically cleaned" table salt is sodium chloride, an unnatural chemical form of salt that your body recognizes as something completely foreign. Dried at over 1,200 degrees Fahrenheit, the excessive heat alters the natural chemical structure of the salt.

Add to this the toxic additives used in table salt. Iodine and fluoride we have been convinced into believing are necessary to maintain health. Calcium carbonate, magnesium carbonate, and aluminum hydroxide are often added to improve the ability of table salt to pour. Aluminum in table salt is a light alloy that deposits into your brain, believed to be a potential cause of Alzheimer's disease.

Ingesting excessive amounts of sodium chloride in table salt can contribute to problems like cellulite build up, rheumatism, arthritis and gout, kidney and gall bladder stones.

Excessive salt intake has been shown to increase blood pressure, possibly leading to heart disease.

Replace with - Unrefined Celtic Sea Salt or Himalayan Salt.

A caution on the Celtic Sea Salt, recently as high as 89% of the producers of Celtic Sea Salt are utilizing refining techniques that lower the nutritional quality of the final product

Himalayan Salt has been shown to contain minerals and trace elements in colloidal form; meaning they are so small your cells can readily absorb them.

Himalayan Salt is mined by hand and hand-washed, avoiding the chemical transformation caused during processing. This product would be considered a healthy alternative to the chemically altered table salt.

Curt

Curt - I've read a lot of pros and cons about refined versus sea salt. The trace minerals that are touted, are really so minor, there's not that much value. If those minerals are found to be deficient, then supplementing with a mineral complex is a better way to go. A lot is just marketing hype.

But...There seems to be some truth to detrimental effect of the added chemicals in the refined so if the expense isn't an issue, then go for the Celtic salt...or similar. I did read it's not worth it to go for the very expensive types...just sea salt

or the Real Salt from the ancient sea beds in the Redmond, Utah mines.

In reality, any type of salt isn't going to do anyone any favors, so it's best not to load up on any salt for any reason.

On the RA problems, I'm sorry to read this. I have a good deal of experience with mis-treatment of RA with my mother. The one thing that is current and emphasized in Functional Medicine circles is that it's imperative to go completely gluten free...and probably dairy free as well.

As difficult as that seems, the results are remarkable. Anyone with elevated antibodies needs to be free of both gluten and dairy if they want to make progress.

Jackie

<http://cardiovascres.oxfordjournals.org/content/59/3/536.full.pdf+html>

Cardiovascular Research 59 (2003) 536–537

Does the Na,K pump current undergo remodeling in atrial fibrillation?

Edward Carmeliet

University of Leuven, Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium

"The sodium pump current has been the subject of many studies, but information on human cardiac tissue is lacking. This gap has been filled by a paper published in this issue in which Workman, Kane and Rankin [1] describe its maximum capacity, the sensitivity to [K⁺] in atrial cells from patients with and without chronic atrial fibrillation. The main conclusions are that the pump current contributes to the resting potential and the duration of the action potential."

[1] Workman AJ, Kane KA, Rankin AC. Characterisation of the Na,K pump current in atrial cells from patients with and without chronic atrial fibrillation. *Cardiovasc Res* 2003;59:593–602.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2639647/>

Heart Rhythm. 2008 June

Cellular bases for human atrial fibrillation

Antony J. Workman, Kathleen A. Kane, and Andrew C. Rankin

"Human atrial cellular refractory period is shortened in chronic AF, likely aiding reentry. The ionic and molecular mechanisms are not fully understood and may include increased inward rectifier K⁺ current and altered Ca²⁺ handling."

Erling

Thought I'd repost this here:

Self Testing Potassium

So, with the discussion of urine pH I've had with Lynn, came across a saliva test for potassium that correlates with serum.

<http://www.hkpp.org/general/cardyKmeter.html>

A Google search on Cardy Potassium Ion Meter shows them selling for about \$240 US.

http://www.hkpp.org/general/saliva_serum_chart.html

Thought this might be of interest.

<http://www.afibbers.net/forum/read.php?f=9&i=3289&t=3289>

George

Going along with George's post on pH... and from the book, "Alkalize or Die" (Baroody), he states something that goes along with Erling's Theory and discussion on voltage.

In part, Baroody says: "from the standpoint of pure energy, pH is the measurement of electrical resistance between negative and positive in the body and measures how much the negative ions (alkaline forming) and positive ions (acid forming) push against one another.

So from this viewpoint, acid and acid forming reactions are purely electro-chemical which means we are not just a conglomeration of chemicals, but are also an entire system of highly organized electrical reactions. We are vibrational beings. The stronger the inner vibration, the healthier we are. The amplitude of body electricity alters in exact proportion to the amount of alkaline and acid forming chemicals internally present at any one moment.

It is calculated by several authorities that a urine and saliva of 6.4 is best for human body function. However, it is very impractical for the average man to test his urine at frequent enough intervals in an ordinary work day."

He says test paper or sticks are too arbitrary and unpredictable and prefers using the values and scales for foods that automatically regulate pH levels over extended hours, days and weeks. (remember this is an old book).

Of interest to afibbers because of the gastric distress connection to afib, Baroody observes that digestive ailments can be the result of low potassium levels.

"Digestive ailments

Potassium chloride occurring naturally in the gastric cells of the stomach appears to be the major source of hydrochloric acid formation in the gastric juice. The lack of potassium signals a direct insufficiency of HCl formation with all its debilitating symptoms. Dr. Baroody finds great benefit to patients when he uses HCl therapy in his practice in the form of betaine HCl especially as it relates to correcting the alkaline/acid balance. He says: "Low HCl production and its resultant acid waste products lie at the core of poor health... proper alkalinity must be established if we are to survive." pp 35-36

He makes an interesting point about the need for adequate stomach acid (HCl) levels which serve to reduce tissue acid waste buildup. When HCl is balanced in the stomach, the alkaline hormone, secretin, causes the pancreas to produce large amounts of a highly concentrated bicarbonate fluid which is very alkaline forming. When HCl is low, the hormone cholecystokinin (CCK) – produced in the small intestine is low. CCK signals the gall bladder to release bile for dispersion of fat globules. Low HCl impairs bile output and interferes with the absorption of nutrients.

Of interest to us in our afib discussions is this causes imbalances in calcium, magnesium, sodium and potassium. Potassium is essential for regulating the heart beat and for the functioning of posterior spinal nerves.

So without adequate stomach acid to digest and utilize the alkalizing minerals, resultant acidic acid waste products will lie at the core of health problems.

A note of interest...Over-alkalinity, if it does occur, happens in the blood and not in tissues and he says: occurs when some form of hyperalkalizing poison like lye is taken. His opinion is that becoming too alkaline overall is one in one thousand.

As Emergency Support, he says Cream of Tartar is a source of natural potassium and it's highly alkalizing. Half a teaspoon can be used in emergencies to neutralize any acid reactions such as allergic response, panting, shortness of breath and anxiety attacks.

On drinking water, he notes that when artificial chemicals, fluoride and chlorine, are added to drinking water, both alter the pH of the water and create positive ion charge which is acid forming.

Source:

Alkalize or Die, Theodore Baroody, Ph.D. Nutrition, DC, ND, CNC, Dipl. Acu
Holographic Press, Waynesville, N.C.

© 1991

Jackie

This seems like an appropriate place to add to the previous post
"25 Key Benefits of Potassium" which was posted originally in Sept. of 2010.

http://www.afibbers.net/forum/read.php?f=8&i=25019&t=25019#reply_25019

Source Reference: "Everything You've Always Wanted to Know About Potassium ... but were too tired to ask" by Betty Kamen, PhD. © 1992

Following are a dozen or so more health benefits provided by potassium excerpted from Dr. Kamen's book. It's more than a bit frustrating to see the dates of these references and realize that some 20-30+ years later, afib patients are still not evaluated more extensively by means of understanding the basic and important role optimizing these key electrolytes as a first-line defense for treating AF.

Caution:

Be sure you understand why you can't just 'add' potassium supplements and expect a quick fix. Intracellular stores of magnesium must be optimal in order for the potassium to work well. Otherwise, adding supplemental potassium can make arrhythmia worse and potassium deficits may not resolve until magnesium deficiency is corrected. Increasing your intake of foods with a high-potassium content is a good start and is generally safe. Just don't over-do sweet fruit and juice as a quick fix since that's counterproductive.

Caveat:

People using potassium-sparing drugs for hypertension, should not use potassium supplements unless supervised by a physician.

Note that missing from the original "25 Benefits" post is the topic of hypertension. Since that's an extensive category and entire books are available discussing this Na/K ratio influence, then if looking for information on high blood pressure, then one cannot do better than the very valuable work by Richard D Moore. "The High Blood Pressure Solution" referenced in Erling's initial Theory post which is the first entry at the top of the page. Dr. Moore is not only an M.D, he's also a PhD biophysicist.

So let's start with an observation about hypertension. Keeping in mind that it's all about the ratio of Potassium to Sodium. So, when you think 'potassium,' you also have to think 'sodium' in the same breath. Optimize potassium; minimize sodium for proper function of the Na/K pumps that operate not only in heart cells but all cells throughout the entire body.

Dr. Kamen spends time discussing the importance of the sodium-potassium pumps, explaining that the Na/K pump facilitates the movement of calcium in and out of muscle cells. Not enough potassium or too much sodium means the cell membranes find it more difficult to remove calcium quickly. Rapid calcium removal from muscle cells induces these cells to relax. If there is too much cellular calcium:

- arterial muscles cannot fully relax
- the average artery size diminishes
- the heart has to work harder to move the same amount of blood
- arteries become less elastic causing turbulence in the blood flow which results in damage to cells lining the inner arterial walls

Thus – the basic relationship between low potassium and high blood pressure. Not enough potassium or too much sodium and the calcium levels in the muscle cells of arteries are likely to be too high. This raised blood pressure. [Too

much calcium inside heart cells can trigger AF.]
As Erling has repeatedly pointed out... this is all about voltage

26. An increased intake of potassium (without a change in dietary sodium) may reduce blood pressure, may suppress the activity of the sympathetic nervous and renin-angiotensin systems, and can prevent development of vascular injury; conversely, potassium depletion has been associated with an increase in stroke and sudden death.
American Journal of Cardiology, 1990, Mar 6 65((10)45E-51E; discussion 52E

27. Potassium deficiency may be as powerful a determinant of cardiovascular morbidity and mortality as sodium excess since potassium can modify both mechanical and electrical properties of the heart and exert diuretic effects. It has been shown to reduce the frequency and complexity of potentially lethal ventricular tachyarrhythmias. Given this central role, the effects can be enhanced or diminished by potassium homeostasis.
American Journal of Cardiology, March 1990, Ibid.

28. It is well known that potassium deficiency contributes significantly to arrhythmias associated with alcoholism.
Ettinger PO et al "Arrhythmias and the Holiday Heart; alcohol-associated cardiac rhythm disorders." Amer Heart Jnl, 1978, 95(5)555-62

29. The sensitive potassium channels play a role in determining coronary responses.
Komaru T et al. "Role of ATP-sensitive potassium channels in coronary microvascular autoregulatory responses. Circ Res. 1991, Oct 69(4):1146-51

30. One study demonstrates that arrhythmia susceptibility is reduced and onset delayed by raising the potassium concentration delivered to a certain coronary area.
Curtis MJ. "The rabbit dual coronary perfusion model: a new method for assessing the pathological relevance of individual products of the ischemic milieu: role of potassium in arrhythmogenesis."
Cardio Res. 1991 Dec, 25(12):1010-12.

31. Most arrhythmias result from malfunction of the sodium channels.
Grant AO Jr. "On the mechanism of action of antiarrhythmic agents." Amer Heart Jnl, 1991 Apr. 123(4 Pt2):1130-6.

32. Potassium-sparing drugs have successfully reduced arrhythmias
Archiv der Pharmazie, 1991 Nov 324(11):895—8.

33. Agents that modulate cardiac and smooth muscle potassium channels have stimulated considerable interest because of their therapeutic potential in a number of cardiovascular diseases. But many of these agents suffer from a side-effect that is directly linked to their specific mechanism of action.
Sanguinetti MC "Modulations of potassium channels by antiarrhythmic and antihypertensive drugs." Hypert, 1991 Mar 19(3):228-36.t

34. After correcting for potassium deficiency, alcoholic patients who have stopped drinking show complete recovery of neurological and neuropsychological function.
Journal Neurology, 1990

35. Dieting and reduced caloric intake decreases potassium levels and thereby glucose and insulin efficiency.
Potassium supplements allow for better insulin and glucose utilization.
Eur Jnl of Clin Invest, 1984

36. A low level of potassium is a predictor of arrhythmia.
Circulation 1985, 71(4):645--6

...

Many studies support or validate supplementation of potassium:
Hypertension, November 1991
Annals of Internal Medicine, No. 1991
Journal of Urology, Sept 1991
The Nutrition Report, August 1991

Post Graduate Medicine July 1991
Journal of Hypertension, May, 1991
Journal Amer College of Nutrition, Apr 1991
Journal Human Hypertension, April 1991
Journal Cardiovascular Pharmacology, Feb 1991
Journal of Hypertension, Feb 1991
American Jnal of Physiology, Jan 1991
Drugs, July 1990
Age and Aging, 1990
...just a few of many listed.

These were a few of the current study listings when Dr. Kamen's book was published nearly 20 years ago.

A current PubMed search for potassium supplementation hypertension/ humans yielded 264 hits.

Jackie

Found this 2004 post from Jackie when I was looking for something else. May be of interest here. Looks like we discussed this conference topic back in 2004? It's unbelievable how much stuff is on this website!!!! Some of the topics we now discuss like this one were discussed in depth years ago. So why have we not "cured" LAF???

Author: Jackie (---.73.203.135.Dial1.Chicago1.Level3.net)
Date: 03-10-04 17:11

Here's a book review by Mike Falcon highlighting the author's opinion on salt in the American diet....

I've not read the book but copied this for a friend interested in the salt problem. Jackie

A book review of The Salt Solution

Excess salt intake --- overwhelmingly common in the USA --- may be far more deadly than we thought. From Alzheimer's to asthma, kidney stones to stomach cancer, the effects of a high salt diet may contribute to a host of major diseases.

And not just for the elderly: the amount of sodium you take in as a young and middle-aged adult could impact high blood pressure --- known as hypertension --- and a number of other diseases throughout your life. It also appears to affect intelligence and memory. And the bad effects can begin very early: At least one major medical study revealed that babies provided a high salt diet had sustained high blood pressure throughout adolescence.

But there is an answer, says the physician and two bio-chemist-biophysics researchers who authored The Salt Solution, a new book that's bound to shake up salt and sodium myths we've lived with for decades. It involves both taking in less salt and more potassium. The two should exist in balance, but rarely do.

Why we crave salt

Our salt cravings "are formerly very efficient survival mechanisms that were essential in helping us take in sufficient sodium necessary for a variety of functions when salt was scarce," notes Dr. Richard Moore, Ph.D., a physician, researcher, and co-author of the book. "But because salt is readily available now, these mechanisms are now maladaptive --- they are not suited to a healthy lifestyle and long life."

Americans routinely take in 4000 milligrams of sodium as table salt each day, about 8 times the minimum daily requirement. At the same time, we ingest just 2500 milligrams of potassium, 1000 milligrams less than the government suggests.

The authors of The Salt Solution suggest both figures are far from optimal, and recommend a 4:1 potassium-to-salt ratio.

This chronic salt excess may have the effect of altering a critical action that takes place within every cell in the body. The balance between salt and potassium in cells is theoretically maintained by the sodium-potassium "pump," which attempts to keep a higher amount of needed potassium within cells and higher concentrations of sodium outside them, where the sodium can eventually be excreted.

This salt-potassium balance creates an electrical charge and balance at the cellular wall, necessary for healthy cellular metabolism. When the balance is chronically taxed by long-term high-salt intake the cell chemistry and the ability of cells to regulate the sodium-potassium balance may be severely compromised. As a result, cellular activity and disease resistance may plummet.

Elevating critical potassium

Bringing the potassium levels up helps enormously, but there are a few problems associated with elevated potassium intake. Changing the potassium intake alone and quickly does not let the cellular pumping action adapt. It can result in irregular heartbeats and even heart attacks, as well as altering calcium absorption.

Additionally, while most minerals can be found in highly concentrated forms, the Food and Drug Administration limits the per-table strength of non-prescription supplements to 99 milligrams of elemental potassium. It would take about 35 tabs a day to reach the suggested amount (the Salt Solution authors suggest 4500 milligrams as a better figure, making supplemental potassium intake even more difficult). This can be corrosive to your stomach lining. And never start potassium pill supplements if you are on high-blood pressure medication, congestive heart failure, or have kidney problems without consulting with your doctor.

Whole foods are a great base. A medium banana or a large apple contain about 500 milligrams of potassium, so eating one of each is a good start, especially since the potassium from whole food sources tends to absorb more evenly, slowly, and completely. Other good potassium sources include other fruits, many vegetables, and meats.

But some people will remain hypertensive and at risk even when they do decrease salt and increase potassium. They're called salt-resistant. One solution to this salt resistance is to take Omega-3 essential fatty oils, which usually come from fish.

You may have heard that low salt actually increases the risk of heart attacks. This was widely reported 2 years ago, but the study and this conclusion are seriously flawed. The study's self-reported low-salt users also reported caloric intakes of under 1000 a day, making this long-term self-reporting questionable, since these 1000-calorie folks weighed the same as the big caloric users. Additionally, when salt-to-calorie ratios were evaluated, it was the high-salt users who had more heart attacks.

Reducing salt painlessly

How can you get rid of salt? Easy. Here's a few starters:

- Watch for the big offenders.

75% of salt intake for most people comes from processed canned foods. In my kitchen cabinet is a major-brand can of canned green beans with 1700 milligrams of sodium. Next to it is a Ralph's "no added salt" can of spinach with 35 milligrams of sodium.

The worst offenders: movie popcorn, pickles, bacon and processed luncheon meats, French fries, salted nuts and potato chips. There are great variances in breakfast cereals and breads as well, so look at all labels closely.

- Order smart at restaurants.

Chicken stir fry with rice sounds healthy, but one serving has over 2300 milligrams of sodium. Restaurant soups are routine sodium disasters. Stick to salads and ask that no salt be added to your grilled meats.

- Try the great new salt substitutes.

A decade ago salt substitutes only looked like salt and tasted like hell. The new Solgar Heart Salt (in some places called Cardia Salt) has 54% less sodium and contains some potassium. Try other seasonings with disease-fighting phytonutrients such as dried onions, garlic, and peppers.

- Read the complete book.

The Salt Solution, complete with references, diet suggestions, and detailed explanations, could save your life.

The Salt Solution: A Complete 9-Step Program to Help Reduce Salt, Increase Potassium and Dramatically Reduce the Risk of Salt

by Herb Boynton, Mark F. McCarty, Richard D. Moore, MD, PhD

Dean

I must stress the following from my above post and the book "The salt solution" and a recent post by Gunnar in the current bulletin board about K possibly causing a death in certain circumstances. So there is obviously a WARNING about K supplementation. Supplementing K is not as safe as many on this board say it is?? Your thoughts please!

Elevating critical potassium

Bringing the potassium levels up helps enormously, but there are a few problems associated with elevated potassium intake.

Changing the potassium intake alone and quickly does not let the cellular pumping action adapt. It can result in irregular heartbeats and even heart attacks, as well as altering calcium absorption."

Author: Gunnar (---.12-2-64736c11.cust.bredbandsbolaget.se)

Date: 02-23-11 20:36

Tikosyn is a potassium blocker and very powerful. During your hospital stay the dosage was adjusted for the potassium level you had there and a prerequisite for treatment with Tikosyn is that the potassium concentration is within the normal range. **Taking supplements for potassium and thereby increasing the concentration of potassium outside the cells could be fatal, as you would change the balance of potassium inside and outside of the heart cells, which would increase the refractory period and prolong the QT, favouring a kind of ventricular tachycardia, called "torsades de pointes".**

<http://www.cvpharmacology.com/antiarrhy/potassium-blockers.htm>

Dean

Dean,

For now I have had to put aside your earlier query on genestein. My focus here is on the Na/K pump and its performance as central to regulation of the ion channels throughout the 'cardiac action potential', hence cardiac rhythm. In particular, we want to understand how various substances and factors influence the pumps performance -- genestein will undoubtedly find its place in this in due time. The hazardous aspect of potassium is well understood and is therefore a frequent topic on the bulletin board - you should consider re-posting there.

'The Salt Solution' was published in 2001, 'The High Blood Pressure Solution' in 1993 and 2001, all based on science solidly established in the '80s, so knowledge of the overall adverse health effects of an out-of-whack dietary K/Na ratio is nothing new. In the 2004 post Jackie disseminated the awareness to the forum via Mike Falcon's review of The Salt Solution. However, what is new is an understanding of the impact of the intracellular K/Na ratio on heart rhythm. We know, for instance, that lowered cell 'membrane potential', from a low IC K/Na ratio, will raise IC calcium, hence a propensity for arrhythmia. In a reply to Mike, above, is this quote from Dr. Moore:

"A diet with a low [K/Na ratio] should result in an increase in EDLS [endogenous digitalis-like substance] in the blood plasma. The... increase will decrease activity of the Na/K pumps... Inhibition of the Na/K pump by elevated EDLS and low serum K levels would increase the level of sodium within the cell and decrease the voltage across the cell membrane. ...as little as a 5% increase in sodium within the cell would be sufficient to elevate the level of calcium by at least 15% to 20%. ...the increase in calcium within the cell could possibly reach as much as 200%, although almost certainly it would be somewhat less."

Of particular importance to address is the complex influence of insulin on Na/K pump activity (George posted a number of relevant links that need to be followed). This 2004 study associated diabetes with AF and high BP: <http://www.ncbi.nlm.nih.gov/pubmed/15287930>. High BP is causally associated with a low IC K/Na ratio.

Atrial fibrillation and its association with type 2 diabetes and hypertension in a Swedish community

CONCLUSIONS: Atrial fibrillation is associated with the combined occurrence of type 2 diabetes and hypertension. Insulin resistance may be a common underlying mechanism.

Erling

Characterisation of the Na, K pump current in atrial cells from patients with and without chronic atrial fibrillation.

Workman AJ, Kane KA, Rankin AC.

Section of Cardiology, Division of Cardiovascular & Medical Sciences, University of Glasgow, Royal Infirmary, Glasgow, UK.

OBJECTIVE: To assess the contribution of the Na, K pump current ($I(p)$) to the action potential duration (APD) and effective refractory period (ERP) in human atrial cells, and to investigate whether $I(p)$ contributes to the changes in APD and ERP associated with chronic atrial fibrillation (AF).

CONCLUSIONS: The Na, K pump current contributes to the human atrial cell $V(m)$, action potential shape and ERP. However, the similarity in $I(p)$ sensitivity to both $[K(+)](o)$ and $V(m)$ between atrial cells from patients with and without chronic AF indicates that $I(p)$ is not involved in AF-induced electrophysiological remodelling in patients.

Full text: <http://eprints.gla.ac.uk/4904/1/4904.pdf>

Erling

Jackie,

Thank you for these posts and the many important references (30!).

The Na/K pump was discovered by biophysicist Jens C. Skou in the late '50's, for which he received the Nobel Prize in 1997: http://en.wikipedia.org/wiki/Jens_Christian_Skou. The fascinating thing is to be linking cardiac rhythm with the activity of the Na/K pump, largely via the science worked out by biophysicist Richard Moore and his colleagues in the '80's.

Erling

Hi Erling

I know you have a "heavy workload" at the moment and I don't want to sidetrack this very interesting conference topic but I do hope you find the time to research genistein in the future as besides its influence on ion channels here is another reason to investigate it:

Erling, you write above- "Of particular importance to address is the complex influence of insulin on Na/K pump activity."

<http://www.ncbi.nlm.nih.gov/pubmed/18661416>

"The study shows that genistein improves insulin sensitivity and kidney function in a dietary model of insulin resistance. We suggest that genistein may have benefits for patients suffering from kidney disease associated with insulin resistance."

Dean

You asked: So why have we not "cured" LAF???

My response would be: because we don't pay attention to the detrimental amount of sodium intake that offsets the benefits of potassium and when the voltage becomes low as a result, the refractory period will be shortened - thus inviting ectopy and AF.

Unless one is eating basically all whole, fresh foods and nothing packed/canned or commercially prepared, chances are, their ratio is skewed in favor of sodium or is, at least, a precarious ratio. Then, some people develop hypertension; others may be prone to arrhythmia.

The emphasis in food prep is taste... typically, we don't like things that are bland or tasteless and adding salt satisfies our craving for that "acquired" taste sensation. Food manufacturers contribute to that salt crave to make sure we keep buying more of their product. (and it works)

It would be unlikely that you could overdose on potassium-containing foods. Paleo man ate 10-15,000 mg a day. If you are on potassium-sparing medications, then supplementation should not be done w/o medical supervision. People with potassium wasting issues need special guidance. We're talking here about the majority of people who function normally but have symptoms as a result of too much sodium and far too little potassium to facilitate the normal Na/K pump operation and all that results downstream.

Torsade patients are typically found to be "profoundly hypomagnesemic, hypocalcemic and hypokalemic"..For treatment, they add both magnesium and potassium to normalize the long QT interval.

A separate discussion in another thread on the pharmacology and why Tikosyn patients must maintain optimal potassium levels would be important. If patients using Tikosyn are unable to maintain serum K levels, they are advised to add supplemental potassium as directed by their EPs.

We aren't attempting to give those directions here. This information is for the standard, generic afibber who is most likely low in both magnesium and potassium and has no subclinical kidney dysfunction. Overt kidney dysfunction is obvious; subclinical may not be and would tend to confound the results.

Jackie

Erling - Thanks for both new links... Great finds. As this unfolds, looks like much more reading and understanding to be done. I'll keep plugging away. Important stuff.

I realize my potassium info was from dated studies... I just included them to show this important info has been around a long time and yet we are still in major darkness when it comes to being treated as patients for these deficiencies of a very important mineral and more importantly, this critical ratio now brought to light thanks to Dr. Moore and others.

Onward---->

Jackie

Technically and historically complete, this is a great look into the process of scientific discovery:
http://nobelprize.org/nobel_prizes/chemistry/laureates/1997/skou-lecture.pdf

The Identification of the Sodium-Potassium Pump
Noble Lecture, December 8, 1997, by Jens C. Skou
Department of Biophysics, University of Aarhus, Denmark

Looking for the answer.

*You hunt it,
you catch it,
you fool yourself;
the answer,
is always,
one step ahead.*

Jens C. Skou

p. 14: "The transport system is a very efficient pump. It pumps 3 Na⁺ out of and 2 K⁺ into the cell for each ATP hydrolysed to ADP and Pi, and for this it uses 70% - 85% of the free energy of the hydrolysis of ATP. With the normal intra- and extracellular concentrations of Na⁺ and of K⁺, the activity of the pump is 10-15% of maximum, i.e. the pump has a considerable reserve capacity. At 37 degrees C, pH 7.4, the enzyme [pump] turns over at a rate of about 160 per second."

Erling

Hi Dean,

This, from your post:

"genistein improves insulin sensitivity and kidney function"

certainly links it to the current discussion with insulin's effect on Na⁺, K⁺, Mg⁺⁺ and Ca⁺⁺ metabolism, and vice versa.

George

Dean and George,

Given that insulin stimulates Na/K pump activity, and that genistein improves insulin sensitivity, does it follow that genistein stimulates Na/K pump activity? Certain renal functions are Na/K pump dependent - does this account for the kidney function improvement by genistein?

Certainly insulin sensitivity/ resistance plays a big role in heart rhythm/ arrhythmia. The links you provided should help clarify this - by raising even more questions.

Erling

=====
<http://physiologyonline.physiology.org/content/7/3/95.abstract>

The Na-K Pump J.C. Skou: "The Na-K pump operates by a stepwise change in Na⁺ versus K⁺ affinities and a gating reaction governed by the reaction with ATP. The activity is regulated by the intra- as well as the extracellular Na⁺-to-K⁺ concentration ratios and is stimulated by insulin and catecholamines."
=====

<http://hyper.ahajournals.org/cgi/content/full/28/3/426> From the journal Hypertension (1996):

Activation of the Sodium-Potassium Pump Contributes to Insulin-Induced Vasodilation in Humans

Cees J.J. Tack; Jos A. Lutterman; Gerald Vervoort; Theo Thien; Paul Smits

"In conclusion, we report that inhibition of Na⁺,K⁺-ATPase by ouabain largely inhibited in vivo insulin-induced vasodilation in humans, which suggests that activation of this enzyme must be involved in the effects of insulin on vascular tone. We hypothesize that insulin could activate Na⁺,K⁺-ATPase at the level of the endothelial cell, which implies that Na⁺,K⁺-ATPase activation will contribute to the endothelium-dependent vasodilator response to insulin. Clearly, the interaction between insulin and Na⁺,K⁺-ATPase should be investigated further at different cellular levels.

Na⁺-K⁺-ATPase and hormones.

<http://ajpcell.physiology.org/content/269/2/C295.full.pdf+html>

Perhaps less apparent is the major role that insulin plays in K⁺ homeostasis through regulation of Na⁺-K⁺ pump activity. This was one of the first reported effects of the hormone. Insulin promotes K⁺ uptake by muscle during the postprandial period simultaneous to its stimulation of glucose uptake. These actions have the purpose of clearing the sudden gain in K⁺ and glucose from the circulation and storing the ion and sugar in muscle tissue.

Insulin is a major anabolic hormone that plays a pivotal role in K⁺ homeostasis. A decrease in plasma K⁺ concentration is mentioned in the first reports of insulin effects on the whole organism.

George

Erling

<http://www.springerlink.com/content/3p73492300v13p76/>

Genistein inhibits voltage-gated sodium currents in SCG neurons through protein tyrosine kinase-dependent and kinase-independent mechanisms

These results suggest that genistein inhibits Na⁺ currents in rat SCG neurons through two distinct mechanisms: protein tyrosine kinase-independent, and protein tyrosine kinase-dependent mechanisms. Furthermore, the Src kinase family may be involved in the basal phosphorylation of the Na⁺ channel.

Erling, you have me at the extreme end of my understanding of all this stuff, I need another drink!. I hope you can make sense of this more than me. If genistein can inhibit Na currents then can it enhance the K in the Na/K pump?

Its voltage or lack of it in the Na/K pump you are looking at isn't it?

Dean

Overview of the pump:

http://www.vivo.colostate.edu/hbooks/molecules/sodium_pump.html

Regulation of Sodium Pump Expression and Activity

Expression of sodium pump activity is regulated at multiple levels and in both acute and chronic timeframes. A functional pump requires synthesis and assembly of both alpha and beta subunits. In many cells excessive beta subunits are produced, making synthesis of alpha the rate-limiting step in expression. It should come as no surprise that such controls are physiologically complex and involve the action of multiple hormones.

Rapid changes in pump activity appear to reflect modulations in kinetic properties, induced by a variety of intracellular signalling pathways. Phosphorylation of the alpha subunit enhances pump activity, presumably by increasing turnover rate or affinity for substrates. A number of hormones stimulate kinase or phosphatase activities within the cell that affect pump activity. Also, it appears that some cell types contain an intracellular pool of pumps that can be rapidly recruited to a functional state in the plasma membrane.

Chronic or sustained changes in pump activity within cells is usually due to increases in transcription rate or mRNA stability.

Major hormonal controls over pump activity can be summarized as follows:

* Thyroid hormones appear to be a major player in maintaining steady-state concentrations of pumps in most tissues.

This effect appears to result from stimulation of subunit gene transcription.

* Aldosterone is a steroid hormone with major effects on sodium homeostasis. It stimulates both rapid and sustained increases in pump numbers within several tissues. The sustained effect is due to enhanced transcription of the genes for both subunits.

* Catecholamines have varied effects, depending on the specific hormone and tissue. For example, dopamine inhibits Na⁺-K⁺-ATPase activity in kidney, while epinephrine stimulates pump activity in skeletal muscle. These effects seem to be mediated via phosphorylation or dephosphorylation of the pumps.

* Insulin is a major regulator of potassium homeostasis and has multiple effects on sodium pump activity. Within minutes of elevated insulin secretion, pumps containing alpha-1 and 2 isoforms have increased affinity for sodium and increased turnover rate. Sustained elevations in insulin causes upregulation of alpha-2 synthesis. In skeletal muscle, insulin may also recruit pumps stored in the cytoplasm or activate latent pumps already present in the membrane.

Pharmacology

The alpha subunit of the Na⁺-K⁺-ATPase is the receptor for cardiac glycosides such digitalis and ouabain. Different isoforms of the alpha subunit have different affinities for such glycosides. Binding of these widely-used drugs to sodium pumps specifically inhibits their activity.

Cardiac glycosides are widely used to increase the strength of contraction of the heart. Inhibition of sodium pump activity in cardiac myocytes results in an increase in intracellular sodium concentration. This leads to an increase in intracellular calcium concentration by sodium-calcium exchange, which appears to be the proximal mechanism for enhancing cardiac contractility.

The above link also has an animated cartoon of the Na⁺-K⁺-ATPase pump.

Sorry my link above requires registration & payment - it didn't the first time I accessed it. One could spend an eternity reading the Cell Physiology journals - real brain cramps!

Here is Dean's link live:

<http://www.springerlink.com/content/3p73492300v13p76/>

George

Brain cramps indeed! For a break I've temporarily moved over, or back to, looking at the parasympathetic neurotransmitter acetylcholine (ACh) and how its activity in "vagal mediated" AF might relate to this. A neuron's 'firing' is an 'action potential' http://en.wikipedia.org/wiki/Action_potential:

"The ionic currents of the action potential flow in response to concentration differences of the ions across the cell membrane. These concentration differences are established by ion pumps, which are integral membrane proteins that carry out active transport, i.e., use cellular energy (ATP) to "pump" the ions against their concentration gradient.[23] Such ion pumps take in ions from one side of the membrane (decreasing its concentration there) and release them on the other side (increasing its concentration there). The ion pump most relevant to the action potential is the sodium-potassium pump...."

Erling

Hi Erling,

What about having a Part Two for this topic. I think we have gone far enough with the brain cramps and scientific study of you theory which I must agree is pretty accurate and convincing for me but as often happens with these conference topics they get bogged down in brain cramps, stagnate and end up in Hans library for posterity.

In the paleo diet K was 4 to 1 in favour to Na.

But hey, we live in the real world and the majority of us have been brought up on a reverse diet of majority Na to K so

hence our problems etc.

So what do we do about it?

Jackie (or should I now say the newly reincarnated version of Fran?) has been advocating very spartan diet ideas about highly restrictive diets to bring the K back into dominance against Na but I say again, living in the real world this is highly impractical to the great majority of afibbers. I most certainly do not want to become a food "monk".

So if my diet is majority Na as against K and I am certainly not going to change my way of eating because I enjoy my diet and life at the moment what can I do to help the K/Na pump gain the upper hand in my diet?

- Can I alter my diet without going on an extreme monk like diet to gradually adjust the balance?
- Do I take supplements to adjust the balance?
- Can eating/supplementing genistein as we discussed help alter the balance with the K/Na pump voltage in our favour? (Jackie, please respond without prejudice to this as I know you are against phytoestrogens and soy)
- Any other ideas?

What do you think? A part two for this topic?

Dean

Hi Dean - I could never attempt to measure up to filling Fran's shoes so I'll decline on the reincarnation, but thanks.

As far as this thread reaching the end...far from it. There are so many facets of this aspect of what goes awry that it is only the beginning and to get it all down for examination is both important and necessary. When we reach what might be considered a reasonable 'conclusion' by examining all the facts, then a summary statement will be appropriate.

As for living in the "real world" and allowing that everyone chooses to eat in a carefree, careless fashion ... one only has to look at the rising prevalence of poor health, escalating dependency on drugs that don't work or cause more side effects...and earlier disabilities.

So, bottom line becomes.... either eat healthy and eat clean or live with the consequences. There is no free pass to eat junk or in a "modern" style that allows for whatever food manufacturers decide we should like and then hope to compensate by throwing in a vitamin or two to offset the damage. It doesn't work that way.

I'm sorry to be blunt and I'm not alone in this approach because anyone interested in sustaining health is on this bandwagon. This is really tough love. Suck it up and get the junk out of one's diet or suffer the consequences. No whining! Back to basics.

To answer your questions:

Q. So if my diet is majority Na as against K and I am certainly not going to change my way of eating because I enjoy my diet and life at the moment what can I do to help the K/Na pump gain the upper hand in my diet?

A. Since you enjoy your lifestyle, then I'd say enjoy life while you can. It may be shorter than you'd like and I certainly don't wish you any misfortune but your attitude is just not smart.

Q. • Can I alter my diet without going on an extreme monk like diet to gradually adjust the balance?

A. Of course... you can alter and adjust gradually... but that doesn't mean you can continue eating bad food. You have to eat whole, fresh foods and watch the sodium intake. Otherwise, what's the goal?

Q• Do I take supplements to adjust the balance?

A. Supplements do not substitute for a poor dietary intake of nutrients or offset junk food eating and poor lifestyle choices. Supplements enhance what might be missing because in some cases, it's difficult to get therapeutic doses of important nutrients solely from food.... ie, Coenzyme Q10 for instance. Magnesium is another...hard to get enough magnesium from food sources.

Q• Can eating/supplementing genistein as we discussed help alter the balance with the K/Na pump voltage in our favour? (Jackie, please respond without prejudice to this as I know you are against phytoestrogens and soy)

A. I have no knowledge of the action of genistein's influence on the Na/K pump action, but as I continue researching this project, I will keep that influence in mind to see if I can learn more. My bias on the soy issue comes from the Functional Medicine circles and from the book, *The Whole Soy Story - The Dark Side of America's Favorite Health Food* by Kaayla Daniel, PhD,.... about 450 pages, fully referenced. I'll check there to see if I can learn anything that may be useful for this discussion.

Q• Any other ideas?

A. Yes... rather than further divert or dilute this focus here in the CR, I'd suggest this topic be moved to the General Health Forum where it can receive more input since many readers don't visit the CR.

Fran was a stickler for pure, clean living and predictably, she not only cured her afib but also her seizures and probably other numerous ailments along the way. She was so inspired by her results, she's now in the process of becoming a naturopathic physician. She sets a wonderful, positive example for all of us to follow. She's certainly my heroine.

Jackie

Dean,

Your comments show that you have not understood this topic's purpose, which is to determine, to the extent possible, the totality of effects of intracellular and dietary K/Na ratios, specifically as it applies to AF. This ratio largely determines the cells' membrane voltage - and our hearts and bodies are indeed electric. This topic is based on the fact that atrial myocyte voltage directly influences the 'cardiac action potential', hence rhythm. You might start over by reading the opening post and its links. For example, in 'Paleolithic nutrition revisited':

<http://www.nature.com/ejcn/journal/v51/n4/pdf/1600389a.pdf> it is shown that our bodies and its systems of homeostasis have not changed significantly since paleolithic times, but for many of us "moderns" the dietary K/Na ratio is now upside down, with huge health consequences. You say: "In the paleo diet K was 4 to 1 in favour to Na." Table 4 shows that in the paleo diet the K/Na ratio was actually about 14/1.

Wishing you good reading.

Erling

George,

You may want to refresh your memory, as I did, with Pat Chamber's excellent article: "LAF vs AF - Shape matters". In it Pat goes into quite a few details about insulin and potassium.

<http://afibbers.org/resources/LAFvsAF.pdf>

Hans

George, I started using the Potassium Cardy Meter you talked about last week and from my initial test, it works fine. I had a lab test about a month ago with a reading of 4, since then I have continued to lower salt intake and added more K to my diet in addition to the supplements. The reading I obtained last night was 4.55 and that is where I want to be. I have noticed less ectopics at that level. Before I tested I did a little research on how to use it and found a site on Youtube where they show how to calibrate the meter and do the test, here they used blood instead of saliva because it gives a more accurate and consistent reading. Simple as a blood sugar test on the strips provided.

After spending \$4000 last year and almost the same amount the year prior, I felt that anything I could get to help me stay in NSR like supplements and a K tester are good investments now that I have had an ablation and it seems to be working at last. I will still get a routine blood test down the road so I know where all the levels are, but knowing what your Potassium level is in a few minutes is peace of mind. Thanks again for bringing the Cardy meter to our attention.

Tom C

Hans,

Thanks for the reminder! I'd forgotten the detail Pat went into on that paper.

One problem I have with the Insulin Sensitivity hypothesis is that I just don't see those people (who are abnormally sensitive to insulin) around me in my life.

My wife is 5'9" and 125 pounds. Clearly on the low end of BMI, WHR, WTR and WC. She also tends to be hypoglycemic. However, when I gave her a glucometer and had her test, her blood sugar would spike and then crater. We've mitigated this with alpha lipoic acid.

At the time of LAFS-11, my WHR, WTR and WC were all below the means of LAFer respondents. Glucometer testing showed poor response to glucose. This ultimately led me to experiment with a ketogenic diet. In this regime, I can keep my blood sugar "perfect" (in the 60-85 mmol/dL or 3.3-4.7 mg/dL) as long as I stick to the program. After 17 months on this program, my BMI is 23.5, WHR 0.85, WTR .45 and WC 32.5. However, if I cheat, I still spike the blood glucose. So all those anthropometric metrics don't correlate with insulin sensitivity, in my case.

I've had other non-diabetics test with a glucometer & even the thin ones all test like they are insulin insensitive.

I'd be willing to bet the ones with WHR, WTR and WC greater than the population means (which are many around me) are also insulin insensitive.

I'm not saying those people don't exist, just not in my life.

I've also not met many non-diabetics who've tracked their blood sugar with a glucometer. I have coached one friend who is trying to do a keto diet as a vegetarian. It is difficult for her, however she's dropped about 30 pounds on a 5'3" frame to a now BMI of 23.5 in the process.

So, I'm convinced that insulin is a big player in the electrolyte equation. I think the number who are insensitive is vastly greater than those who are too sensitive.

Cheers,
George

Tom,

Thanks for posting this. I look forward to ongoing reports. It will be interesting if others try this testing, too.

I wonder if reducing Na in the diet will increase serum K?

Could be answered with testing.

George

Since many of us take potassium supplements to help the K/Na Ratio, thought this might be of interest or at least tangentially related:

http://www.hkpp.org/physicians/b_12_pp.html

"Patients taking long-term K+ may need B-12 injections

Patients who take potassium supplements long-term, i.e., potassium chloride and potassium citrate, are at high risk for developing vitamin B-12 deficiency. Potassium supplements such as K-Dur, Micro-K, Slow-K, K-Lyte, etc. interfere with the absorption of vitamin B-12 and eventually lead to the depletion of body stores of this crucial vitamin. (1, 2, 3) "

George

George - this B12 issue with potassium probably relates to the form of potassium similar to some forms of magnesium being better absorbed than others. Since the Chloride versions can be highly irritating to the stomach and GI tract, this may be the key. B-12 formation depends on adequate HCl production and then, of course, some people are missing the intrinsic factor so that becomes another issue as well, although not as prevalent as low stomach acid. Perhaps the KCl versions compete/interfere with adequate stomach acid.

Dietary intake is the preferred source of potassium and is repeatedly stated throughout Moore and others on this topic. However, I've been supplementing modestly for a number of years and B12 and methylation typically tests out normal.

On the insulin sensitivity/resistance topic:

A clip from *The Salt Solution* by Moore:

When insulin resistance is present, it takes greater-than-normal levels of insulin to stimulate proper uptake of glucose from the blood. But the abnormally elevated blood insulin levels produce its own problems. These higher-than-normal insulin levels are known to be at least part of the cause of several abnormalities: high blood LDL cholesterol levels, low HDL cholesterol levels, development of abnormal (muscle-bound) structure of arterioles, and perhaps increased blood volume. Moreover, since insulin shifts calories into fat storage, elevated insulin levels are a large factor in causing and maintaining obesity. Of course severe insulin resistance leads to elevated blood glucose levels and is essentially the same thing as type II or non-insulin diabetes that becomes so common in people as they become older.

And, remember that the presence of "insulin resistance" apparently does not diminish the hormone's effect upon ion transport mechanisms such as the Na/K pump and sodium reabsorption by the kidney. To look at this in more detail, we have to consider the fact that elevated levels of insulin have specific effects upon body cells other than, and independent of, just stimulating glucose uptake." (pp 154-55)

Jackie

George - you said: I wonder if reducing Na in the diet will increase K...

If you check back to the many quotes Erling has provided, and the teeter-totter analogy, it will become clear that is exactly what happens and it won't happen any other way. If sodium does down, potassium goes up and the reverse. However, if potassium very low and sodium is very high, it will not be enough just to reduce sodium a little bit, obviously.

Erling posted in the AF forum about reducing sodium slowly over a period of time so one doesn't experience adverse "withdrawal" effects from lowering sodium.

Author: Erling (---.ptld.qwest.net)

Date: 03-07-11 12:43

Hi Justine,

It's all about our evolutionary past and how our kidneys were configured to hang on tight to what little sodium was available. Now that the problem is too much sodium, the kidneys have 'down-regulated' the activity (and numbers?) of their sodium-retaining Na/K pumps so that excessive sodium will be discharged into the urine. When switching to a low-sodium intake, it takes a while for the kidneys to 'up-regulate' to a sodium retaining mode. If one reduces sodium intake too quickly and radically, the result will logically be a temporary sodium deficiency. It's great that you proved this by adding back a bit of salt, thereby raising your (logically lowered) blood pressure just enough to take care of the light-headedness.

Recommended reading: *The Salt Solution* by Herb Boynton, Mark McCarty, Richard Moore MD, PhD. Here are some relevant quotes:

p. 89: "Remember the three lessons you've learned from this book. One is that cutting salt is important. The second is that increasing potassium is equally important. And the third is that cutting your salt intake to any significant degree, and increasing your potassium intake to any significant degree, will significantly improve your health.

"One important caution before you start: Don't change your potassium and salt intakes suddenly and drastically! Every cell in your body currently has adjusted to your usual intake of potassium and sodium, and an abrupt change in this ratio can overwhelm your body's adaptive ability to handle potassium [and less sodium].

"So start gradually. Take at least a week to decrease your salt consumption; then gradually increase your intake of potassium containing foods"

p. 13: "As you'll recall, our bodies are designed to hang on to sodium, which was scarce in the prehistoric human diet. Thus, the Na/K pumps in your kidneys, which are somewhat different from your body's other Na/K pumps, have a special job: to save sodium that otherwise would be washed away in the urine by causing it to be transported back into the bloodstream.

"Clearly, if you're eating too much salt [sodium], you don't want this to happen. Your problem is too much salt, not too little! So your body releases compounds, called natriuretic substances... that slow down the Na/K pumps in your kidneys, allowing your kidneys to excrete more sodium into your urine. That's good in the short run because your body is getting rid of excess salt.

"The problem is that if you continually overload your body with salt, these natriuretic substances begin to inhibit all of of the Na/K pumps in your body, not just the pumps in your kidneys. So if you chronically eat too much salt, the natriuretic hormones your body secretes to defend itself against a sodium overload will chronically suppress the Na/K pumps in every cell of your body. This leads to an imbalance of potassium and sodium in every cell -- an imbalance that's much more extreme if there's too little potassium in your diet."

Erling

Hi Jackie,

Thinking along the empirical testing line - Tom is using the Cardy Potassium Ion Meter to test his saliva & it can also test blood. <http://www.afibbers.net/forum/read.php?f=9&i=3693&t=3693>

Cardy also has other ion test meters - such as sodium. Other providers have testers for other ions. How about testing the saliva or serum (or urine) ratio of K+/Na+ directly. What else could be reasonably measured on an ongoing basis? What could be learned with intensive monitoring?

Lynn and now Mike are measuring urine and saliva pH <http://www.afibbers.net/forum/read.php?f=9&i=3500&t=3500>
The are both correlating pH patterns with their afib (Lynn) & ectopy (Mike).

It is very interesting when I measure something on an ongoing basis. This includes serum glucose and ectopics. At the very least, patterns normally develop.

George

George, Cardy meters are intended for agricultural testing as you know and some very bright person figured out you could test saliva or blood and made a chart to utilize these measurements. However I have not found an article yet on using a Cardy Sodium tester to measure human blood sodium levels. Having both measurements available with home testing would be ideal.

Tom C

Someone with a BioChem background could figure it out.
Molar mass of Na = 22.989770 g/mol

Cardy sodium meter

Measurement range: 23~2300ppm(10^{-3} ~ 10^{-1} mol/L)

from <http://www.envcoglobal.com/catalog/product/water-quality-pocket-meters/cardy-sodium-ion-meter.html>

Molar mass of K = 39.098 g/mol

Cardy potassium meter:

Measurement range: 339~3,900ppm(10^{-3} ~ 10^{-1} mol/L)

from <http://www.envcoglobal.com/catalog/product/water-quality-pocket-meters/cardy-potassium-ion-meter.html>

Conversion chart:

http://hkpp.org/general/saliva_serum_chart.html

In the chart, there is a constant relationship between saliva ppm and saliva mmol/l. saliva mmol/l =saliva ppm * 0.0625

The relationship between saliva mmol/l and serum mmol/l is:
serum mmol/l = 3 + (saliva mmol/l * 0.0625)

I'm not sure how to develop a relationship between saliva ppm and serum mmol/l for sodium. However, I believe you could get information just collecting the data together and correlating it with any adverse (or positive events). A Google search on

Salivary Sodium Potassium Ratio
turns up some interesting articles

<http://tinyurl.com/4s75vva>

The influence of moderate reduction in dietary sodium on human salivary sodium concentration

"Twenty-four healthy subjects were placed for 12–13 weeks on diets that reduced average sodium intake from 145 to 74 m-equiv. Na⁺/day as determined by multiple 24-h urine collections before and during the diet. Whole-mouth resting and stimulated saliva was collected and analysed for flow rate and sodium concentration several times before and during the low-sodium period. Sodium restriction did not influence salivary flow rates but salivary sodium levels fell 25 per cent for resting and 17 per cent for stimulated saliva. Thus moderate reductions in sodium intake are accompanied by significantly lower salivary sodium levels."

<http://www.nejm.org/action/showImage?doi=10.1056%2FNEJM196211292672207&iid=f001>

The Salivary Sodium-Potassium Ratio — A Useful Screening Test for Aldosteronism in Hypertensive Subjects

David P. Lauer, M.D.†, Roger B. Hickler, M.D.‡, and George W. Thorn, M.D.§

N Engl J Med 1962; 267:1136-1137 November 29, 1962

The high incidence of hypertension in cases of primary aldosteronism, the recent association of an elevated aldosterone secretory rate in malignant hypertension and the case reports of aldosteronism associated with unilateral renal arterial stenosis have all focused clinical attention on the functional status of the adrenal gland in hypertensive subjects. However, this investigative enthusiasm is often dampened by duration and cost of sodium-potassium metabolic-balance studies and limited availability of the determination of tritium-labeled aldosterone secretory rate....

http://www.salivalis.com/handlbody_E.htm

Saliva function laboratory manual

If I were to approach this, I'd just try to sample consistently and then correlate my data with AFIB outcomes.

George

George, thanks for the info., it does not seem that it would be that difficult to establish the parameters similar to the potassium ion test. I am going to try and contact someone at the Periodic Paralysis website, they should be interested in what we are discussing here, it would seem to tie in with their research.

Tom C

Another thought - reading some of the saliva articles, sodium concentration in saliva is related to flow rate. Serum testing might be a better answer.

George

All,

My suspicion has been that "vagally mediated AF" is initiated via acetylcholine inhibition of the Na/K pumps in atrial myocytes, thus reducing membrane potential, ultimately shortening the refractory period. Brain-cramping through "the literature" for understanding, this rough beginning is just that and needs much work:

-- "Carbachol is a parasympathomimetic that stimulates both muscarinic and nicotinic receptors."

<http://en.wikipedia.org/wiki/Carbachol>

-- "Cholinergic Inhibition of Na/K-ATPase via Activation of Protein Kinase C in Madin-Darby Canine Kidney Cells"

<http://jasn.asnjournals.org/content/4/2/195.full.pdf>

-- For background, an earlier BB thread: http://www.afibbers.net/forum/read.php?f=9&i=836&t=429#reply_836, which includes this from the University of Washington School of Medicine: "Acetylcholine as a Neurotransmitter"

<http://courses.washington.edu/chat543/cvans/sfp/acetylch.html>

-- This has a description of the neuro-muscular junction between vagus nerve axon and muscle cell membrane (sarcolemma): http://webanatomy.net/anatomy/muscle2_notes.htm

Erling

George, you provided some excellent information at <http://www.afibbers.net/forum/read.php?f=9&i=495&t=429&v=t>. Your logical conclusion re: anticholinergics in vagal AF: "So, if you keep the Mg and K up, you don't need to take the PB or another anticholinergic med."

With further understanding this should probably read: "... if you keep the Mg and K up, **and the Na down...**"?

Erling

The idea that 'vagal AF' is 'mediated' via acetylcholine inhibition of the Na/K pumps with consequent lowering of the atrial myocytes' membrane potential, thus shortening the ERP, gains credence with the following from the BB:

http://www.afibbers.net/forum/read.php?f=9&i=3853&t=3843#reply_3853.

By Hans (excerpt):

"The reason for the increase in heart rate after an ablation is that a significant portion of vagal nerve endings is damaged during the RF ablation procedure. Because the vagal nerves imbedded in the myocardium serve as *speed controllers* counteracting the adrenergic influence, a reduction in the number of effective vagal nerves would be expected to lead to an increased heart rate. Thus, it is possible that a more *aggressive* ablation, as indicated by a higher heart rate after the procedure, is more likely to be successful."

<http://europace.oxfordjournals.org/content/7/5/415.abstract>

Increased resting heart rate following radiofrequency catheter ablation for atrial fibrillation

Excerpt:

"PV isolation in patients with AF may result in increased HR, which positively correlated with the ablation success."

Erling

From the book Healing is Voltage by Jerry Tennant, MD: <http://www.tennantinstitute.com/>

Quotes, p. 39 and on:

The Chemistry vs. The Biophysics Paradigm

Myth: The human body is controlled primarily by chemistry.

Fact: The human body is controlled primarily by electronics (physics), not chemistry.

You will hear statements like "all disease occurs when you are acidic". What this is really saying is that all disease occurs when your voltages are low or in an electron-stealer state.

You will hear statements like "alkalize or die". What this means is that you must have electrons available to do work or your cells will die.

We heal primarily by making new cells. To make a new cell requires a voltage of ~ -50 mV.

[A chart follows correlating cell voltage from -50 to $+30$ mV with cell pH from 7.88 to 6.48. On this chart 20 to 25 mV equates to pH 7.35 to 7.44, this range being shown as 'Normal for adults']

Salivary and urinary pH are about 0.8 pH units less than the cell pH. Urinary pH is a rough indicator of the voltage in the fluid around cells. When normal, both should be 6.5. If you add 0.8 to 6.5 you get a pH of 7.3. This equates to -20 millivolts.

[Of course 'electrically excitable cells' such as neurons and cardiomyocytes have voltages that vary from their 'resting membrane potential' to zero throughout their 'action potential']

Thus we see that chronic disease is always defined by having low voltage. One cannot cure chronic disease without inserting enough electrons to achieve -50 mV.

p. 55: If your body has lower voltage than the earth, walking barefoot on the dirt or grass will cause electrons to flow from the earth into your body, recharging you.

Erling

Hi Erling,

Personal experiences:

I've been sleeping on a grounded sheet for about six months. I have experienced somewhat better sleep. As to heart rhythm, I've seen no difference in recorded ectopic counts/hour during sampling.

As to cellular voltage, I have no idea. However my urine consistently tests pH of 5.5 and saliva of 7.5 (could be higher as this is the limit of my pH paper). In The Jeremiah Metzger Lecture on Ketosis

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2441301/pdf/tacca00109-0225.pdf> the chart on p.9 (of the PDF) shows the changes of urine composition caused fasting (or perhaps ketosis in general). On p13 (of the PDF), bear hibernation is described. The hibernating bear exists in ketosis, also excreting little urine as nitrogen is conserved. I've experienced this, as in ketosis, I can exercise all day at 12,000' elevation, without drinking or urinating (or any adverse effects). Also, at the end of the day, when I do urinate, it is a pale yellow color, indicating no dehydration. (As an aside, I never have to wake up urinate at night eating this way)

I would suggest that urine pH is at least partially controlled by the relative proportion of the various constituents. My urination pattern would suggest I'm experiencing the conservation of nitrogen discussed. However, as ammonia has a basic pH and uric acid an acidic pH, and ketosis has relatively more ammonia than uric acid, I'd expect more of a basic pH. Urea has more of a neutral pH.

Cheers,

George

The following AHA article supports the theory that inhibition of the Na/K pumps is arrhythmogenic via slowing of the Na⁺/Ca⁺⁺ exchanger pumps in the cardiomyocyte membranes. See p. 64, Richard D. Moore, MD, PhD. The High Blood Pressure Solution (2001).

During my AF years occasional ECGs had "Low voltage" on the printout. Today it seems obvious that this low voltage was directly associated with the AF at that time, and was actually causative of the AF. It could be useful for this discussion to know what is a "low cardiac resting membrane potential". Texts generally seem to agree that 'normal' is on the order of ~-96 mV?

Erling

<http://circres.ahajournals.org/cgi/reprint/CIRCRESAHA.108.176677v1>

Circulation Research. Published online Jul 17, 2008

Burst Emergence of Intracellular Calcium Waves Evokes Arrhythmogenic Oscillatory Depolarization via the Na⁺-Ca²⁺ Exchanger. Simultaneous Confocal Recording of Membrane Potential and Intracellular Ca²⁺ in the Heart

Katsuji Fujiwara, Hideo Tanaka, Hiroki Mani, Takuo Nakagami, Tetsuro Takamatsu

Abstract

Intracellular Ca²⁺ waves (CaWs) of cardiomyocytes are spontaneous events of Ca²⁺ release from the sarcoplasmic reticulum (SR) that are regarded as an important substrate for triggered arrhythmias and delayed after-depolarizations. However, little is known regarding whether or how CaWs within the heart actually produce arrhythmogenic membrane oscillation because of the lack of data confirming direct correlation between CaWs and membrane potentials (V_m) in the heart. On the hypothesis that CaWs evoke arrhythmogenic oscillatory depolarization when they emerge synchronously and intensively in the heart, we conducted simultaneous fluorescence recording of intracellular Ca²⁺ ([Ca²⁺]_i) dynamics and V_m of ventricular myocytes on subepicardial surfaces of Langendorff-perfused rat hearts using in situ dual-view, rapid-scanning confocal microscopy. In intact hearts loaded with fluo4/acetoxymethyl ester and RH237 under perfusion with cytochalasin D at room temperature, individual myocytes exhibited Ca²⁺ transients and action potentials (APs) uniformly on ventricular excitation, whereas low-K⁺ -perfused (2.4 mmol/L) hearts exhibited CaWs sporadically between Ca²⁺ transients without discernible membrane depolarization. Further [Ca²⁺]_i loading of the heart, produced by rapid pacing and addition of isoproterenol, evoked triggered activity and subsequent oscillatory V_m, which are caused by burst emergence of CaWs in individual myocytes. Such arrhythmogenic membrane oscillation was abolished by ryanodine or the Na⁺-Ca²⁺ exchanger inhibitor SEA0400, indicating an essential role of CaWs and resultant Na⁺-Ca²⁺ exchanger-mediated depolarization in triggered activity. In summary, we demonstrate a mechanistic link between intracellular CaWs and arrhythmogenic oscillatory depolarizations in the heart. Our findings

provide a cellular perspective on abnormal $[Ca^{2+}]_i$ handling in the genesis of triggered arrhythmias in the heart.

Erling,

Here is an ECG I recorded in May 09 - no ectopics. 60 Seconds of data.

I used this device: <http://www2.vernier.com/booklets/ekg-bta.pdf>

Excel file: <http://dl.dropbox.com/u/4012052/ECG%20May%2009.xls>

This Excel file includes the mV data, sampled at 0.01 second intervals, and two graphs. The second shows 10 seconds of data, so you can see the QRS signature. The data are noisy as it was sampled while wearing a Polar heart rate monitor transmitter in addition to the ECG electrodes.

The Excel ECG looks a lot like the example graph in the manual.

If I remember, the sample was taken using a Lead II configuration.

Here is one more ECG data set, 10 seconds sampled at 0.005 second intervals.

It is less noisy, so may not have had the Polar transmitter on simultaneously.

<http://dl.dropbox.com/u/4012052/ECG%20Smooth%20May%2009.xls>

George

Low Voltage defined:

"Low voltage in the limb leads was defined as a QRS amplitude of < 5 mm in all limb leads, and low voltage in the precordial leads was defined as a QRS amplitude of < 10 mm in all precordial leads."

So it depends whether chest or limb placements are used for electrodes. As I recall, my data are from precordial placement (however I could be mistaken).

source: <http://chestjournal.chestpubs.org/content/124/6/2064.full>

Default scales: "The amplitude scale refers to standard ECG signals; the default scales (10 mm/mV and 25 mm/sec) "

source: <http://www.physionet.org/physiotools/wug/node54.htm>

http://www.gp-training.net/protocol/cardiovascular/ecg_reporting.htm#Voltage

Low Voltage

Diagnostic Criteria

* Voltage of entire QRS complex in all limb leads <5mm.

* Voltage of entire QRS complex in all precordial leads < 10mm.

* Either criteria may be met to qualify as "low voltage".

(again 10 mm = 1 mV - I checked a number of sites & this seems to be the standard.)

Differential Diagnosis

An increase in the distance between the heart and the ECG leads, infiltration of the heart muscle itself and metabolic abnormalities are all associated with low voltage.

1. Increased Distance
 - * Pericardial effusion
 - * Obesity
 - * COPD with hyperinflation
 - * Pleural effusion
 - * Constrictive pericarditis
2. Infiltrative Heart Disease
 - * Amyloidosis
 - * Scleroderma
 - * Hemochromatosis
3. Metabolic Abnormality
 - * Myxoedema

George

Thanks George - this is all very helpful. It is clear that the term "low voltage" is in reference to the QRS amplitude measured on the ECG, 1 cm = 1 mV, and is quantified as such. It is also clear that the term does not refer to the Phase 4 'resting membrane potential' (voltage), but perhaps that is inferred from the QRS amplitude? Obvious question: can low QRS voltage be the result of low Na/K pump performance?

The following are a few excerpts from your posts with my comments [in brackets]:

-- I used this device: <http://www2.vernier.com/booklets/ekg-bta.pdf>

[quote: "The inside of the cell is at a potential of about 90 millivolts (mV) less than the outside of the cell membrane. The 90 mV difference is called the resting potential." (Of course they mean 0.90 mV?)]

-- Excel file: <http://dl.dropbox.com/u/4012052/ECG%20May%202009.xls>

[My close look interpretation: the first QRS - .19 sec. to .23 sec. - amplitude 1.856 mV. The RMP appears to be ~ 1 mV]

-- Here is one more ECG data set, 10 seconds sampled at 0.005 second intervals.

<http://dl.dropbox.com/u/4012052/ECG%20Smooth%20May%202009.xls>

[Yes, the data and graph are quite clear and correlate as in the above]

-- Low Voltage defined:

"Low voltage in the limb leads was defined as a QRS amplitude of < 5 mm in all limb leads, and low voltage in the precordial leads was defined as a QRS amplitude of < 10 mm in all precordial leads."

[< 5 mm = < .5 mV. < 10mm = < 1 mV]

So it depends whether chest or limb placements are used for electrodes.

[Yes - that's clear]

-- source: <http://chestjournal.chestpubs.org/content/124/6/2064.full>

Default scales: "The amplitude scale refers to standard ECG signals; the default scales (10 mm/mV and 25 mm/sec) "

source: <http://www.physionet.org/physiotools/wug/node54.htm>

[This is clear]

=====

Ref. http://en.wikipedia.org/wiki/Cardiac_action_potential

The 'cardiac action potential' graph shows Phase 4 (resting membrane potential) to be -96 mV and Phase 1 to be +52 mV. Here again: these values are obviously lacking a decimal point and should be -0.96 mV and +0.52 mV respectively, making the Phase 4 - Phase 1 amplitude 1.48 mV, about 1 1/2 cm on the ECG (1 cm = 1 mV). (Or am I still confused?) See also <http://en.wikipedia.org/wiki/Electrocardiography>

Erling

Just for fun, and just kidding (I think):

<http://en.wikipedia.org/wiki/Electrocardiography>

"The first to systematically approach the heart from an electrical point-of-view was Augustus Waller, working in St Mary's Hospital in Paddington, London."

http://en.wikipedia.org/wiki/Augustus_Desir%C3%A9_Waller

Augustus Desiré Waller (18 July 1856 - 11 March 1922) was a British physiologist and the son of Augustus Volney Waller. He was born in Paris (France). He created the first practical ECG machine with surface electrodes

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC482113/?tool=pmcentrez>

Waller--pioneer of electrocardiography. British Heart Journal, 1979, 42, 61 – 64.

Erling,

Near as I can tell, the "cardiac action potential" refers to one cell. What the ECG measures is the average of action potential for all the heart cells. So I don't think there is a decimal point missing on membrane potentials.

So... "It is also clear that the term does not refer to the Phase 4 " (voltage), but perhaps that is inferred from the QRS amplitude?" I don't think so. A cellular membrane potential is not measured by the ECG.

Had to root around on this one. No reference uses a decimal point when referring to resting membrane potential.

George

George, thanks for this:

"Low voltage in the limb leads was defined as a QRS amplitude of < 5 mm in all limb leads, and low voltage in the precordial leads was defined as a QRS amplitude of < 10 mm in all precordial leads."

<http://chestjournal.chestpubs.org/content/124/6/2064.full>

However, the QRS amplitude is measured from the ECG 'baseline', which by definition is the Phase 4 voltage of the ventricular myocytes. This baseline is an extension of the 'isoelectric' T-P interval. See **Rational Choices in Antiarrhythmic Pharmacotherapy** http://www.turner-white.com/pdf/brm_Card_V10P1.pdf: "The resting membrane potential (Phase 4 of the action potential or the TP interval on the ECG)..."

That being the case, it seems that "low voltage", being defined as low QRS amplitude, also means low Phase 4 membrane voltage. (?)

Erling

http://library.med.utah.edu/kw/ecg/ecg_outline/Lesson3/index.html

" QRS Complex

The QRS represents the simultaneous activation of the right and left ventricles, although most of the QRS waveform is derived from the larger left ventricular musculature.

QRS duration < 0.10 sec

QRS amplitude is quite variable from lead to lead and from person to person. Two determinates of QRS voltages are:

Size of the ventricular chambers (i.e., the larger the chamber, the larger the voltage)

Proximity of chest electrodes to ventricular chamber (the closer, the larger the voltage) "

ECGs are measuring 3D spatial data in a 2D plane. The QRS amplitude will depend upon the orientation of the electrodes.

See: <http://bit.ly/hqep6e>

Different people can have different heart orientations.

George

Thanks George,

There are of course a multitude of variables in the QRS amplitude, so my statement "...low QRS amplitude, also means low Phase 4 membrane voltage" was 'off the wall' wrong (which I knew the moment I hit Post). However: baseline "Phase 4 membrane voltage" is one of the variables, but is apparently never considered or mentioned.

Related: A clue from my 1990 palpating cardiology work-up was "depressed ST segment" on the treadmill ECG. The cardiologist was concerned that it might reflect ischemia, but that was ruled out via a nuclear stress test. He apparently did not know that a lowered ST segment can be caused by low serum K (I learned that later), or he might have recommended K supplementation (see: Hypokalemia <http://www.sharinginhealth.ca/presentations/hypokalemia.html> - 'ECG changes' - 'depressed ST segment'). But surely it does not have to be outright 'hypokalemia' (<3.5 mEq/L) to depress the ST segment (voltage). And, my ST segment depressed voltage was likely not caused by low K per se, but rather by a combination with high Na. Not knowing any better, I had always been enjoying salty foods, while not paying any attention to the need for high K vegetables. Adding to that was Denver's (Colorado) low Mg/ high Ca tap water with its Na/K pump inhibiting fluorine. Full AF followed in '95.

It's always amazing to be reminded that this science had all been worked out and published by Dr. Seelig et al by the '80's, by biophysicist Dr. Moore and colleagues also in the '80's, published in '93 in The High Blood Pressure Solution and again in '01 along with The Salt Solution.

Erling

<http://www.ellenscorner.reocities.com/CapeCanaveral/lab/1141/papers/ajp99crn.pdf>

Am. J. Physiol. 275 (Heart Circ. Physiol. 44): H301-H321, 1998.

Ionic mechanisms underlying human atrial action potential properties: insights from a mathematical model

Marc Courtemanche, Rafael J. Ramirez, and Stanley Nattel
Research Center, Montreal Heart Institute, Montreal, Quebec

"The mechanisms underlying many important properties of the human atrial action potential (AP) are poorly understood. Using specific formulations of the K^+ , Na^+ , and Ca^{++} currents based on data recorded from human atrial myocytes, along with representations of pump, exchange, and background currents, we developed a mathematical model of the AP. The model AP resembles APs recorded from human atrial samples and responds to rate changes, L-type Ca^{++} current blockade, Na^+/Ca^{++} exchanger inhibition, and variations in transient outward current amplitude in a fashion similar to experimental recordings."

"Results: "The model has a stable resting potential near -81mV. All intracellular concentrations are stable at rest..."
"Figure 14 shows a model AP generated during stimulation..."

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<http://www.cvphysiology.com/Arrhythmias/A007.htm>

Cardiovascular Physiology Concepts - Richard E. Klabunde, Ph.D. <http://www.cvphysiology.com/>

"Note: An 18 minute mini-lecture on this topic can be viewed at the end of this page.

"The resting potential for a ventricular myocyte is about -90 mV, which is near the equilibrium potential for K^+ when extracellular K^+ concentration is 4 mM. Since the equilibrium potential for K^+ is -96 mV and the resting membrane potential is -90 mV, there is a net electrochemical driving force (difference between membrane potential and equilibrium potential) of 6 mV acting on the K^+ . The membrane potential is more positive than the equilibrium potential, therefore the net driving force is outward due to K^+ having a positive charge. Because the resting cell has a finite permeability to K^+ and the presence of a small net outward driving force acting upon K^+ , there is a slow outward leak of K^+ from the cell. If K^+ continued to leak out of the cell, its chemical gradient would be lost over time; however, a Na^+/K^+ -ATPase pump (<http://www.cvphysiology.com/Arrhythmias/A007b.htm>) brings the K^+ back into the cell and thereby maintains the K^+ chemical gradient."

<http://www.ncbi.nlm.nih.gov/pubmed/12034138>

Int J Dev Neurosci. 2002 Apr;20(2):77-81.

On the mechanism of the inhibition of Na/K-ATPase activity caused by homocysteine.

Streck EL, Zugno AI, Tagliari B, Sarkis JJ, Wajner M, Wannmacher CM, Wyse AT. Departamento de Bioquímica, ICBS, Universidade Federal do Rio Grande do Sul, Rua Ramiro Barcelos, 2600-Anexo, CEP, 90035-003 Porto Alegre, RS, Brazil.

"In the present work, we investigated the kinetics of the inhibition of Na/K-ATPase activity caused by homocysteine (Hcy)... It is proposed that the inhibition of Na/K-ATPase by Hcy may be one of the mechanisms related to the neuronal dysfunction observed in human homocystinuria."

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2203122/pdf/710.pdf>

The Mechanism of the Calorigenic Action of Thyroid Hormone. Stimulation of Na/K-ATPase activity

Faramarz Ismail-Beigi and Isidore S. Edelman. From the Cardiovascular Research Institute and the Departments of Medicine, and Biochemistry and Biophysics, University of California, San Francisco, California 94122

"...In this study, the effects of triiodothyronine (T3) on total oxygen consumption (QO₂), the ouabain-sensitive oxygen consumption [QO₂(t)], and NaK-ATPase in liver, kidney, and cerebrum were measured... These results indicate that thyroid hormones stimulate Na/K-ATPase activity."

<http://onlinelibrary.wiley.com/doi/10.1046/j.1432-1327.1999.00111.x/pdf>

Eur. J. Biochem. 260, 1±8 (1999) q FEBS 1999. Yvonne Shao, Thomas A. Pressley and Faramarz Ismail-Beigi. Department of Medicine, Case Western Reserve University, Cleveland, OH, USA; 2Department of Physiology, Texas Tech University, Lubbock, USA

Na,K-ATPase mRNA^{b1} expression in rat myocardium ± effect of thyroid status

"The abundance of Na,K-ATPase and its a and b subunit mRNAs is upregulated in cardiac and other target tissue by thyroid hormone (T3). Multiple Na,K-ATPase mRNA^{b1} species encoding an identical b1 polypeptide are expressed in the heart."

<http://www.ncbi.nlm.nih.gov/pubmed/8392583>

J Membr Biol. 1993 May;133(3):203-11. Wiener H, Nielsen JM, Klaerke DA, Jørgensen PL. August Krogh Institute, Copenhagen University, Denmark.

Aldosterone and thyroid hormone modulation of alpha 1-, beta 1-mRNA, and Na,K-pump sites in rabbit distal colon epithelium. Evidence for a novel mechanism of escape from the effect of hyperaldosteronemia

"Aldosterone and thyroid hormone regulation of Na,K-pump biosynthesis has been examined..." "... consistent with thyroid hormone having a permissive role for the aldosterone stimulation of Na,K-pump biosynthesis."

Homocysteine modulates sodium channel currents in human atrial myocytes

Toxicology Volume 256, Issue 3, 27 February 2009, Pages 201-206

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/19110030>

Full text:

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TCN-4V3545X-1&_user=10319418&_coverDate=02%2F27%2F2009&_rdoc=1&_fmt=high&_orig=gateway&_origin=gateway&_sort=d&_docanchor=&_view=c&_searchStrId=1697996557&_rerunOrigin=google&_acct=C000050221&_version=1&_urlVersion=0&_userid=10319418&md5=dda746c585ee33b71e0e4858d87cf847&searchtype=a

"Hyperhomocysteinemia has been proposed as an important risk factor for cardiac arrhythmias and ischemia worldwide... the resting membrane potential of human atrial myocytes was obviously depolarized by elevated homocysteine levels... Taken together, the data presented in this study first revealed that increased homocysteine levels caused the abnormality of sodium currents in human atrial cells by slowing the inactivation and promote the recovery of sodium channels, which provides a better understanding of hyperhomocysteinemia associated cardiac arrhythmias and ischemia."

Erling

Another plus for paleo, at least in some implementations- increased choline & lowered homocysteine:
<http://thepaleodiet.blogspot.com/2010/02/paleo-diet-q-homocysteine.html>

<http://lpi.oregonstate.edu/infocenter/othernuts/choline/>

A large body of research indicates that even moderately elevated levels of homocysteine in the blood increase the risk of cardiovascular diseases (5). For more information on homocysteine and cardiovascular diseases, see the article on Folic Acid. Choline, when oxidized in the body to form betaine, provides a methyl group for the conversion of homocysteine to methionine by the enzyme, betaine-homocysteine methyltransferase (BHMT). See diagram. Despite its relevance, the relationship of betaine and choline to homocysteine metabolism has been only lightly investigated in humans.

Homocysteine alters glutamate uptake and Na(+),K (+)-ATPase activity and oxidative status in rats hippocampus: protection by vitamin C.

<http://www.ncbi.nlm.nih.gov/pubmed/21287399>

Results showed that chronic hyperhomocysteinemia decreased glutamate uptake and the activities of Na(+),K(+)-ATPase, catalase and superoxide dismutase in hippocampus of rats. Reactive species levels were increased by chronic homocysteine administration. Concomitant administration of vitamin C significantly prevented these alterations caused by homocysteine.

Folate, B6 & B12 can lower homocysteine:

<http://www.ncbi.nlm.nih.gov/pubmed/21389855>

RESULTS: We found a significant increase in basal ($P<0.02$) and adenosine-induced ($P<0.05$) coronary blood flow in patients who received folic acid/vitamin B12 for 24 months, compared with placebo or vitamin B6 alone.

George

Returning to ATP (Na/K-ATPase) for a moment (and magnesium):

http://www.mpwhi.com/magnesium_for_life.pdf

“Of the 325 magnesium-dependent enzymes, the most important enzyme reaction involves the creation of energy by activating adenosine triphosphate (ATP), the fundamental energy storage molecule of the body.

Dr. Garry Gordon wrote, “If you have compromised cell membranes or low ATP production for any reason, then the cell has trouble maintaining the normal gradient. This is because the usual gradient is 10,000 times more calcium outside of cells than inside; when this is compromised you will have increased intracellular calcium, which seems to always happen at the time of death. Whenever intracellular calcium is elevated, you have a relative deficiency of magnesium, so whenever anyone is seriously ill, acute or chronic, part of your plan must be to restore magnesium.”

“Mg²⁺ is critical for all of the energetics of the cells because it is absolutely required that Mg²⁺ be bound (chelated) by ATP (adenosine triphosphate), the central high energy compound of the body. ATP without Mg²⁺ bound cannot create the energy normally used by specific enzymes of the body to make protein, DNA, RNA, transport sodium or potassium or calcium in and out of cells, nor to phosphorylate proteins in response to hormone signals, etc. In fact, ATP without enough Mg²⁺ is non-functional and leads to cell death. Bound Mg²⁺ holds the triphosphate in the correct stereochemical position so that it can interact with ATP using enzymes and the Mg²⁺ also polarizes the phosphate backbone so that the 'backside of the phosphorous' is more positive and susceptible to attack by nucleophilic agents such as hydroxide ion or other negatively charged compounds. Bottom line, Mg²⁺ at critical concentrations is essential to life,” says Dr. Boyd Haley who asserts strongly that, “All detoxification mechanisms have as the bases of the energy required to remove a toxicant the need for Mg-ATP to drive the process...”

Magnesium is a crucial factor in the natural self-cleansing and detoxification responses of the body. It stimulates the sodium potassium pump on the cell wall and this initiates the cleansing process in part because the sodium-potassium-ATPase pump regulates intracellular and extracellular potassium levels. Cell membranes contain a sodium/potassium

ATPase, a protein that uses the energy of ATP to pump sodium ions out of the cell, and potassium ions into the cell. The pump works all of the time, like a bilge pump in a leaky boat, pumping K⁺ and Na⁺ in and out, respectively. "ATP production is essential for every cell to have an ample supply to deal with the challenges of metal overload, as it is required to even permit the cell to keep on pumping out calcium. Lack of ATP then is the underlying cause of abnormal calcification of tissues," wrote Dr. Garry Gordon Potassium regulation is of course crucial because potassium acts as a counter flow for sodium's role in nerve transmission. The body must put a high priority on regulating the potassium of the blood serum and this becomes difficult when magnesium levels become deficient.

Glutathione synthetase requires B-glutamyl cysteine, glycine, ATP, and magnesium ions to form glutathione.

Magnesium and ATP "Mg²⁺ is critical for all of the energetics of the cells because it is absolutely required that Mg²⁺ be bound (chelated) by ATP (adenosine triphosphate), the central high energy compound of the body. ATP without Mg²⁺ bound cannot create the energy normally used by specific enzymes of the body to make protein, DNA, RNA, transport sodium or potassium or calcium in and out of cells, nor to phosphorylate proteins in response to hormone signals, etc. In fact, ATP without enough Mg²⁺ is non-functional and leads to cell death. Bound Mg²⁺ holds the triphosphate in the correct stereochemical position so that it can interact with ATP using enzymes and the Mg²⁺ also polarizes the phosphate backbone so that the 'backside of the phosphorous' is more positive and susceptible to attack by nucleophilic agents such as hydroxide ion or other negatively charged compounds. Bottom line, Mg²⁺ at critical concentrations is essential to life," says Dr. Boyd Haley who asserts strongly that, "All detoxification mechanisms have as the bases of the energy required to remove a toxicant the need for Mg-ATP to drive the process. There is nothing done in the body that does not use energy and without Mg²⁺ this energy can neither be made nor used."

Low levels of ATP have commonly been found in people with fibromyalgia, and it is believed that this plays an important role in many of the fibromyalgia symptoms. Thus, a magnesium deficiency would definitely be a factor in worsening those symptoms. Magnesium is extremely necessary for proper ATP synthesis, because ATP is stored in the body as a combination of magnesium and ATP, which is known as MgATP. ATP requires magnesium in order to be stable. Without magnesium, ATP would easily break down into other components, ADP and inorganic phosphate. The brain heavily relies ATP for many functions. In fact, 20% of total body ATP is located in the brain. Thus, low levels of ATP can diminish brain cognitive functions, a common problem in people with fibromyalgia.

George

Thanks George - Excellent find.

The last segment on low ATP and fibromyalgia.... this is why ribose is a miracle supplement for those with FM....he should have mentioned how ribose fits into this picture... and it's not just for those with FM.

Jackie

Interim summary:

1. The theory for the potassium/sodium ratio in AF is an extension of 'The Strategy - What Metabolic Cardiology Means to Afibbers' (<http://www.afibbers.org/resources/strategy.pdf>) and is based on electrical energy generated by ubiquitous Mg-ATP powered Na/K pumps continuously pumping three Na⁺ ions out of the cell in exchange for two K⁺ ions pumped in. This 3-to-2 separation of positive electrical charges provides the energy for energy-dependent cell functions. Na/K pump activity determines the membrane potential (voltage), and the cardiac action potential via regulation of electrolyte flux. The degree of Na/K pump activity is determined largely by the cellular K/Na ratio, which reflects the dietary ratio. A low cellular K/Na ratio results in lowered Na/K pump activity and reduced membrane voltage, which encourages AF by slowing the rate of depolarization, thus shortening the cells' refractory period. If membrane voltage becomes too low, the myocytes may not be excitable, and conduction through the heart may be delayed, increasing the risk for AF.

-- Biophysicist Richard D. Moore MD, PhD: Biophysics is that realm of science that looks at the living cell as a whole system. In so doing, biophysics takes into account not only the molecules of the cell, but also electrical forces and

fields and how these are all interrelated... Our new understanding of the living cell clearly shows that all variables (such as sodium, potassium, magnesium, and calcium) are interrelated. The living cell is a multivariable system - not a machine made up of discrete parts. Although it is almost never explained in textbooks, every living cell has its own electrical system. The living cell generates the electricity to charge its battery by a mechanism called the sodium-potassium pump... If the sodium-potassium pump is slowed, after awhile the concentration of sodium and potassium inside the cell will come closer to the concentrations outside, and the membrane voltage will become much smaller. (The High Blood Pressure Solution, 1993, 2001)

-- Biophysics researcher, orthopedic physician Robert O. Becker, MD: Most biochemists and doctors aren't much closer to the "truth" about life than we were three decades ago... Mechanistic chemistry isn't adequate to understand these enigmas of life... medical biology is afflicted with a kind of tunnel vision... Erwin Chargaff, biochemist, wrote of biology, "No other science deals in its very name with a subject that it cannot define." (The Body Electric - Electromagnetism and the Foundation of Life. 1985)

-- Biophysicist Jens C. Skou, MD, PhD: The gradients for Na⁺ into and K⁺ out of the cell sustained by the pump represent an energy source which is used for the creation of a membrane potential... the potential reaches a value of about 70 mV, at which point the rates of the two fluxes are equal, a steady state situation. (1997 Nobel Lecture http://nobelprize.org/nobel_prizes/chemistry/laureates/1997/skou-lecture.pdf) (Paul D. Boyer, John E. Walker, and Jens C. Skou shared the 1997 Nobel Prize in Chemistry for elucidation of the synthesis of ATP, and for identification of the enzyme Na,K-ATPase (Na/K pump). http://nobelprize.org/nobel_prizes/chemistry/laureates/1997/press.html)

-- Physician, biophysics researcher Jerry Tennant, MD:
Myth: The human body is controlled primarily by chemistry.
Fact: The human body is controlled primarily by electronics (physics), not chemistry.
Modern medicine assumes the body is Newtonian. Newton's laws work for large objects, but they do not work for atoms... You will hear statements like "all disease occurs when you are acidic"; what this is really saying is that all disease occurs when your voltage is low... Thus we see that chronic disease is always defined by having low voltage. (Healing is Voltage, 2010)

-- Cell biologist Bruce H. Lipton, PhD: ...even after the discoveries of quantum physics, biologists and medical students continued to be trained to view the body only as a physical machine that operates in accordance with Newtonian principles... the quantum perspective reveals that the universe is an integration of interdependent energy fields that are in a meshwork of interactions. Biomedical scientists have been particularly confounded because they often do not recognize the massive complexity of the intercommunication among the physical parts and the energy fields that make up the whole... Cellular constituents are woven into a complex web of crosstalk, feedback, and feedforward communication loops. A biological dysfunction may arise from a miscommunication among any of the routes of communication flow... The physical sciences have already embraced quantum physics with sensational results... It's been a long time coming, but the quantum biological revolution is nigh. The medical establishment will eventually be dragged, half kicking and screaming, full force into the quantum revolution. (The Biology of Belief, 2011)

2. Depending on cell type, there are between 800,000 and 30 million Na/K pumps in each cell. http://www.vivo.colostate.edu/hbooks/molecules/sodium_pump.html

-- thus there are many quintillion (10 to 18th power) Na/K pumps in the ~ 50 trillion cells of the human body.
-- "The Na/K pump turns over at a rate of about 160 per second." (Skou, the Nobel Lecture)

3. Optimal cellular K/Na ratio allows generation of optimal membrane voltage.

-- optimal cellular K/Na ratio reflects optimal dietary K/Na ratio.
-- optimal cellular Mg is required for optimal cellular K and K/Na ratio.
-- therefore, cellular Mg deficiency will cause cellular K and K/Na ratio to be less than optimal.
-- poor Mg absorption may cause cellular Mg deficiency.
-- Mg transporter channelopathy may be a cause of intracellular Mg deficiency.

4. Optimal membrane voltage is reflected in:

-- optimal functioning of voltage-gated electrolyte channels.
-- optimal cardiac action potential.

- optimal refractory period duration.
- optimal intracellular pH.
- optimal intracellular calcium.

5. Na/K pumps are powered by the energy molecule ATP complexed with magnesium (Mg-ATP).

- ATP is synthesized within the mitochondria (<http://en.wikipedia.org/wiki/Mitochondrion>)
- Synthesis of ATP requires oxygen, fatty acids, CoQ10, carnitine, ribose, Mg, numerous enzymes encoded in mitochondrial DNA and nuclear DNA, cofactor vitamins and minerals.
- Each cardiomyocyte may contain several thousand mitochondria.

6. Some factors/ substances that stimulate Na/K pump activity, optimizing membrane voltage:

- high cellular K/Na ratio, reflecting high dietary K/Na ratio.
- Mg-ATP sufficiency.
- insulin, e.g.: <http://hyper.ahajournals.org/cgi/content/full/28/3/426>, <http://hyper.ahajournals.org/cgi/content/full/28/3/426>
- T3 thyroid hormone.
- catecholamines (sympathetic NS).
- genistein, e.g.: <http://www.ncbi.nlm.nih.gov/pubmed/18661416>

7. Some factors/ substances that inhibit Na/K pump activity, thereby lowering membrane voltage:

- low cellular K/Na ratio, reflecting low dietary K/Na ratio.
- statin drug inhibition of CoQ10 synthesis.
- mitochondrial dysfunction/ reduced ATP synthesis.
- EDLS (endogenous digitalis, ouabain), digoxin, 'cardiac glycosides'.
- fluoride.
- homocysteine.
- acetylcholine (parasympathetic NS)
- genistein?

Cell biologist Bruce Lipton wrote: "Biomedical scientists have been particularly confounded because they often do not recognize the massive complexity of the intercommunication among the physical parts and the energy fields that make up the whole... Cellular constituents are woven into a complex web of crosstalk, feedback, and feedforward communication loops. A biological dysfunction may arise from a miscommunication among any of the routes of communication flow..."

The following article is "the state of the art" (as of 2000) in untangling the 'complex web' of regulation of various Na/K pump isoforms in various tissues. Parts of the web are shown in Tables 1 and 2 (pp. 13 and 15).
<http://ajpcell.physiology.org/content/279/3/C541.full.pdf+html>

Am J Physiol Cell Physiol 279: C541-C566, 2000.

Mechanisms of sodium pump regulation

Alex G. Therien and Rhoda Blostein
Department of Biochemistry, McGill University, Montreal, Quebec, Canada

Introductory paragraphs:

"The Na,K-ATPase, or sodium pump, is the membrane-bound enzyme that maintains the Na⁺ and K⁺ gradients across the plasma membrane of animal cells. Because of its importance in many basic and specialized cellular functions, this enzyme must be able to adapt to changing cellular and physiological stimuli. This review presents an overview of the many mechanisms in place to regulate sodium pump activity in a tissue-specific manner. These mechanisms include regulation by substrates, membrane-associated components such as cytoskeletal elements and the g-subunit, and circulating endogenous inhibitors as well as a variety of hormones, including corticosteroids, peptide hormones, and catecholamines. In addition, the review considers the effects of a range of specific intracellular signaling pathways

involved in the regulation of pump activity and subcellular distribution, with particular consideration given to the effects of protein kinases and phosphatases.

"In 1997, the Nobel Prize in Chemistry was shared by Danish researcher Jens C. Skou for his discovery of the Na,K-ATPase. Although the existence of an active 'sodium pump' had been previously hypothesized, Skou was the first to suggest, in 1957, a link between transport of Na⁺ and K⁺ across the plasma membrane and a Na⁺ and K⁺ activated ATPase activity (307). The significance of this discovery is underscored by the subsequent publication, each year, of scores of reports relevant to various aspects of Na,K-ATPase structure and function. Although much information about the enzyme has become available in the years since its discovery, one area of pump research that is not completely understood, despite recent advances, is that of pump regulation."

Erling

Hello Dean,

Sorry for being so slow! Two months ago (!) you posted the successful resolution to your long history of AF. I'm very happy for you! During this time I have honestly tried to get smart enough to help explain your good fortune, as you asked, but with no success so far. From your notes I constructed this timeline:

- Late 1990s SVTs became LAF.
- Start PPI 2001.
- AF free since 2003.
- 2003 attempted catheter ablation, but too many hot spots.
- Started Natto early 2004, which eliminated SVTs, reduced ectopics, normalized BP, but loss of strength/ muscle mass.
- Stopped Natto 8- 2009 (5 1/2 yrs. use)
- Stopped PPI 2-2010 (9 yrs. use). Strength now back to normal.
- No ectopics since 8-2010 - can't even be provoked.
- Heart now normal again (reported 2-2011).

Here are a few quotes from your post:

"The most amazing thing is that for the last 6 months all ectopics have disappeared. I can't even stimulate them with coffee, alcohol, exercising etc. So far, I have for all intents and purposes a normal heart again...

"Is the phytoestrogen and tyrosine kinase inhibitor, Genistein, in the natto food the reason? Has the Genistein altered the cardiac ion channels in my heart?"

"...this Genistein research is so technical and beyond me - will you have a look at some of the research papers and comment in layman's terms what it means?"

This is beyond me also. I've studied the research papers you referenced but became quite confused. For additional confusion I've read many other studies, such as this one showing genestein can be pro-arrhythmic:

<http://www.ncbi.nlm.nih.gov/pubmed/12145529>

Genistein inhibits the inward rectifying potassium current in guinea pig ventricular myocytes.

"We suggest that genistein directly blocks the inward rectifying K(+) current in ventricular myocytes, and one should be cautious of its pro-arrhythmic effect in clinical use."

Here again is the 2000 article highlighting the complexity of such issues, 'Mechanisms of sodium pump regulation': <http://ajpcell.physiology.org/content/279/3/C541.full.pdf+html>, wherein Tables 1 and 2 list 80+ studies on Na/K pump regulation by just two specific kinases, PKA and PKC. The References section lists 362 papers on Na/K pump regulation studies.

This is interesting. We should continue looking for an answer as soy/genistein consumption is prevalent. I wish you continued freedom!

Erling

A Hundred Years of Sodium Pumping

Ian M. Glynn, MD, PhD.
Professor of Physiology, Cambridge University, England
Annu. Rev. Physiol. 2002. 64:1–18

Abstract

This article gives a history of the evidence (a) that animal cell membranes contain pumps that expel sodium ions in exchange for potassium ions; (b) that the pump derives energy from the hydrolysis of ATP; (c) that it is thermodynamically reversible — artificially steep transmembrane ion gradients make it run backward synthesizing ATP from ADP and orthophosphate; (d) that its mechanism is a ping-pong one, in which phosphorylation of the pump by ATP is associated with an efflux of three sodium ions, and hydrolysis of the phosphoenzyme is associated with an influx of two potassium ions; (e) that each half of the working cycle involves both the transfer of a phosphate group and a conformational change — the phosphate transfer being associated with the occlusion of ions bound at one surface and the conformational change releasing the occluded ions at the opposite surface.

<http://einstein.ciencias.uchile.cl/Fisiologia2008/Lecturas/DWolff/100YearsSodiumPumpingARP2002.pdf>

Erling

More on the Cardy meter from the regular board:

Horiba potassium and sodium instruments

Author: Wil Schuemann

Date: 04-06-11 20:43

I purchased the Horiba C-131 potassium and C122 sodium instruments.

I was scheduled to have a basic metabolic blood test last week.

I got up at 0600.

At 0700 I obtained saliva readings of 5.3 mMol/L for potassium, and 200 ppm for sodium, from the Horiba instruments.

(I've not been able to find a correlation table to convert saliva sodium ppm to sodium blood plasma mMol/L)

The blood sample was taken at 0800. The results were 4.1 MEQ/L for potassium and 136 MEQ/L for sodium.

At 0900 I obtained saliva readings of 4.5 mMol/L for potassium and 93 ppm for sodium from the Horiba instruments.

Assuming the Horiba readings are meaningful, and the Horiba saliva potassium measurement changed linearly between 0700 and 0900; that would give a potassium value of 4.9 mMol/L from the Horiba, compared to 4.1 from the blood test.

Author: Tom C
Date: 04-07-11 05:02

Wil, the test is more accurate if you use blood instead of saliva, just use a diabetic lancing device. You then take the first reading you get when the measurement stabilizes, I wait about 8 seconds after the number stays the same. I noticed that it will continue to climb slowly but the initial level is the correct one. There are a couple of very informative videos on Youtube (CardyMeter) about how to calibrate and use the tester, it takes a few times to do it correctly. If you repeat the test and get close to the same result, that is most likely the correct reading. You could keep going back to the lab for tests to compare readings but that would defeat the purpose of why I bought the meter in the first place. I have noticed a direct correlation between the readings and adding more Potassium, or less Sodium to my diet. I have also noticed less ectopics now that I have increased my Potassium and decreased the salt.

I was going to purchase the Sodium meter, but as you said there is no conversion chart at this time that I have been able to locate, I am sure that a good biochemist could put one together or come up with the math formula in short order.

I also thought that those people who have Periodic Paralysis Syndrome who initially used the CardyMeter because Potassium levels are very important to control episodes, would be interested in our latest Conference Room topic on the correlation between Sodium and Potassium, but their forums aren't quite as accessible as this one. I again thank GeorgeN for informing us about the CardyMeter.

Author: GeorgeN
Date: 04-07-11 09:18

Tom and Wil,

I'm glad you two took my bait and purchased the Cardy meter(s).

I concur with Tom that direct blood testing is preferred over saliva. From what I've read, saliva concentrations can have an additional variable of flow rate. This can cause sodium concentrations to change.

Here is a post of mine in SESSION 72: Potassium/Sodium Ratio in Atrial Fibrillation (February 7 - February 28, 2011) <http://afibbers.org/conference/index.htm> (for future reference to get to the session when it has been closed) Here is the direct link:
http://www.afibbers.net/forum/read.php?f=5&i=923&t=844#reply_923

My approach would be to a) test blood for potassium (and sodium if I had both meters), b) correlate with intake of both potassium and sodium, c) correlate with afib and/or ectopic count outcomes.

I look forward to more reports!

George

Author: GeorgeN
Date: 04-07-11 19:43

My experience with a diabetic lancing device is you don't need to lance the pad of your finger. Along the side of the finger works just fine.

Also wonder if magnesium intake will have an effect on serum potassium, I suppose I should get a meter and find out.

George

Author: GeorgeN
Date: 04-08-11 07:22

Manuals for these products:
<http://www.specmeters.com/pdf/2400%20CARDY%20K%20Meter.pdf>
<http://www.specmeters.com/pdf/2500%20CARDY%20Na%20Meter.pdf>

Youtube calibration video: <http://www.youtube.com/watch?v=S-roOpSTC0>
blood test video <http://www.youtube.com/watch?v=jB3pJCFRiI8&feature=related>

I wonder if the Periodic Paralysis Syndrome people are aware of the need to have magnesium at a sufficient level for the potassium to be effective?

George

Author: Jackie
Date: 04-08-11 11:23

George - Good point about the low magnesium factor. So few are aware that potassium can't function without optimal IC magnesium. Even in the hospital when serum K shows up as low, they often just give potassium rather than a 'cocktail' that addresses the whole functional approach.

Jackie

Author: Tom C
Date: 04-10-11 06:04

It took 5 months for my ablation to kick in and no more afib, and after finally getting off the meds I felt good about my progress but I was still dealing with ectopics (occasional missed beats). I have been supplementing with the Mag., Potassium and Taurine and a few other vitamins and have been working out again to reduce blood pressure and post ablation heart rate. But right about the time the first threads were started in the latest conference room about the Sodium, Pot. connection I started to really look at my Sodium intake. To have total control I stopped all eating at restaurants and started preparing every meal myself. I scrutinized every label and started to see that you did not have to give up on your favorite foods, you just had to prepare them yourself with the reduced salt alternative, for example: there is regular canned corn with 250 mg. of Sodium and there is "natural" corn in a national brand for a few cents more with 15 mg. the taste was about the same, you have to understand that a lot of products have added salt for a longer shelf life and the general population is so salted up that it takes more Sodium to make it noticeable. When you reduce your salt for a period of time you will really notice the salt content of foods simply by taste, you will be much more sensitive to its flavor. There are low salt breads, tomato based products are loaded with salt, even your basic ones, however you can find low salt alternatives if you look at labels, initially this takes a lot of time standing around the aisles in a grocery store just staring at labels, you will be shocked at the amount of salt listed, going to a store with a good selection is the key here. Then you have to learn how to cook in low salt mode. After awhile it really wasn't that hard when you know what products to buy and get used to the recipes. After a few weeks of this diet I noticed my missed beats reducing and now they are gone. I also bought a Cardymeter to test my own blood for Potassium and that has been a real help as well. I recently left the country for a week of vacation and had to eat restaurant food for a short time, I took extra Potassium to counteract the salt however I did notice a few missed beats and when I got home my Pot. reading was lower. It took a week or so to get back on my usual diet and the ectopics are gone again.

I tested my blood levels for Pot., Sodium etc. when I stopped my post ablation meds. and they were all normal in the mid range of the scale but I was still having ectopics, that is why when you are prone to afib you have to test on the higher range of normal for Potassium and the lower range of Sodium to stay out of trouble.

A 2007 report on stroke prevention, offered a segment was devoted to sodium.

Tip #3 - Don't assume that you can tell sodium by taste.

It's estimated that 150,000 lives could be saved each year from stroke and heart disease if we cut sodium by 50% in processed and restaurant foods. (Stephen Havas, VP for Science, quality and public health at the AMA). The needless loss of lives that is due to the excess salt intake must stop."

This article focuses on stroke, heart attack and elevated blood pressure as consequences for high sodium intake, which should be important to us all, but for afibbers, as noted in here in this session, the sodium/potassium pump operation directly affects our tendency to allow AF to flourish.

Depending on the source, it's estimated the average American eats about 3500 milligrams of sodium every day. Almost one-fourth of that sodium is naturally contained in food. The rest plus more is added with the salt shaker or contained in the processed, packaged, restaurant food we eat.

To allow for the recommended ratio of potassium-to-sodium for health (4:1), it would mean that if we consumed the average amount of 3500 mg daily of sodium, then we'd need 14,000 mg intake of potassium from foods just to stay healthy...avoiding hypertension, MI, and of course, AF. How many of us take in that much potassium? How many easily meet or exceed the 3500 mg sodium? (a teaspoon of salt is about 2300 mg of sodium) and most whole, raw foods naturally contain some amounts of sodium.

There are loads of charts online that list sodium and potassium content of foods. You'll note that some medications and OTC products contain sodium. Read labels.

Remember that restaurants often use commercially prepared broths as a base for soups and sauces and these are just loaded with sodium and often MSG and other flavor enhancers.

While some of stated sodium content in foods may be currently different from what was stated in 2007, it's close enough to still be relevant.

Common foods – sodium content...

Bagel, cinnamon raisin 2.5 oz - 338 mg sodium ...
Bagel, egg 530
Bread, cracked wheat 153 /slice
Pita Pocket, whole wheat 6" dia 350 mg
Plain English muffin 2 oz 290
Pumpnickel Rye bread, 1 slice 190
Salted peanuts - 250
Hot dog (1) 600-800 mg
Ham, cured, 3 ounces 837 mg
Corned beef, 3 ounces 800 mg
Chicken –roasted.. white meat only no salt added 3 oz... 43 mg.
Bullion cube – 960 mg
Breakfast cold cereals, on average around 250
Corn Flakes 350
Canned chicken noodle soup - average 1100/serving
Cocoa drinks - high sodium content

Examples of typical convenience foods...

Canned soup 800 mg
McDonald's fries – 330 mg
McDonald's Quarter Pounder 730
Big Mac 1010
Grilled Chicken Sandwich 1240
5-pieceChickenSelects Premium Breast Strips w/o sauce 1550
Asian or Caesar Salad 1000mg w/o the dressing. 1500-1700 mg with dressing
Sitdown restaurants are worse because the portions are typically larger.

Repeating the take-home message, you can't always tell sodium by taste... BUT... when you reduce your sodium intake down to the recommended levels as discussed in here in CR 72. Everything you eat in restaurants will taste salty...and it is.

If you watch the Food Networks or cooking shows, you'll be amazed at how much salt those chefs grab to throw on food.

Even grilled meats are abundantly laced with salt before hitting the fire. You need to remember to request no added salt.

It may be difficult because often, meats receive a prep coating of both sugar and salt to enhance flavor. When you order a salad, choose olive oil and vinegar on the side so you don't risk a high sodium content in commercial salad dressings. Lemon wedges and olive oil work well too.

So the bottom line in controlling your AF: Address your salt (sodium) intake in foods that are not whole, fresh and cooked from scratch. Make a list of a typical day's food intake and calculate the sodium for each serving you put in your mouth and compare that in the same manner to your potassium intake.

You can't talk about potassium helping AF until you address sodium intake in the same breath.

Jackie

Ref:

Nutrition Action Healthletter, March 2007

<http://www.collectivewizdom.com/SodiumInCommonFoods-FastFood.html>

I'm fascinated by all of this but it begs one basic question in my brain. If we are all so out of sync, why don't more people get afib?

Nancy

Hi Nancy,

Said differently, why do so *few* people get afib? How does the heart ever manage to perform "normally"? As complex as its workings are, this life-giving pump is amazingly tolerant of insult, not the least of which is feeding it in a way that is completely contrary to how evolution designed it to be fed -- notably the cellular, hence dietary ratio between potassium and sodium, which today is way "out of sync". How *does* the heart put up with it! Most amazing.

Great credit to the kidneys, which under the same constant insult manage to keep the K/Na ratio at the heart cells at least reasonably workable, so that a critical majority of the billions of atrial cells have the voltage they need to do their rhythmical contracting/relaxing in coordination. Some people's hearts are just closer to the ragged edge, is all -- just a bit more sodium, a bit less potassium, a bit hypo- or hyper-thyroid, add one of any number of 'triggers', a bit of fibrosis, not quite enough ATP, not quite enough magnesium, on and on, and there goes the rhythm...

And, unfortunately, more people *are* getting afib - see the current Afib report: "There is now general consensus that atrial fibrillation is an epidemic." Afib, for the most part, is without any doubt a "disease of civilization", and as the nutritional value of 'food' continues to decline, while sodium (salt) consumption will likely continue to be outrageously high, the prevalence of Afib can only increase. Add to this the effect on the cells from the electrical-field 'soup' we live in, and there it goes.

So, the advice, as always, is to follow the recommendations in Jackie's 'The Strategy' --

<http://www.afibbers.org/resources/strategy.pdf> -- and be sure that the diet takes in *at the very least* four times as much potassium as sodium.

Best wishes, and be well!

Erling

Nancy,

My assumption is that there is a genetic component that makes some more likely to get afib than others. A possible answer for this are p cells in the pulmonary veins.

<http://www.ncbi.nlm.nih.gov/pubmed/12890038>

George

As Bruce Lipton, PhD, would say when discussing The New Biology, "genes are not controlling our body"and then that brings up that whole other topic that could be explored in another thread.

We may have a gene flaw, but as Garry Gordon, MD points out, he has many broken genes but controls the expression of them by creating a favorable environment conducive to health and healing.

What we do, think and are exposed to in our personal environment has direct influence on gene expression.

Jackie

Jackie:

I can attest to but one thing; after a couple of months of ZERO salt excepting what is naturally carried by the meats that I eat (nothing cured... all baked, boiled or BBQ'd) I can tell before I put the food in my mouth if it is laden with salt. I can no longer eat store bought prepared foods or sauces at all and even some bottled waters, when examined at close range, suddenly appear to have huge quantities of salt. Coca-cola is an offender and their brand(s) of bottled water are loaded with salt which I discovered this past Winter by accident. I had left two bottles of water in my car outdoors overnight. The next morning one was frozen as solid as a rock and the Coke brand water was still liquid. Hmmmmm.

We add salt to NOTHING and if a guest wishes salt they are free to add it.

Hopefully we have reduced our sodium intake sufficiently at this point that our potassium/sodium intake is in a better ratio as we have also supplemented potassium intake with fresh foods and low sodium V8 (which we now find to be salty).

One must be especially careful in eating anywhere but at home as everyone and every restaurant will heap on an abundance of salt in the mistaken belief that they are doing you a favour and that it will not harm. We generally request that foods come TOTALLY unseasoned and we add what we want to the basic foods that we will tolerate eating outside. And as a matter of FURTHER interest, one needs to be careful of salads and salad bars as the so-called fresh vegetables are VERY often soaked in chemicals to maintain their green colour and prevent spoilage.

Your best bet is to eat at home, where you know what you are ingesting.

We no longer even put salt on the table and tend to serve potassium rich foods where possible.

Murray

Thanks Murray. I've found the same thing is true with the taste of prepared foods. I don't cook with salt and don't use prepared food products.

I crave salt. (low-functioning adrenals). I put the powdered potassium gluconate in an empty shaker and add that to food. It adds just enough 'salty' taste that seems to satisfy most of the time. When I absolutely must add salt, then I do it sparingly and always take a dose of potassium along with it.

This CR topic is extremely important for everyone and not just afibbers.

Glad to see you're here and reading.

Jackie

Mitochondrial DNA in Aging and Disease Scientific American, August 1997
<http://www.nslc.wustl.edu/elgin/genomics/Bio3055/3055/projects/readings/mitDNA.pdf>
Douglas C. Wallace, Ph.D.*

Mitochondrial synthesis of ATP is central to Na/K-ATPase (Na/K pump) performance, hence cardiac performance. To meet this high ATP demand each cardiomyocyte has many thousand mitochondria.

The essential positions of CoQ10 (Coenzyme Q) in the 'electron transport chain' within the inner membrane of mitochondria is shown at Complex I -> III and at Complex II -> III. At the terminus 'ATP Synthase' synthesizes new ATP and recycles 'spent' ADP.

*Professor of Molecular Genetics, he received his Ph.D. in microbiology and human genetics from Yale University.

Proton Pump Inhibitors are Associated with Focal Arrhythmias (<http://innovationscrm.com/showarticle.aspx?id=79>)

Excerpts:

"We found that PPI use was significantly more common in patients with focal tachyarrhythmias than controls... This finding was consistent with both the AT [atrial tachycardia] and the RVOT [right ventricle outflow tract] automaticity groups, alone exhibiting a greater proportion of PPI use than the control group. After adjusting for potential confounders, PPI use was associated with a statistically significant fivefold greater odds of focal atrial tachycardia.

For more than a decade, animal studies have demonstrated evidence of H⁺/K⁺-ATPase [proton pump] activity in myocardium... Most recently, this protein has been shown to be present in human myocardium. In that study, PPIs resulted in increased intracellular calcium attributed to a PPI-dependent inhibition of sarcoplasmic reticulum Ca/ATPase (SERCA), resulting in a reduction in sarcoplasmic reticulum uptake of calcium."

(PPI examples by name: http://en.wikipedia.org/wiki/Proton-pump_inhibitor#Examples)

Erling

I should note that some have "low blood volume." I was initially made aware of this issue by a post on this board. My wife is subject to this. Increasing her sodium intake helped a lot. Here is the original post <http://www.afibbers.net/forum/read.php?f=6&i=12232&t=12232> If this applies to you, I would not suggest lowering your sodium intake.

GeorgeN

George,

"Low blood volume" and the article at <http://www.afibbers.net/forum/read.php?f=6&i=12232&t=12232> suggest aldosterone insufficiency? <http://en.wikipedia.org/wiki/Hypoaldosteronism>:

"Na⁺ is lost in the urine. K⁺ is retained, and the plasma K⁺ rises. When adrenal insufficiency develops rapidly, the amount of Na⁺ lost from the extracellular fluid exceeds the amount excreted in the urine, indicating that Na⁺ also must be entering cells. When the posterior pituitary is intact, salt loss exceeds water loss, and the plasma Na⁺ falls. However, the plasma volume also is reduced, resulting in hypotension, circulatory insufficiency, and, eventually, fatal shock. These changes can be prevented to a degree by increasing the dietary NaCl intake. Rats survive indefinitely on extra salt alone, but in dogs and most humans, the amount of supplementary salt needed is so large that it is almost

impossible to prevent eventual collapse and death unless mineralocorticoid treatment is also instituted"

See also: http://en.wikipedia.org/wiki/Addison%27s_disease: "... wherein the adrenal glands produce insufficient steroid hormones (glucocorticoids and often mineralocorticoids [aldosterone])."

Erling

George - typically when one improves blood volume by adding sodium, it indicates an adrenal problem that should be formally addressed. While adding sodium may work physically, there's more to the whole picture...as Erling's clip indicates.

Jackie

Erling,

The Wiki description: "Rats survive indefinitely on extra salt alone, but in dogs and most humans, the amount of supplementary salt needed is so large that it is almost impossible to prevent eventual collapse and death unless mineralocorticoid treatment is also instituted" is a bit severe in my wife's case. She had previously been treated for adrenal insufficiency, which treatment is ongoing.

This quote from the July 2007 link fits her pretty well:

"He grasps my left hand as though he has something upsetting to tell me. He doesn't. He wants to see if my hands feel cold. They do, as they almost always do. Ditto my feet. Watkins nods knowingly. "Do you ever get light-headed when you stand up?" Sometimes. "Dry eyes?" Constantly. "Feel run down, easily fatigues?" Yup. "

I forwarded this to my wife when it was first posted. She subsequently followed the advice in the article - adding more sodium and drinking more water. This helped her a lot. Maybe she has rat genes...

GeorgeN

Jackie,

In theory, the integrative docs are doing this, and were doing it long before I gave my wife the post. I asked tonight and she says the increased sodium and water has helped a lot. I know they gave her some potions to address this; however the simple salt and water help more...

GeorgeN

George, I understand that the water and sodium help... it's just like giving an aspirin to relieve a headache, but it doesn't address the underlying cause, just makes the symptoms go away. Adrenal dysfunction treatment goes deeper into functional restoration and it is, from my experience at least here in this area, difficult to find someone who is knowledgeable in that area.

Jackie

<http://www.geneticorigins.org/mito/theory.html>

This in-depth science on mitochondria adds important detail to the article [Mitochondrial DNA in Aging and Disease](#) by Douglas C. Wallace:

<http://www.nslc.wustl.edu/elgin/genomics/Bio3055/3055/projects/readings/mitDNA.pdf>

Seminars in Nephrology 25:312-321 2005

Hormonal and Nonhormonal Mechanisms of Regulation of the Na,K-Pump in Collecting Duct Principal Cells
Manlio Vinciguerra, David Mordasini, Alain Vandewalle, and Eric Feraille

Service de Nephrologie, Fondation pour Recherches Medicales, Genève, Switzerland.
Faculté de Médecine Xavier Bichat, Paris Cedex, France.

Introductory paragraph:

In the kidney, the collecting duct (CD) is the site of final Na₊ reabsorption, according to Na⁺ balance requirements. In this segment of the renal tubule, principal cells may reabsorb up to 5% of the filtered sodium. The driving force for this process is provided by the basolateral Na,K-adenosine triphosphatase (ATPase) (sodium pump). Na,K-ATPase activity and expression in the CD are modulated physiologically by hormones (aldosterone, vasopressin, and insulin) and nonhormonal factors including intracellular [Na₊] and extracellular osmolality. In this article, we review the short- and long-term hormonal regulation of Na,K-ATPase in CD principal cells, and we analyze the integrated network of implicated signaling pathways with an emphasis on the latest findings.

Full text:: http://medlib.yu.ac.kr/eur_j_oph/sem_nephrol/sem_n_pdf/SemNep_25_5_312.pdf

Erling

The hormone aldosterone in paroxysmal AF cyclicly. Aldosterone stimulates the activity of all Na,K pumps in all 50 trillion cells of the body.

<http://www.afibbers.net/forum/read.php?f=9&i=6385&t=6385>

GeorgeN

George,

It was a "rush to judgment" on my part to conclude that "Aldosterone stimulates the activity of all Na,K pumps...". Also not supported by the literature was my assumption that cardiac myocyte Na/K pumps are stimulated by aldosterone - the yr. 2000 article below seems to conclude otherwise, although research into that question is likely ongoing: "Although much information about the enzyme [Na/K pump] has become available in the years since its discovery, one area of pump research that is not completely understood, despite recent advances, is that of pump regulation."

<http://ajpcell.physiology.org/content/279/3/C541.full.pdf+html>

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<http://circres.ahajournals.org/cgi/content/full/86/1/37>

Circulation Research. 2000;86:37. American Heart Association.

Hyperaldosteronemia in Rabbits Inhibits the Cardiac Sarcolemmal Na⁺-K⁺ Pump

Excerpt:

Metabolic Effects of Hyperaldosteronemia and the Na⁺-K⁺ Pump

"Because hyperaldosteronemia can be associated with K⁺ depletion and because K⁺ depletion has been reported to affect the Na⁺-K⁺ pump in skeletal and cardiac muscle, the possibility that K⁺ deficiency accounts for the decrease in I_p in our study should be considered. However, the decrease in serum K⁺ in our study was considerably less than the decrease usually associated with downregulation of the pump. Because skeletal muscles contain {approx}75% of the total body K⁺ content, a major effect of aldosterone on K⁺ balance should also be reflected in the skeletal muscle K⁺ content. We did not find an aldosterone-induced reduction in K⁺ contents of skeletal muscle or myocardium. An effect of aldosterone on K⁺ balance is associated with a decrease in the abundance of Na⁺-K⁺ pump units. There was no such decrease in skeletal or cardiac muscle in our study. It is also important to note that spironolactone completely abolished the effect of aldosterone on I_p without having any effect on the decrease in serum K⁺ that developed during treatment with aldosterone (see Figure 6Up). Finally, it should be noted that K⁺ depletion in rabbits increases rather

than decreases electrogenic pump activity in cardiac myocytes. Therefore, it is likely that the aldosterone-induced decrease in I_p in our study is independent of an effect of aldosterone on K^+ balance.

Because hyperaldosteronemia can be associated with a decrease in levels of thyroid hormone and because hypothyroidism can reduce Na^+-K^+ pump function in rabbit heart, the possibility that hypothyroidism accounts for the decrease in pump function in the present study should also be considered. However, given that thyroid hormone regulates synthesis of Na^+-K^+ pumps, the absence of an effect of aldosterone on the abundance of Na^+-K^+ pump units suggests that the aldosterone-induced decrease in I_p is not related to thyroid function. To obtain independent support for this, we measured levels of triiodothyronine and thyroxine in 6 rabbits before and after treatment with aldosterone. There was no detectable effect on thyroid function by aldosterone treatment (data not shown).

Clinical Implications of Aldosterone-Induced Na^+-K^+ Pump Inhibition

Serum levels of aldosterone in patients with congestive heart failure are {approx}3-fold higher than levels in patients without heart failure. Both clinical and experimental evidence suggests that chronically elevated aldosterone levels have an adverse effect on the heart. High intracellular Na^+ levels in the myocardium of patients with heart failure may at least in part be related to aldosterone-induced Na^+-K^+ pump inhibition. Because of the steep, nonlinear dependence of intracellular Ca^{2+} on the transmembrane Na^+ concentration gradient, this is expected to cause a large increase in intracellular Ca^{2+} . Cellular overload of Na^+ and Ca^{2+} is believed to be important in the pathogenesis of cardiac arrhythmias, a common complication of congestive heart failure. Aldosterone-induced Na^+-K^+ pump inhibition may also contribute to cardiac remodeling in heart failure, because pump inhibition can cause activation of key growth-related genes in cardiac myocytes and contribute to myocyte hypertrophy. The present study suggests that aldosterone receptor antagonists offer a rational therapeutic approach, a notion supported by recent reports of clinical benefits of such drugs."

Erling

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Jeremiah Stamler

ABSTRACT

The INTERSALT Study is a standardized, worldwide epidemiologic study of large sample size ($n = 10,079$ men and women aged 20-59 y from 32 countries) that tested both within- and cross-population prior hypotheses on 24-h sodium excretion and blood pressure. For individuals, a significant, positive, independent linear relation between 24-h sodium excretion and systolic blood pressure (SBP) was found. With multivariate adjustment for underestimation, the estimated effect of a sodium intake higher by 100 mmol/d was higher SBP/DBP (diastolic blood pressure) by $\sim 3\text{-}6/0\text{-}3$ mm Hg. This relation prevailed for both men and women, for younger and older people, and for 8344 people without hypertension. In tests of prior cross-population hypotheses ($n = 52$), significant, independent relations were found between sample 24-h median urinary sodium excretion and sample median SBP and DBP, prevalence rate of hypertension, and slope of SBP and DBP from age 20 to 59 y (median sodium intake greater by 100 mmol/d was associated with a 30-y increase in SBP/DBP, ie, at the age of 55 y compared with 25 y, of 10-1 1/6 mm Hg. The INTERSALT results, which agree with findings from other diverse studies, including data from clinical observations, therapeutic interventions, randomized controlled trials, animal experiments, physiologic investigations, evolutionary biology research, anthropologic research, and epidemiologic studies, support the judgment that habitual high salt intake is one of the quantitatively important, preventable mass exposures causing the unfavorable population-wide blood pressure pattern that is a major risk factor for epidemic cardiovascular disease.

Continue, full text: <http://www.ajcn.org/content/65/2/626S.full.pdf>

Erling

Summary Statement

Those who have been fortunate enough to find and read CR session 72 have been witness to a most significant revelation. Coupled with the focus of The Strategy,[15] this information helps close the circle and capture all of the critical elements that bring to a light an elusive and often overlooked factor. While it's true that many critical nutritional elements are needed and they all work synergistically to help maintain a normal heart rhythm, one glaring important fact has been consistently overlooked or at the very least, under-emphasized. That fact is that unless or until the sodium/potassium (Na/K) pump function is facilitated, ensuring normal sinus rhythm (NSR) can be elusive, at best.

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Jackie

Addendum

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