THE AFIB REPORT
Your Premier Information Resource for Lone Atrial Fibrillation
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VIRTUAL LAF CONFERENCE

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SUBJECT: LAF AND THE HORMONE CONNECTION

Revision 1 (includes references) – January 20, 2003

The many excellent postings on the subject "What terminates an Afib episode" have, to say the least, been incredibly stimulating and certainly have given the old grey cells a great workout. Specifically, they have stimulated me to come up with a hypothesis that could explain many, if not all, aspects of the mechanism underlying paroxysmal LAF. I am sure there are quite a few "holes" in it, but I am hopeful that these can be "filled in" during further debate in the Conference Room.

So here goes – a play in three acts.

The LAF Cycle or The Theory of Everything

Background:

Many afibbers, myself included, have noticed that it feels like something is building up in the body that is eventually released by an afib episode. Some, again myself included, have also noticed an increase in PACs and/or PVCs in the days prior to an episode and a total lack of ectopic beats in the first few days following an episode. I believe this observation is crucial to discovering what terminates an episode.

THE PLAYERS

ANP: atrial natriuretic peptide.
A hormone formed by stretching of the walls of the atria. It helps regulate blood pressure and salt (Na) and water balance in body fluids. Its main action is to cause the excretion of sodium and water via the kidneys and urine. [1,2]

Here is what we know about ANP

- ANP levels are lower in people with LAF than in "normal" people. [3]
- ANP levels decline with age and increased duration (years) of afib. This is probably due to the increase of fibrosis of the arterial wall over time.[3,4,5]

- ANP is released during exercise. A stronger release predicts a better chance of staying in normal sinus rhythm (NSR). [6]
- ANP inhibits the excretion of cortisol, DHEA and aldosterone in a dose-dependent manner. [1]
- ANP may possess anti-inflammatory properties. [7]
- ANP levels are higher during an afib episode than during normal sinus rhythm. [3]
- ANP levels are higher when laying on the right side (right lateral decubitus position) [8]
- A higher ANP level predicts a quicker return to sinus rhythm. [3]
- ANP blocks the calcium channels in cardiac myocytes. [9]
- ANP suppresses the RAAS (renin-angiotensin-aldosterone system). [10,11]

BNP: brain natriuretic peptide.
A hormone formed by stretching of the walls of the ventricles.

Here is what we know about BNP
- BNP causes the excretion of sodium and water via the kidneys and urine. [11]
- BNP suppresses the renin-angiotensin-aldosterone system, lowers aldosterone level and inhibits the release of norepinephrine and other catecholamines. [12,13]
- BNP has been synthesized and is available as a drug called nesiritide. This drug has the same effects as BNP itself. It has no effect on potassium levels nor does it cause arrhythmias. [13,14,15]

Renin-angiotensin-aldosterone system (RAAS).
The body's main system for dealing with a decrease in blood pressure that is too great to be dealt with by the autonomic nervous system alone.

Here is what we know about the RAAS
- The primary purpose of the RAAS is to increase blood pressure by preserving (hoarding) sodium (Na) and water. The RAAS is normally activated by hypotension caused, for example, by a sudden shift from supine to standing position.
- It works as follows:
- The low blood pressure is first sensed by the kidneys which proceed to secrete a small peptide called renin. Renin is transported to the liver where it helps to produce angiotensin I from a large protein called angiotensinogen. Angiotensin I in turn is carried by the blood to the lungs where it is converted into angiotensin II. Angiotensin II (inhibited by ACE inhibitors) is the most potent vasoconstrictor in the body. It causes the blood vessels to constrict and potentiates the sympathetic nervous system resulting in an increase in blood pressure. [16,17,18]
- Angiotensin II also acts on the adrenal gland to produce the hormone aldosterone. Aldosterone causes sodium and water to be retained by the kidneys thus increasing the body's fluid content and thereby the blood pressure. [16,17,18]
- The action of the renin-angiotensin part of the RAAS may take seconds to minutes to kick in, but it may take days or even weeks before the full effect of the steroid hormone, aldosterone is felt. [18]

Aldosterone.
This hormone deserves special attention as it is one of the main actors in the play.

Here is what we know about aldosterone
- Aldosterone secretion is also stimulated by ACTH, the same hormone that stimulates the production of cortisol. [17]
- An excessive production of aldosterone is involved in the disorder aldosteronism Aldosteronism results in a constant overload of sodium and water as well as a deficiency in potassium (hypokalemia). Aldosteronism can be caused by a benign tumour

(adenoma) on the adrenal gland or simply by an enlargement (hyperplasia) of the adrenal gland. Hyperplasia itself has been linked to prolonged exposure to stress. [19,20,21]
- Adrenal tumors are fairly common and can be genetically "ordained". [21]
- A magnesium (Mg++) deficiency causes an increase in aldosterone production and subsequent hypokalemia. [22]
- An excess of calcium (Ca++) increases the secretion of ACTH. [23]
- DHA (docosahexaenoic acid), a component of fish oils and GLA (gamma-linolenic acid) both inhibit the production of aldosterone. [24]
- Excessive aldosterone exposure causes myocardial fibrosis which may contribute to arrhythmias through ANS disturbances and electrolyte abnormalities. [25]

11-beta-hydroxysteroid dehydrogenase (Type 2)
which we shall nickname "Beta", is an enzyme that facilitates the uptake of cortisol and aldosterone by their respective receptors. It is instrumental in the conversion of cortisol to its inactive metabolite cortisone. [26,27]

Here is what we know about Beta

- Beta is inhibited by licorice (glycyrrhizic acid) and low levels of this enzyme can also occur due to a genetic defect. [20,27,28]
- Beta helps preferential binding of aldosterone, rather than cortisol, to mineralocorticoid receptors. [26,29]
- Beta (Type 1) can convert cortisol to cortisone and vice versa while Type 2 can only convert cortisol to cortisone. [30]
- A reduced Beta activity leads to increased cortisol levels in the blood which can result in an increase in blood pressure, the development of hypokalemia (low potassium level) and suppression of the RAAS. [26,28]

Cortisol
is one of the body's main stress hormones. It is released in response to long-term stress while epinephrine (adrenaline) is released in response to an acute stress situation.
- Cortisol causes blood glucose levels to rise resulting in an insulin response and the possibility of hypokalemia.
- Inhibition of Beta causes an increase in cortisol levels resulting in hypertension, hypokalemia and metabolic alkalosis. [26,28,29]
- Exposure to stress increases both cortisol levels and PACs, but to the best of my knowledge a cause and effect relationship between cortisol levels and PACs has not been established. [31]

Electrolytes
Four electrolytes (ions) are essential for the proper operation of cardiac myocytes (muscle cells): Sodium (Na+), potassium (K+), calcium (Ca++), and magnesium (Mg++).
The membranes of myocytes act as small pumps that pump sodium, potassium and, to a lesser extent, calcium and magnesium ions in and out of the cells. When the cell is at rest the concentration of potassium is high inside the cell (intracellular) and the concentration of sodium is high outside the cell (extracellular). At certain times the ion channels which allow entry of sodium into the cell open and sodium ions rush into the cell causing it to discharge an electric charge (depolarization) and contract. The contractions proceed from cell to cell making the whole muscle fiber contract and ultimately making the whole atria contract.

Potassium leaks out of the cell during the depolarization period, but as soon as the depolarization is over it begins to flow back into the cell during what is called the rest or refractory period. Atrial fibrillation is characterized by a total lack of refractory periods. Calcium and magnesium ions follow the sodium and potassium ions respectively, but at a slower rate. Thus sodium and calcium are "excitatory" ions while potassium and magnesium can be viewed as "calming" ions.

This underscores the importance of having adequate intracellular levels of both potassium and magnesium and also explains why a magnesium infusion sometimes halts AF.

Hypokalemia
is an abnormally low level of potassium in the extracellular fluid surrounding the myocytes. It can be caused by a magnesium deficiency, aldosteronism, a low Beta level, an excessive insulin release, alcoholism, a high cortisol level, diarrhea or vomiting, the use of diuretics and calcium channel blockers and metabolic alkalosis.

High carbohydrate meals
release large amounts of insulin which can cause hypokalemia.

In addition to these main actors a cast of "the usual suspects" also participates in the "LAF Cycle". These include:

- The autonomic nervous system (ANS)
- An abnormally sensitive heart tissue
- Fish oils
- Insulin
- Ion channels
- Membrane modifying drugs (antiarrhythmics)
- Calcium channel blockers (verapamil, diltiazem and cousins)
- PACs and PVCs

THE PLAY

PROLOGUE

Everything is calm and serene. Cortisol levels are low, electrolytes are perfectly balanced and PACs and PVCs are non-existent or at least few and far between – Life is good!

ACT I

Aldosterone and Beta are on center stage as the curtain opens. Aldosterone may have gotten there because of an adrenal adenoma, hyperplasia of the adrenal gland, perhaps caused by many years of excessive stress or it may just be there because of a serious magnesium deficiency or a calcium overload. Beta is there to help aldosterone do its job and to help convert cortisol to cortisone.

The presence of aldosterone diverts beta from its role in converting cortisol into its inactive metabolite cortisone. This causes cortisol (stress) levels to rise and PACs and PVCs to make their presence felt again. This effect will be magnified if Beta levels are low or Beta production is inhibited. The rising cortisol levels induce glucose and insulin production which in turn encourages intracellular migration of potassium (K+) and subsequent hypokalemia.

In the meantime aldosterone begins to do what it is supposed to do, that is, instruct the kidneys to hoard sodium (Na+) and water so as to cause an increase in blood pressure.

The end result is a pronounced shift in Na+/K+ balance favouring Na+. Combine this with the increase in PACs accompanying the cortisol build-up and the stage is set for an afib episode. The situation becomes even more "explosive" if a high carbohydrate meal is ingested and is of cause exacerbated if a genetic predisposition to LAF is present.

ACT II

The frequency of PACs increases with rising cortisol levels. The autonomic nervous system (ANS) becomes increasingly frantic in trying to keep things under control, but eventually it is overwhelmed by some event (trigger) that initiates an afib episode. The ANS of an afibber is exceptionally sensitive (dysfunctional) and the episode may be initiated by an inappropriately exuberant response to a trigger from either the sympathetic (adrenergic) or parasympathetic branch of the ANS.

In the very early stage of an episode it may be possible to abort it by doing a Valsalva manoeuvre, taking a beta-blocker (adrenergic afibber) or antiarrhythmic drug or moving around (vagal afibber). However, within five minutes or so the ion channels in the cardiac myocytes are likely to have been altered to the point where these approaches are no longer effective. At this point the ANS is basically out of the loop and the heart is left with its uncontrollable, chaotic beating.

It is still possible to terminate the episode by infusing a membrane-modifying drug (anti-arrhythmic) that will close down a sufficient number of sodium channels to bring the heart back into normal sinus rhythm. In other words, the effect of the drug is the same as what would be obtained by a sudden lowering of Na+ levels.

It is also possible to lower the heart rate by infusing or taking orally a calcium-channel blocker. The effect of this drug is similar to what would occur with a drop in Ca++ concentration.

However, without pharmacological intervention, the afib episode will carry on until it terminates on its own.

ACT III

The violent movement and stretching of the atria and ventricles caused by the fibrillation result in the release of ANP and BNP. These hormones immediately start dumping Na+ and water through the kidneys causing the “big pee” and normalizing the Na+/K+ ratio. ANP partially blocks the calcium channels in cardiac myocytes and thereby helps slow the heart rate. ANP also suppresses the whole RAAS system causing aldosterone to leave the stage. This frees up Beta to concentrate on converting cortisol to inactive cortisone resulting in a normalization of cortisol levels.

Once the Na+/K+ ratio and cortisol levels have been normalized the factors sustaining the afib have been removed and the ANS will once again be able to take control and terminate the episode. The return to normal sinus rhythm can sometimes be facilitated by light exercise, which is known to release additional ANP.

The duration of the afib episode will depend on the vigour of the ANP response. This response is less pronounced in older afibbers and in afibbers with LAF of long standing because of the progressive fibrosis of the heart tissue caused by many episodes.

LOUD AND SUSTAINED APPLAUSE!!!

EPILOGUE

Everything is calm and serene. Cortisol levels are low, electrolytes are perfectly balanced and PACs and PVCs are non-existent or at least few and far between – Life is good!

AND THEN THE CYCLE STARTS ALL OVER AGAIN!!

ADDITIONAL MUSINGS

It is not clear in my mind whether a Beta deficiency in itself would be sufficient to support afib or an abnormal aldosterone level is needed as well. It is conceivable that a low Beta level could cause cortisol to "dock" at the aldosterone receptors and thereby cause all the effects of aldosteroidism. I'm afraid we may need an endocrinologist to sort that one out. [30,32]

If Beta inhibition is indeed the culprit is it possible that something in the diet or environment, other than licorice, may be the cause of the inhibition?

It may be possible to verify or negate the presence of abnormally high aldosterone levels as a cause of LAF by measuring the levels immediately before and after an episode. The presence of aldosteronism can be determined by measuring plasma aldosterone-renin ratio.

Alternatively, is it possible that LAF is a form of subclinical aldosteroidism or – far out – that LAF is actually the body's first line of defense against the development of permanent hypertension?

Is it possible that the anti-inflammatory properties of ANP may be a subsidiary effect that helps stop an afib episode?

IMPLICATIONS FOR THE MANAGEMENT OF LAF

It is clear and supported by the analysis of the diets of afibbers who have "kicked the habit" that a high magnesium and potassium intake combined with a low intake of sodium and calcium are essential factors in preventing afib episodes. My hypothesis (The Play) supports this.

High carbohydrate meals with their resulting insulin release and hypokalemia should clearly be avoided. An overly exuberant insulin release can also be avoided by ensuring that each meal and snack contains some protein.

One of the LAF surveys found that vagal afibbers who supplemented with calcium had significantly more LAF episodes than vagal afibbers not supplementing. There was also a trend for all paroxysmal afibbers to have longer lasting episodes if they supplemented with calcium. These findings fit well with the hypothesis.

It is possible that a potassium-sparing diuretic such as spironolactone may help lengthening the interval between episodes by counteracting the effects of aldosterone and low Beta levels. [20] Spironolactone is probably not a viable long term solution though due to its side effects including breast enlargement in men. However it may be worth a try to see if the idea is sound. A non-potassium-sparing diuretic may also work, but would need to be accompanied by potassium supplementation.

Neseritide (synthetic BNP) or carpetitide (synthetic ANP) may prove to be useful for terminating episodes and would almost certainly have far fewer side effects than currently used antiarrhythmics.

Large doses of vitamin C, phosphatidylserine and Moducare (sterols and sterolins) have all been found to be effective in helping to keep cortisol levels under control. Could they be effective in preventing LAF episodes?[33]

Sustained, vigorous exercise (more than about 40 minutes) sharply elevates cortisol levels. Could going easy on exercise help prevent afib episodes?

FUTURE DIRECTION

It is time for me to pass the talking stick. Fellow afibbers, please start picking some serious nits!

Hans

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I think you are on the right track Hans but what seems to be entirely missing is objective data. Could we arrange with one of the saliva endocrine testing organisations to provide a 10 day x 4 samples a day profile of say 10 of us VMAF customers? We might then have something quite exciting. You have a copy of my sine wave graph of hours in AF - I don't see how this could be attributed to anything but an endocrine cycle. Interestingly, my moving onto Disopyramide has also (so far) eliminated a tendency I had for vasovagal syncope (which was not a heap of fun). Another endocrine connection?

Bill

Wow!

I think I need to read this a few more times but I really like the idea of trying to figure out the whole cycle.

My first nit pick (somewhere in Act1): Although I don't measure my blood pressure on a daily basis I've never been measured as having a high blood pressure (I'm usually around 120/70 regardless of where I am in my AF cycle). Wouldn't you expect a rise in blood pressure concomitant to the increase in K+?

Is there anyone out there that has spotted an increase just before AF? (and is there anyone out there who takes regular measurements but has not seen an increase)
--
James D

Sorry, my mistake I should have said, wouldn't you expect a rise in blood pressure concomitant to the increase in Na+? (due to sodium hoarding)

James D

James...A rise in Potassium will more than likely REDUCE blood pressure, since a rise in potassium leads to a concomitant reduction in sodium concentration. That's one reason who many docs like their BP patients to eat fruits and veggies.

As for Hans, you brilliant bugger, you! Perhaps you've coordinated much of the discourse on the BB over the last year, and encapsulated it into the makings of a coherent theory of initiation.

I agree that a large sampling will be required to verify this. If we can get one going, count me in. I will also provide ALL of my own data about my endocrine samplings, some of which I expect any day now.

Last, I have to ask about the role of BNP in Congestive Heart Failure, and whether or not you see a connection within your theory. Recent research shows that high detectable levels of BNP upon presentation for medical treatment are being used to determine the existence of CHF in some patients.

What say you on that?

Great Work.

Jerry

Jerry,

I am glad you liked the play - it obviously needs a lot of verification, but will hopefully lead to a lot more scrutiny being given to the hormone connection.

I can't think of a connection between LAF and congestive heart failure involving BNP other than the fact that the ventricles are forced to work harder both in CHF and during an afib episode and therefore produces more BNP.

Hans

Right, and apparently it's the presence of that extra BNP that serves as a marker for the disorder (CHF). I'll work back to the sites where BNP was referenced, and offer up what I find.

If the Hormone Connection proves out, there ought to be ways to manipulate our hormone balance, so as to diminish the risk of onset, as well as reduce the frequency and duration.

Here's hoping...***Jerry***

Hans...A quick search led me to this, from the LEF site:

"New test diagnoses congestive heart failure in minutes...

Congestive heart failure (CHF) is the fourth leading cause of hospitalization in the United States, and the leading cause of hospitalization in people over sixty-five. The condition has been defined as that occurring when the heart is incapable of maintaining a cardiac output adequate to accommodate metabolic requirements and the venous return. Diagnosis of CHF is sometimes difficult, with symptoms and signs such as shortness of breath and edema being diagnostic of several conditions and physical examination prone to error. Although markers such as cytokines and catecholamines are elevated in CHF, they are hard to measure and often not elevated until the disease becomes severe. Echocardiogram is effectively employed in CHF diagnosis, but is time-consuming and expensive. A new blood test has been developed which can diagnose CHF in fifteen minutes. The test measures blood levels of a peptide called B-type natriuretic peptide (BNP) which is released in response to increased pressure load of the heart's ventricles, the lower chambers of the heart.

In a study published in the February 2, 2001 issue of the Journal of the American College of Cardiology, 250 patients with shortness of breath who were seen in urgent care and emergency departments had blood samples drawn and BNP levels measured without their attending physicians being informed of the results. Two cardiologists evaluated the patient's clinical data and symptoms to provide a diagnosis. Using the cardiologists' diagnoses as the standard, concentrations of 80 pg/mL BNP were 95% accurate in diagnosing congestive heart failure, and values lower than this were 98% accurate in ruling out the condition. Thirty cases of congestive heart failure diagnosed by the cardiologists were missed by the urgent care physicians, but a

BNP test could have brought this figure down to one. Study coauthor Alan S Maisel MD remarked that the test has greater diagnostic accuracy than does the PSA for prostate cancer, mammogram for breast cancer or a PAP smear for cervical cancer. In view of the fact that one study estimated up to 20% of all congestive heart failure cases as being misdiagnosed, the new test will enable urgent care physicians to provide a more rapid, accurate diagnosis for this group of patients. [February 5, 2001]"

I'll keep searching, since I know that BNP is all over the Google network.

Jerry

If it is true that elevated BNP is a marker for CHF, what implications might that have for the use of BNP as a therapeutic intervention in AF? Seems to me that it might be contraindicated for our disorder, if the effects might include increasing the risk (or severity) of CHF?

Still searching...***Jerry***

Hans,

Concerning hypokalemia and Ca channel blockers:

If one uses Ca channel blockers in an "on demand" basis, wouldn't doing this just continue to create a hypokalemic effect messing up the Na/K ratios and thereby increasing the length of the afib episode? This is what I am doing now & sometimes when I take NO Ca blockers it seems the episode is in fact shorter. My rate is around 100 without any drugs (in afib), around 80 with Ca blocker. The 100 rate really doesn't bother me, but I worry about the effect on the heart (which is probably not a big deal). At night in bed is when I notice it the most and am more apt to reach for the Ca blockers- so I can sleep better.

If one is taking a controlled release Ca channel blocker every day, then I'm assuming a hypokalemic effect would be continuous and therefore maybe contribute to afib??? I've been wondering about this for some time. What do you and others think??

Thanks in advance,
Jim

Jerry,

I think BNP is produced by the ventricles in response to CHF and as such is a marker only and unrelated to etiology. The natriuretic polypeptides appear to be counter-regulators of angiotensin II. BNP is definitely produced in the heart (and the brain too I think) and most of the experts ascribe its secretion to the stretching of cardiac muscle cells. ANP is also commercially available and it's called carpeditide.

PC, MD v54

Hans,

Great stuff.... I'll - like James - have to read it a few times before I'm fully on board!

Further to PC's comment about commercially available ANP (known to be low in those with a-fib) does anyone here know if any a-fibbers have tried carpeditide for their a-fib?? Surely this is too obvious-a-solution not to have been tried??

Mike F.

I would think that carpeditide and neseritide would work best for "on demand" termination of an episode. For long-term prevention I feel it would be better to deal with the underlying problem that is, (assuming the hypothesis is correct) aldosteronism or Beta inhibition.

Hans

Jim,

I have also noted an inverse relationship between the intensity (World War II or gentle butterflies) of an episode and its duration. This would make sense according to the hypothesis in that a more gentler episode would presumably generate less ANP and BNP per minute (hour) and therefore take longer to turn things around.

This could also be one reason why the use of calcium channel blockers, even though they make the "experience" more tolerable may also make it last longer.

Hans

I have just come across an interesting article that may support the hypothesis. Here is an excerpt from the abstract (1):

"Modern imaging modalities lead to frequent detection of adrenal masses, most of them incidental findings. Although the majority of adrenocortical and adrenomedullary tumors are benign, there are no reliable...."

In other words adrenal adenomas, which might be associated with aldosteronism are more common than previously thought.

Also, it is quite evident that the research into 11beta-hydroxysteroid dehydrogenase (Beta in the Play) is really heating up. The December and January issues of the Journal of Clinical Endocrinology and Metabolism have at least half a dozen articles on the subject.

By the way, there are two types of Beta. Type 1 supports both the conversion of cortisol to cortisone and vice versa while type 2 only supports the conversion of cortisol to cortisone.

Hans

(1) Koch Ca et al, The molecular pathogenesis of hereditary and sporadic adrenocortical and adrenomedullary tumors. J Clin Endocrinol Metab 2002 Dec; 87 (12):5367-84

Hans...Is there a known "best mechanism" by which one can discover the existence of such benign tumors? I presume that, if such medical inquiry exists, it would best be done by an endocrine doc?

Jerry

James,

You've become quite the electrophysiologist and have certainly exceeded my understanding of the electrophysiology of AF. Everything you state is correct. I was only trying to point out that wavelets do not propagate in the traditional layman's sense of the word, e.g., as waves propagate to the shore. Wavelets exhibit movement but they do not "propagate" anymore than eddies and swirls propagate. More importantly, I think we are wasting time and effort in pursuit of mastery of the nuances of electrophysiology, unless one of us is contemplating an ablation. Like you, however, I find it all so fascinating. The solution to the LAF riddle is going to come from mastery of the pertinent biochemistry and human physiology.

Et al.,

I find "the play" by Hans Larsen to be highly intellectually stimulating. That part of it that I find most intriguing is not the hormone connection but the enzyme connection. Hans has brought "beta" onto the stage. As far as I know, Mg++ is not required for it to work properly. There are a large number of steroid related enzyme deficiencies that are associated with specific signs and symptoms. Furthermore decreased activity (not complete deficiency) has also been described in association with various disease states. Some of these latter have overlap with Mg++ deficiency related disease states. At the top of the enzyme list are monoamine oxidase and dopamine beta-hydroxylase. The former catabolizes (breaks down) catecholamines and dopamine and the latter just dopamine.

Neither require Mg++ (they require copper instead). Many studies have shown depressed activity of both these enzymes in schizophrenia, migraine and alcoholism (Human Platelet Monoamine Oxidase Activity in Health and Disease: A Review; Plasma Dopamine-Beta-Hydroxylase in Familial and Sporadic Paranoid Schizophrenia; Platelet Monoamine Oxidase, Plasma Dopamine beta-Hydroxylase Activity, Dementia and Family History of Alcoholism in Chronic Alcoholics are just a sampling). These three disease states also rank high on the list in those deficient in magnesium.

In past postings I've mentioned that Mg++ is required for the enzyme cholinesterase to work properly, thereby causing a more vagotonic state. Mg++ is also required for the proper action of catechol-O-methyl transferase (COMT), one of several enzymes that breakdown dopamine and catecholamines. Hans' posting and some other postings about the defective substrate of LAFers vs dysfunctional ANS have opened my eyes to the possibility that a genetic component manifest through decreased (but not completely deficient) enzyme activity may be lurking in the background. My father and his brother died of AF. My mother has AF. My father had a distinct subtype of migraine associated with scotomata (visual field defect due to vasospasm of the visual cortex in the occipital lobe). I have this. He was also an alcoholic (I actually hate alcohol), as was at least one of my brothers. I have another brother who is schizophrenic (many of you may think me mentally ill too). I know these are all common diseases, but it would be interesting to know how many of you suffer from these same problems/family history.

Furthermore, the single most common cause of an "adrenergic" episode for me is sex. As I've previously posted (12/17/02), this appears to be mediated by excess dopamine. It often puts me into bigeminy and sometimes into AF. It occurs subsequently when my heart rate is just above 50 but contractions are quite vigorous. This latter is due to the well known ionotropic (strength of

contraction vs number of contractions = chronotropic) effect of dopamine. Dopamine is commonly used in the hospital to elevate blood pressure. I believe arrhythmia results under such circumstances because ionotropism is associated with an increase in intracellular Ca++, making the heart cell more prone to PACs (bigeminy = PACs with automaticity). This same mechanism would be operative in both VMAFers and LAFers. Most experts feel that electrical remodeling is caused by excessive cytosolic Ca++.

So the long and the short of it is that the defective substrate may be actually neither the heart nor the ANS but a defective enzymatic substrate. Whether one manifests this defect(s) via neuromuscular (cramps, asthma, AF, etc.) or neuropsychiatric (migraine, schizophrenia, depression, etc.) routes is dependent on the individual. Mild Mg++ deficiency, critical in about 350 enzymes, only exacerbates an existing condition.

PC, MD v54

PC,

Further to your comment in your post at the end of the 'Termination and the ANS thread', my own experiences with sexual activity and PACs is almost exactly the same as yours (probably every other time). But in response to another comment of your afore-mentioned post more in keeping with this new thread.....

Most interesting about the enzymatic substrate: I too find it an intriguing possibility that the latter may be the culprit - this would accord with the fact that most members of the wider population get the occasional PAC, but only a relative few (in their younger years at least) get a lot of PACs/a-fib - i.e. every adult heart has the ability (what we have called myocyte substrate) to produce ectopics (and can, for that matter, be induced into a-f).

After having read Hans' excellent 'play' a few times, I looked into the possibility of some tests here in the UK. Whilst I can get homocysteine (£36-00), CRP (£20-00), LPa (£38-00), and aldosterone (£47-00), even BARTS hospital in London hasn't heard of what Hans calls II-beta-hydroxysteroid-dehydrogenase..... I wonder could it be called something else here in the UK??

Mike F.

PC

I could really relate to your last post. I can't pretend to understand half of it, or should I say a tenth, at the moment, but would like some clarification. What hormone (if there is one), enzyme deficiency do you see as significant to your family history?

You ask about others with a genetic component manifest itself through enzyme activity and give some examples of you and your family history.

My own symptoms have some brain component in that I have been diagnosed with migraine (which I see as headache, sometimes with flashing lights – but often wonder if I feel pain the same as others as I never get unwell). As well as my unknown seizures.

My family history is strange in that there were no diagnosis forthcoming, and the ones that have been got since all have no known underlying reason. We never got taken to Dr's (my mother was a nurse and treated us all). We were all brought up being told we were remarkably healthy family.

But since leaving home (and caring for my father prior to his death) and in hindsight realise this is so far from the truth. I have discovered that on my fathers side there is a history of early onset dementia of unknown origin (great grandmother in an asylum at a young age, grandmother went 'doolally' and was 'always a bit strange'. My father was initially diagnosed with schizophrenia at 60 after my mum threw him out, but on further investigation was found to have severe atrophy of the cerebral cortex. Obviously in hindsight this manifested itself in my fathers behaviour as often he would not recognise us as kids or would be living on a different planet to us (but we took it for granted and didn't know any different). My mother had Vasovagal syncope if standing too long. She also suffered paranoid delusions and over reactions, and has always had them which made for a really weird and sometimes frightening childhood. My younger sister faints, has absent moments. My other sister has Rheumatoid arthritis and a host of other conditions that they say is part of RA, but is not, she is sure. All say their heart races at times, other than with exercise.

I know this does not add to the gnat straining, but it may open another throw on it.

Also you asked in a previous post about AF terminating with sleep.

In the beginnings when I still had PAF my AF always terminated in my sleep. I could always be assured that AF would terminate during sleep and things would be fine when I woke up. In the end when I was chronic AF on waking was not half as bad as AF would be when I lay down to go to sleep. Lying down made it so much more uncomfortable and it would get even faster. But something happened during sleep that evened the balance out and I always loved the mornings.

Fran

Fran,

Thank you for reading and responding to my post.

I don't necessarily have an enzymatic deficiency in my family history. However, monoamine oxidase (MAO) and dopamine beta hydroxylase (DBH) would be good candidates for decreased activity.

The point of my post is that there is increasing technological ability to evaluate enzymatic activity and correlate the results with specific disease states. An abnormal dopamine/serotonin ratio in the CNS (central nervous system) has for years been felt to be directly correlated with depression.

Parkinson's Disease is due to a deficiency of dopamine. There are numerous neurotransmitter and related substances that when not in balance, result in otherwise well defined neuropsychiatric diseases. Why are they not in balance. Is it a genetic problem? Probably to some degree. We already know that schizophrenia has a distinct genetic component. But there is a definite environmental component, e.g., post viral encephalitis in Parkinson's. Well what about a dietary deficiency? Mainstream medicine does not seem to be interested in this angle. We all know the reason why? All I'm postulating is that there is a well described genetic predisposition to some of these disease and we are just now little by little beginning to uncover the specifics of their etiology. Magnesium is such an unbelievably important requirement in so many of the body's reactions, especially anything that involves a nerve, that I would be surprised if future research didn't implicate it in many of these neuropsychiatric diseases. We already know about its role in many neuromuscular diseases. Perhaps LAF is the tip of the Mg++ deficiency iceberg. As we grow older, LAF melds imperceptibly with AF. Since we all have some degree of heart disease even now, we eventually just give up and accept our fate as beyond our control, even as our GI tracts become less efficient at absorbing an increasingly rare dietary item. The partial solution

could be right under our noses. Actually I'm trying to get my hands on a list of all the 350 or so enzymes that require magnesium to some degree. If anyone knows where this can be found, I'd be most interested to know.

PC, MD v54

James

I normally have low BP. I don't know if this is normal, but during AF when I was measuring BP I got a fright a few of times. I always stand through these readings keeping the cuff at heart level. My BP was very high (for me) at 115/105. I could not believe my eyes so took another reading. This one was very low. Took it again and realised at this point my BP was not being maintained as it was all over the place. The next one was midway. Then it dropped then got really high again. I wondered if you would pass out or something worse if the diastolic met the systolic as at times there was not much in it. The Dr explained to me that BP in AF will fluctuate due to the differing forces of blood being pumped by the irregular heart (don't know whether he was scientifically correct or just giving me a plausible answer to make me feel better). This seemed to make sense to me as if you corresponded my BP to the heart rate it was very high when the BP was high, and BP was lower when heart rate was lower, but not low. I wish had kept the read outs I was taking.

This phenomenon has been observed and asked about by others with AF who have been monitoring heart rate and BP.

I'm trying to make sense of RAAS. Would this initiate such a quick response - in the time it takes to take BP readings?

Fran

Love the theory.

Hi Fran, I think my argument would still be that if the shift in Na+ theory is correct surely we'd see a rise in BP quite some time BEFORE AF kicked in?

I know that once AF has kicked in BP fluctuates from beat to beat so can be notoriously hard to measure (and the very act of measuring it will change it - Heisenberg is everywhere!) but I think this is simply a case of poor haemodynamics when we are in AF. I'm not sure I'd like to read much else into these fluctuations.

--
James D

Your doctor's answer was accurate, Fran. BP will fluctuate as a result of the pumping force and the degree of arterial resistance, etc.

Jerry

Reading the postings over the past few weeks has made me realize just how much I do not know or understand!

Related to hormones, what role might heavy metal poisoning play? In searching for the root cause of my VAF, I discovered that I am highly mercury toxic. For the last year and a half I have been undergoing several forms of chelation. It is my understanding that mercury interferes with enzymatic reactions, and that would appear to be important.

Also, in all of my VAF episodes, (they generally start at night upon going to sleep and terminate on their own the following morning), my average heart rate is always around 60. Is this significant?

Philip

I'm playing devils advocate again. (I actually really like the idea of a hormonal cycle - it fits my AF like a glove!) Sadly, my knowledge of biochemistry is terrible but I'll see how much I can bluff :) ...

The job of going from observation to inference is really quite hard and I hope we are not jumping the gun.

I'd like to agree on a lot of the above...

Yes - increased PACs often precede AF.
Yes - atrial stretching in AF releases ANP
Yes - ANP results in a loss of Na
Yes/Perhaps - this loss of Na is helpful in reverting to NSR.

I don't think we can infer from any of the above that too high a concentration of Na is what starts the ball rolling. Has anyone measured a raise in blood pressure BEFORE AF starts? Why does ANP only kick in when we are in AF? (If there was too much sodium around wouldn't ANP kick in BEFORE AF?) The loss of Na may well be helpful but it may be out of balance when AF terminates rather than when it starts.

If it's Ca overload that gets the ball rolling could we expect to see any other symptoms?

Whilst this seems intuitively correct is the any evidence that this is true? Might the crazy mechanics of AF result in atrial stretch regardless of blood volume?

I've done the simple experiment of not re-hydrating when I'm in AF but have seen no change in duration (I've not tried adding salt). Has anyone noticed a difference in duration by not re-hydrating?

If anything I've noticed the opposite (if you are suggesting a vigorous ANP response will shorten an episode). For me there's a correlation between fast rates (and in particular strong palpitations) and the amount of toilet visits - the more unpleasant the AF the more toilet trips I make. If anything (and it is only marginal) the duration of these AFs are longer.

I should also mention that the toilet trips stop long before my AF. (Normally only in the first 5-10 hours, my AFs average around 26 hours)

What about Ca? (you mention Ca overloading) If I understand it correctly the SA node is not really interested in Na. Long pauses at the SA node are good candidates for inducing ectopics at other locations. Once the heart is in AF isn't intracellular Ca overload responsible for shortening

the AERP further and keeping us there? Do we need to get rid of intracellular Ca to lengthen the AERP??

If we can't get rid of the overload of Ca then ditching some Na might be the next best thing?

Hope some of this makes sense and helps the thought process :)
--
James D

Fellow fibbers,

There has been a certain sense of euphoria or at least a more optimistic tone on the BB of late. Jerry has expressed this. Hans has. I too think we are getting closer to solving the riddles of LAF. Like many of you, I'm obsessed with this.

Way back toward the end of November Hans brought up ANP in a discussion regarding the decrease in PACs immediately post AF. Hans' implied the following sequence: increased PACs, AF episode, atrial stretching, release of ANP, loss of Na in the urine (natriuretic means sodium in the urine), favourable change in the intracellular/extracellular Na/K gradient, reversion to NSR with decreased PACs, end of atrial stretching and cessation of ANP release, slow deterioration of the favourable gradient with gradually increasing PACs and you're back to square one.
On 12/8/02 I posted a proposed mechanism for conversion of AF. It went basically as follows:

"I believe that in addition to this mechanism (the above) there is an additional one involving aldosterone, keeping in mind that autonomic activity at any point in time is a measure of the sympathetic/parasympathetic tug of war. With the decrease in plasma Na through urinary excretion there is loss of water, thereby helping the atria to minimize their required stretch. With this decrease in hydration there is decreased sympathetic tone or increased vagal tone. It is this increasing vagal tone that is responsible for the increasing refractoriness of AF during the first half of the episode. However this decreased hydration stimulates the activation of the renin angiotensin aldosterone system (RAAS). The aldosterone jumps into action and perceives a need to conserve water. After all, the stretching induced release of ANP is due to AF not some actual over-hydrated state. This it does through renal sodium absorption. This causes water retention and an increase in sympathetic tone, which directly opposes the vagal tone created by ANP."

In "the play" (about hormones) Hans has placed the hormone aldosterone in the lead role. One big piece of information in his post that caught my attention was "the action of the renin-angiotensin part of the RAAS may take seconds to minutes to kick in, but it may take days or even weeks before the full effect of the steroid hormone, aldosterone is felt." This was news to me. Then Bill quickly responds with his "sine wave graph of hours in AF" and how this cannot be attributed to anything but an endocrine function. I think that one can make a strong argument for the aldosterone cycle to be the cause of the "cycle of AF". It takes days or weeks, as Hans states, before the full effect is seen. ANP inhibits aldosterone in a dose-dependent manner. ANP at the start of AF is probably entering an environment of relatively high intracellular sodium and calcium. In VMAF Mg deficiency may play more of a role in allowing this Na/K imbalance (through the malfunctioning Na/K ATPase pump that requires Mg). In ALAF increased ACTH and cortisol from stress and age are probably quite instrumental in creating this imbalance (through increased aldosterone that dictates renal absorption of Na at the expense of K). It takes many hours of natriuresis to rectify the Na overload and before aldosterone is able to overcome this ANP induced inhibition and to start conserving Na at the expense of K. At termination of AF aldosterone would be at its peak concentration and then would slowly begin its decrescendo in the ensuing days as we begin again to accumulate intracellular Na (not enough Mg to maintain the Na/K ATPase pump and/or excessive aldosterone). The particulars would vary only slightly between VMAF and ALAF.

Onset and duration of AF is primarily about a Na/K imbalance. These latter are more dynamic electrolytes and fluctuations in either can precipitate or terminate an episode. Mg (through the various ATPase pumps) is critical in maintaining the balance. I know of an individual who can often terminate an episode within 30 minutes by drinking OJ supplemented with one gram of K on an empty stomach after onset of AF.
http://www.med-edu.com/HyperNews/patient/thread.pl/arrhythmias/afib-egulars/45.html?dir=next-in-thread

I'd imagine that this would have to be fairly early in the episode. Mg infusion is also well known as a method for termination of AF. The mechanisms for each are quite apparent (correction of the intracellular Na/K imbalance via the Na/K exchanger which is passive and does not require energy and thus Mg). Aldosterone may mediate termination of VMAF by increasing sympathetic tone (by increasing vascular volume). The day that I took my sublingual scraping and smear for intracellular mineral analysis was ironically the day I went into AF (about 10 hours later on Christmas). Therefore this represents a snapshot of the intracellular electrolyte environment that favors AF. It revealed an upper limit of normal Ca, nearly upper limit Na and lower limit of normal Mg and P and lowish K.

Intracellular Ca overload is associated with increased PACs and shortening of the refractory period. Variations in Ca concentration throughout the atria cause increase in atrial dispersion. The situation would appear to be ripe for an episode of AF, as it proved to be. AF occurs on a backdrop of an increased intracellular Ca/Mg. This results in the Na/K imbalance and is also at the heart of electrical remodeling. Until rectified it will sustain an AF friendly environment. As I've said previously, perhaps drinking less water and ingesting a little salt intake would hasten the dehydration. This should expedite the entry of aldosterone onto the stage and shorten episode duration. Spironolactone (a potassium sparing diuretic) or carpeditide (commercial ANP) might lengthen the interval between episodes by restoring Na/K balance.

These are just my ever-evolving thoughts on this complex topic. Much of the pertinent physiology can be read at the below webpage: http://www.ub.rug.nl/eldoc/dis/medicine/r.g.tieleman/c10.pdf

PC, MD v54 .

PC...Fine post today. Your thinking is becoming more succinct about the mechanisms of AF onset and termination. Your descriptions are more and more "coned down," as they say in the x-ray department, and that's to the good, from my point of view. Why? Because it begins to suggest an elegance of thought about the issue, one of the stages in the process of intellectual discovery and creativity. As the processes are more and more understood, it seems we are returning more and more to an endocrine/electrolyte view of this disorder. Once again, all to the good.

One thing that pops out at me today, as on prior days, is the evident need for all of us with AF to take deliberate measures to minimize salt intake as a matter of course. The Na/K balance being so crucial, it seems important that we sustain our potassium intake and remain vigilant about how much sodium we're taking in via diet.

Looking forward to the breakthrough!

Jerry

From my non-physician's point of view, I would predict that there would most definitely be an increase in BP prior to AF onset, AT LEAST IN VAGAL A-FIBBERS. If that is accurate, then such a precursor event would fit with PC's theory.

I would assert that, in susceptible hearts (as in those of us whose endocrine function is now in question, and whose electrolyte balance must be in a state of flux either undetected or insufficiently measured), ANP might very well "kick in" BEFORE active onset of AF, but that the beneficial effects (to include natriuresis) of ANP are not detected until the symptoms and effects of AF are detectable. As for me, I remain uncertain that we know for sure that ALL afibbers can say without hesitation or error that their AF is present before ANP is operating. In my case, I urinate well before my irregular heartbeat is triggered, and I feel intense vagal tone in my upper chest prior to an episode. To me, that suggests that the ANP is at work, struggling to decrease my sodium levels.

It's important for me to state that, since ACTIVELY REDUCING SODIUM intake every day (the usual volume being well under 1000 mg) and maintaining adequate potassium intake via diet alone (apples, pears, etc), I have not had any issues or episodes. I have not had any excessive urination, and I am not plagued by the kind of pre-episode high-vagal tone that once made my life so miserable. That is NOT to suggest that low-sodium, high-potassium is the answer. Rather, that a change has occurred in me.

I ask PC and HANS, especially, to pay close attention to what I just wrote:

My K levels are excellent, while my serum Mg levels remain low-normal. I have almost NO symptoms on a daily basis. Put it together, and it suggests to me that the ONLY reason I remain largely AF episode-free today is because I have a steady level of K available. If my K were to fall precipitously, I would predict that the severity of my symptoms would increase dramatically.

I must also add that my serum potassium has ALWAYS been and continues to be nearly 5.0 at EVERY doctor's visit for which a lab report was ordered. At the same time, I can report that my serum magnesium has ALWAYS been and continues to be at the lowest end of normal, DESPITE the fact that I've been taking hundreds of milligrams of magnesium daily for two years.

As for hydration, it is known in the medical community that sub-clinical dehydration can be a cause of elevated blood pressure. If we lose large amounts of fluids during an episode, and if we fail to rehydrate during an episode, then some degree of dehydration might result. If so, then PC and Hans would be correct that the blood volume reduction would allow for less atrial stretching, hence less ANP release. If ANP is the vehicle by which episode duration is affected, then it would seem that ongoing hydration during an episode would be a good thing, flushing sodium while helping to maintain ANP release. Yes/No?

Also, the removal of Ca is an intriguing issue. As most of us know, the intracellular level of Ca should be 10,000 times LOWER than the internal concentration. We might want to consider the Ca/Na Exchange Pump and its role in AF. When the concentration of Ca is too high, it is far easier for Na to enter the cell, thus driving up BP and discharging the Na/K membrane pump. In that situation, 3 Na ions are driven into the cell, and 1 only Ca ion is driven out. The greater the Ca concentration of a muscle cell, the greater the degree of contraction. The muscle cells that surround our arteries are led to maintain higher TONE when the Ca concentration is higher, and that's not a good thing for us. [It is said that a 5% increase in cellular Na yields a 15-20% increase in cellular Ca. That's 4-to-1.]

All the while, the cell is trying to keep Ca out, even as it drives internal Ca out. In essence, the cell is working like hell to maintain a favourable balance. Too much sodium, and not enough potassium, allows the cell membrane voltage to discharge to a certain extent, and that voltage discharge allows Ca to leak into the cells through the ion channels. That's why Magnesium is such a strong calcium channel blocker, and our ingestion of that vital mineral should NEVER

stop. Too much Na will allow too much Ca into the cells. When too much Ca is present, arterial muscle cell contraction increases, narrowing the artery and elevating BP. An increased level of Ca in the Sympathetic Nerves would increase the transmission of epinephrine/adrenaline, a process that would increase the contraction of smooth muscle cells in and around the small resistance arteries.

With that in mind, isn't it true, then, that the ANP natriuresis that comes about during an episode reduces the Na concentration, which recharges the cellular membrane that keeps Na outside the cell, thus driving Ca concentration down by forcing more Ca out of the cell, a process that is supported in vital ways by the overall cellular Mg concentration? Wouldn't that be why ANP (taken either prophylactically or upon AF onset) might shorten duration, and lower BP at the same time?

In addition, we might want to consider the cellular Acid Pump (Na/H Exchange), which also obtains its energy for chemical equilibrium from the Na/K pump. The acid pump works by driving Hydrogen ions (H+) out of the cell, thus increasing cellular alkalinity. However, if our Potassium concentration falls, then the Sodium/Potassium Pump is allowed to discharge, as is the Acid Pump, and the loss of membrane voltage allows acid to accumulate inside our cells (cellular acidosis). An increase in cellular pH (alkalinity) is related to beneficial protein synthesis and new-cell growth. We've been drinking WW, which allows Bicarb to bring Mag into our cells, thus elevating our pH. It would seem to me that even WW will be doomed to failure if we discharge the Sodium/Potasium membrance pump by ingesting too much NA, thus driving K levels down. Cellular Na and K are always in reciprocal relationship to each other: when one goes up, the other must go down.

Next post--HORMONES and KIDNEYS.

Jerry

PC

Further to your post and musings on schizophrenia have you considered exorphins (from milk and wheat) as a possible candidate? It seems that exorphins also have an effect on gastrointestinal function, hormonal release, and appetite.

Fran

Fran,

I eat plenty of both. Please educate me on this.

PC, MD v54

PC

I'm not much of an educator in the accepted sense of the word. Certainly not at the level you are used to. However a few links and some anecdotal evidence might help. There are at least two people who have stopped AF (on the Yahoo message board) by avoiding the opoids in dairy. There has been quite a lot of research done on exorphins and schizophrenia/autism. Anyway here goes with some links:

http://www.paleodiet.com/autism/cadelet.txt

This is a cached version from Google as this link about some research is now gone.
http://216.239.39.100/search?q=cache:qQcQt4ZEDJMC:www.rikshospitalet.no/view/readforskat.asp%3FnPubID%3D795+exorphins+and+schizophrenia&hl=en&ie=UTF-8

Exorphins from http://membres.lycos.fr/xbeluga/addictivefoods.html

Pieces of milk and wheat proteins (peptides) can act like the body's own narcotics, the endorphins, and were described by Zioudro, Streaty and Klee as "exorphins" in 1979. Other food proteins, such as gluten, results in the production of substances having opiate- (narcotic) like activity. These substances have been termed "exorphins." Hydrolyzed wheat gluten, for example, was found to prolong intestinal transit time and this effect was reversed by concomitant administration of naloxone, a narcotic-blocking drug.[MorleyJE. Levine AS et al. Effect of exorphins on gastrointestinal function, hormonal release, and appetite. Gastroenterology.1983 84(6) 1517-23.] Digests of milk proteins also are opioid peptides. [Opioid activities and structures of casein-derived exorphins. Loukas S. Varoucha D., Zioudrou C. at al.1983 Biochemistry 22:4567-4573] The human brain effects of exorphins have not yet been studied, but may contribute to the mental disturbances and appetite disorders which routinely accompany food-related illness. The possibility that exorphins are addictive in some people is a fascinating lead which needs further exploration.

Another mechanism, similar to dependency on food-derived neuroactive peptides such as exorphins, would be a dependency on gastrointestinal peptides, released from the bowel during digestion. Deficiencies in the bowel production of regulatory addictive peptides, such as endorphins, would likely be associated with cravings and compulsions to increase food ingestion. There are a large number of gut-regulatory peptides feeding back to brain control centers to form the brain-gut axis. The information flow between the gut and brain is likely critical in regulating feeding behaviors.

Eugenio Paroli reviewed the peptide research, especially the link between food and schizophrenia. He suggested: "The discovery that opioid peptides are released by the digestion of certain food has followed a line of research that assumes pathogenic connections between schizophrenic psychosis and diet."

Milk and wheat proteins have been studied and shown to yield active peptides. These substances may be numerous in the digestive tract after a meal and several effects could occur in sequence. The absorption of larger peptides may be irregular, with variation in symptom production after meals, making the interpretation of milk and wheat disease difficult. Other foods are likely to yield similar peptides.

From our basic understanding of protein digestion, we should predict that there will be regular traffic of peptide information passing from food digests into the body. Ingestion of normal food may result in information-molecules streaming into our bloodstream from stomach or small intestine with all the impact of narcotic drugs! A "Gluten Stimulatory Peptide" is also described with narcotic (opiate) antagonist properties. It has been suggested that gluten hydrolysates, digests of wheat protein, have mixed opiate agonist-antagonist activity and, like two drugs with mixed narcotic activating and blocking actions (nalorphine and cyclazocine), produce dysphoria and even psychotic symptoms. Loukas and colleagues have derived the structure of cow's milk-derived exorphins: Opioid activities and structures of casein-derived exorphins. These two peptides carry information by finding and binding to brain receptors which ordinarily respond to endorphins. The message is go to sleep, feel bad, but go back for more.

Fran

PC...Thanks for your response. My PAC's and PVC's rarely ever occur—unless I fail to maintain my regimen. If, for example, I allow my magnesium ingestion to diminish for any reason, I am susceptible to ectopics. If I ingest chocolate, caffeine, etc (the usual AF triggers), then my ectopics would begin. So, in answer to your question, I can say that PAC's and AF-related episodes have gone away together, arm in arm. I wish them a good journey.

As for the type and amount of magnesium, I have for two years been taking increasing doses of magnesium glycinate (first by Solgar, now by Metagenics). In the initial months (January 2001 to July 2001), I took no more than 100 mg of magnesium. Even at that time, the effect was miraculous. All AF-type dysrhythmia stopped upon initial ingestion—that very night--and I slept fairly well, for the first time in months. I continued that does level through the end of the year, believe it or not. Starting in early 2002, I began to increase the doses, first to 200 mg, then to 300-350 as of August 2002. All the while, I remind you, I had annual physicals, follow-up echo's, and an extensive array of blood profiles. My serum K was always excellent, and my serum Mg was always near the bottom of clinical normal. Intracellular levels of minerals (including Na) have NEVER been done, but I will be doing that quite soon. Report to follow.

In my own case, I chalk my AF reduction down to the use of magnesium, the elimination of known triggers and excitatory foods, the consistent use of vitamin and mineral supplements, and the genetic accident of reasonably high K levels (without which, I believe, my AF would be dramatically different). My own onset and symptoms suggest to me that I am vagal, with tone increasing late in the day. I am ACTIVELY exploring (via physician consult, lab profiles, and my own analysis) the role of my endocrine system in this matter. I have believed for a very long time that my cortisol and other key hormone levels are at least modestly deranged, as evidenced by sleep problems, shifts in waking and sleeping states, general feelings of internal function increase (including BP, etc), all of which point to strange endocrine workings that should be (and will be) fully sussed out.

As for my active sodium reduction, I begin by saying that I am an avid label reader. I will not eat foods that are hyper-sodium (most breads, soups, most packaged goods of all kinds), and I never salt any food. I count the mg's of Na that I ingest, to the extent possible. I also actively ingest fruits that are high in K, so that the reciprocal chemical effect comes into play--as my K increases, my Na decreases proportionately. I've found a wonderful diuretic effect from added K through fruits, and that process may have contributed to my current absence of AF symptoms.

I learned about the assertion that sub-clinical dehydration can cause elevated BP from Dr. Lam's website, which discusses that very effect under Lam's BP protocol. Were it not for that citation, I would not have mentioned it in my post. From my point of view, hydration and BP have an interesting relationship, since hydration would tend to assist cellular membrane function, and the pumps discussed would be allowed to dispose of intracellular Na and Ca more readily when fully charged. The constrictive effects on peri-arterial muscle cells would then be reduced, so that related BP effects would be diminished as well.

[I hasten to add that I'm not a physician--I just play the part on this BB. Do you remember the US aspirin commercial that ran for years?]

I find the idea that sustained hydration could well increase the duration of an AF episode quite intriguing. I would love to see a de facto trial of that claim within the population of this BB. If duration were to increase with hydration, then we might have to reconsider our beliefs about Na effects, wouldn't we? Or, would we have to give even more serious thought to the endocrine hormones, and the interplay that allows ionic imbalance to occur, thus discharging cellular pumps, or at least reducing their efficiency?

My non-professional prediction is that hydration would not prolong an episode, and that, coupled with proper K and lower Na, hydration would diminish the length of an episode, if only because the atrial stretching caused by increased volume would force the auricle cells to emit ANP. Of course, all current evidence is found in sporadic anecdotal assertions or descriptions of personal experience. We might want to rigorously gather such information, so that we can properly assess what's going on with volume, ANP, hydration and length of episode(s). I will be unhappy if duration is not diminished. Why? Because it will make the correction of AF a little bit harder, from my point of view. On the other hand, it might point us to a more focused review of hormonal actions, which may very well be at the heart of this disorder, pardon the pun.

Would it be ethical for a physician/researcher to gather a group of known AF patients and establish a rigorous trial of prophylactic ANP use? If such a trial were to occur, and if the trial led to a reduction or elimination of AF episodes (even if it caused lifestyle disruptions because of frequent urination), then we would have a lot of additional information to consider, would we not? The implications of such a trial would be extensive, since either the trial would lead to a) AF elimination/reduction, or b) no such beneficial effect. Right now, we're assessing uncontrolled anecdotal evidence. Always difficult to get perspective, or organized data and results, that way.

As I understand it, there are long-term downside effects of routine/repeated stretching of atrial tissue. If prophylactic ANP administration were to be tried, wouldn't the ANP trigger natriuresis WITHOUT a prerequisite atrial stretch? Wouldn't the chemistry of the synth-ANP excite the natriuresis, without a requisite atrial tissue precursor? If so, we would get the beneficial effect, without the potentially detrimental long-term risk to atrial tissue.

A bit simple, but it's based on a hopeful outlook, and a hunch.

If you were to follow on your idea of taking a K-sparing diuretic such as spironolactone, you would still have to monitor your K intake very closely, wouldn't you? Perhaps even more rigorously than you do now?

Lastly, I want to dig a bit more deeply into the assertion made by traditional medicine that hypervolemia always increases BP. That, in my opinion and from my research, appears to be based on the belief that BP elevation is almost always the result of increased volume and the arterial inability to accommodate such volume? I would like to ask whether or not medical science has made the answer harder than the problem (as is so often the case in medicine). Why must we assert that too much volume is the CAUSE of the BP elevation? Why can't it be that a stricture in the vessels leads to BP elevation, that stricture coming from the reactive effects of ionic shifts that allow the vessel constriction in the first place? More Potassium, for example, would promote vessel dilation, thus allowing more volume to flow, unimpeded by vessel contraction.

If my theory holds, then our vessels are more capable of tolerating increased volume. Not forever, of course, but long enough for some biophysical alteration to be made by the individual (via exercise, diet, etc). If vessels are so capable, then hypervolemia would not in and of itself cause BP elevation, nor would hypervolemia be the only mechanism by which the atrial auricle trigger ANP release in AF patients. [I'm presuming that synth-ANP could also be used.] If healthy vessels are so capable, then sustained hydration would not elevate BP via hypervolemia (if healthy vessels have proper ionic balance in membranes, meaning lower Na and Ca and higher K, hence pump efficiency and greater dilation), and an increased intracellular Na would drive BP up by discharging the Na/K pump, thus allowing the membrane to lose vital K and its BP-lowering benefit.

I ask you to remember that a) I am AF-symptom free, b) I am ectopic free, as long as I make no "trigger mistakes" in diet, etc, c) I have lots of K available in my system, d) I reduce Na in my diet every day, e) I sustain K in my diet every day, f) I noted INCREASED TONE PRIOR TO my previous AF events, g) I'm not convinced that such increased tone ever diminished, ended or

eliminated any of my prior AF episodes. With those thoughts, and my prior paragraphs, in mind, I have to say that this post constitutes both an anecdote of my experience, AND a proposition about AF. Neither is intended to be the oracular declaration of AF.

We'll do this again soon.

Jerry

As I said in my post in response to that of Jerry's, I'm not assuming that retention of Na results in an increase in BP. I think most of it ends up inside cells because of a somewhat leaky membrane (Na in and K out). ANP doesn't kick in because of too much Na inside the cells or outside. It kicks in because atrial cells are being stretched. Forget about Na wrt stimulating release of ANP in LAF. Although natriuretic peptides are secreted in CHF to decrease blood volume, LAF is kind of a false alarm. There is no real fluid overload in LAF, as there is in CHF.

I certainly can't argue with you on the possibility/probability of a post AF Na/K imbalance. That is all speculation on my part. It would seem reasonable to me that this imbalance would more favorable at the end rather than at the beginning, given the activity of ANP providing a more favorable gradient for active removal via pump or passive diffusion via an exchanger of intracellular Na. Regarding duration of episode and amount of ANP secreted, I'd say that you might be right. We're all looking for objective evidence. If your HR is higher during a particular episode, then renal perfusion (blood flow through the kidneys) would be higher with larger production of urine, all else being equal. This might explain your more frequent trips to the loo. But all this depends on fluid intake as well, because ADH is always lurking in the background. The fact that your frequent trips to the loo stop long before your AF suggests that aldosterone (the anti ANP hormone) or ADH is becoming active well before termination of AF.

Calcium overload is aggravated by AF or tachycardia. This happens because the cell doesn't have enough time between beats to move it back outside the cell along with the Na. This is called loss of physiologic rate adaptation. Within 15 minutes of onset of AF there is a buildup of extracellular K. And yes increased Ca in the cytosol causes shortening of the AERP and the logical thing for the cell to do would be to remove it. It does this through the Na/Ca exchanger (operates by passive diffusion and does not require energy), because the ATP requiring pumps are not operating very well. This brings Na in and Ca out. That obviously aggravates the intracellular Na picture, but I think the continuing natriuresis rectifies some of this. The intracellular Ca picture is probably bad at the beginning of AF and possibly/probably worse at the end. This is the primary cause of electrical remodeling during AF. This and Mg keep us on the knife's edge of AF. However, I think the Na/K picture is what determines actual onset of AF. Who knows what the real mechanism is in the absence of objective data. Perhaps a little trial of spironolactone at the right point before an episode of AF might shed some light on all this.

PC, MD v54

I just re-read something that was written on the general BB, and it gave me pause. Someone wrote that he believed that AF episodes and their effects might have more to do with the mechanism by which ion transfer/exchange occurs than on the actual levels of potassium or other minerals. Brilliant.

While I still believe that K levels are vital to the reduction/elimination of the problem we face, I was struck by the elegance of that post, although it is quite likely that the individual who wrote it could not have known that it would trigger thoughts in people like me.

In my own case, my K levels have ALWAYS been at the top of normal, even though I NEVER actively tried to sustain K intake until late last year (2002). At the same time, my magnesium levels are at the barely discernible baseline of normal, even though I HAVE TRIED to sustain substantial Magnesium intake for nearly two full years.

K levels high WITHOUT trying; Mag levels low WHILE TRYING.

Now, to the point: As I've already written, here and on the BB, I have no ongoing AF symptoms, nor do I have routine ectopics about which I become concerned, and my symptoms went away as soon as I began taking Magnesium.

Think about that from my point of view. I have clinically minimal levels of Magnesium, but high levels of Potassium. My AF symptoms disappeared with the ingestion of Magnesium, even though I STILL have clinically minimal levels in my serum.

Doesn't that point to the very real possibility that a) my initial onset and symptoms in January 2001 came about when my systemic Magnesium depletion could no longer be tolerated by my body; b) that the ingestion of minimal amounts of Magnesium was all that was needed to minimize (later, eliminate) my symptoms and episodes; and c) that the small amounts of Magnesium that I ingested could well have been just enough to provide the electrolytic kick that my cellular membranes needed in order to fully utilize the substantial Potassium levels that were (and are) apparently available within my body? And the only way my electrolytes could be used to my physiological benefit was to ensure that the cell membrane integrity was maintained or restored, thus allowing for the more efficient functioning of cellular pumps.

In essence, my own case seems to provide A CLINICAL IRONY in terms of AF:

- We are trying to ingest more K and more Mg in an effort to reduce or eliminate our AF symptoms and episodes;

- We are drinking bicarbonate water with Mg in an effort to more effectively deliver systemic Mg and, at the same time, minimize sustained cellular acidosis;

- We are not ALL gaining the desired physiological benefit(s) of those efforts, either to the same extent or in the same form or for the same amount of time;

- Yet, in MY own case, my minimal Magnesium absorption is apparently enough to sustain my symptom-free condition on a long-term basis, most likely because I am the fortunate beneficiary of a naturally high level of serum K.

What is the logical outcome of this analysis? If there is any merit to my hunch at this moment, it might be that my own ingestion of Magnesium is sufficient to provide the cellular charge necessary for my membranes to allow for the uptake of available Potassium, without which my symptoms and episodes would return, perhaps in a more dramatic way. I've done little to provide my body with the K it needs, but the Magnesium has apparently provided a synergy in which my cellular membranes are allowing the efficient exchange and use of K ions. If I'm right, then those folk whose membranes are not so charged would have greater difficulty reducing or eliminating their episodes, especially if they allowed dietary intervention and mineral ingestion to waver or decline.

If that is true, then it could be that cellular membrane integrity, coupled with ionic balance of key minerals, sustains an AF-free condition. By extension, it would then seem to me that we would be wise to consider endocrine function as the source of cardiac/electrolytic balance, the CPU-controller of electrolyte levels and their transfer and cellular utilization. In short, the endocrine

system might well be the biochemical scaffold onto which the Cardiac Theory of Everything could be assembled.

Think of those of you with Thyroid problems (endocrine). Think of Erling, who has eliminated his AF with membrane integrity (use of WW, Omega 3, etc). Think of Fran, PC, Mike, James, and so many others of you who have stated your problems and offered your corrections, as they have benefited you. Don't they all seem to fit into a matrix of endocrine function?

However anyone else applies those things, I can say that, from my point of view, they seem to organize themselves around endocrine function, either as a primary or a secondary biophysiological function.

Thoughts for you to contemplate. Valid or invalid, that's where I am today.

All the best...***Jerry***

Jerry,

Thanks for the post. I, and I think all of us, love hearing a success story.

Regarding the apparent effect of your low salt diet, it would seem to me that one less disciplined in this area could theoretically accomplish the same thing by intermittent judicious use of spironolactone. This, as you know, is an aldosterone antagonist and allows diuresis through Na excretion vs the usual K excretion. This could be used to periodically wash out the excess accumulated intracellular Na (more of a problem in those with leaky membranes due to Mg deficiency). The decrease in plasma Na would provide a better gradient for extrusion of this excess intracellular Na (the Na/H exchanger might be less effective if plasma pH were high normal vs low normal). One could possibly restart the interval (between AF episodes) clock by this method just as ANP (according to our theory) does this during an AF episode. I'm still hopeful that my more aggressive approach to Mg supplementation ala Dr. Mansmann (dubbed magnesium dosing technology by Bill) will prolong that interval. Close attention to K intake is an important corollary to the regimen. If this fails, then I would like to see if the above spironolactone theory has any merit. Carpetitide (synthetic ANP), by the way, doesn't seem to be listed in my Physicians Desk Reference. Spironolactone is recognized for the treatment of hypokalemia. Although many meds are contraindicated while taking spironolactone, including potassium supplements, it otherwise appears fairly innocuous, assuming good renal function.

Regarding the Lam statement about dehydration and blood pressure, I've read what he says on this (p. 191 -192 of his book). "One of the primary causes of high blood pressure is the loss of fluids." On p. 104 of his book Hans states, "MDs ... have found that drinking large quantities of water (500 ml) significantly increases sympathetic activity." To clear up what otherwise appears to be a conflict or at least a contradiction, let me say this. There are basically two treatable forms of high blood pressure, one that is caused by excess blood volume and which is corrected by a "water pill" (diuretic) and one that is caused by excessive vascular tone (constricted blood vessels) and which is corrected by a beta-blocker (inhibits the contraction of the smooth muscle around the blood vessels). When Dr Lam encourages us all to drink more water, from a BP standpoint he is counting on the normal homeostatic mechanisms of the body to counteract what would otherwise result in an elevation of BP, i.e., there will be a commensurate decrease in circulating catecholamines as well as down regulation of the RAAS (renin angiotensin aldosterone system). This is a very good thing. During dehydration the opposite will be brought into play and that is a bad thing, if prolonged over time. However, I think that perhaps, as raised in James' post yesterday, the DEHYDRATION of AF mediated by ANP causes activation of the RAAS and this enhances sympathetic tone. This I think is the real determinant of when a cholinergic (vagal) episode is terminated. And that is why avoiding fluid intake might shorten AF

duration. Taking a little salt would allow for renal excretion of slightly more Na and absorption of just that much more K.

Hope this doesn't sound too complicated.

PC, MD v54

Hi everyone,

I'd like to share what happens when I have one of my main triggers ALCOHOL (other triggers include lack of food and dehydration). I have briefly discussed this on the board before but thought about it again while reading the posts on the forum. Its pretty basic stuff you may already know it but it's my way of making sense of it as some of the posts just baffle me.

James D asked a question," has anyone measured a raise in blood pressure before AF starts?"

Do some of our triggers cause changes in blood pressure?

I have read that when you first have an alcoholic drink your blood pressure initially rises and then drops. Is it something in the alcohol or the change in blood pressure that puts me in danger of AF (apart from dehydration, loss of magnesium etc)?

My first drink of the night is always accompanied by palpitations and a very flushed face, then after another one, things tend to calm down about.

Another AF trigger for me has been getting in a hot bath, I was told later in casualty that the hot water dilated my blood vessels and lowered my blood pressure quickly causing the AF.

As we are talking about hormones and i don't want to bore you guys maybe this is one for the ladies on the board. I am more prone to palpitations on my premenstrual bloat, also after when you lose the excess water when the progesterone levels drop. Add to that the stress and the feeling of wanting to hurl abuse at everyone, it sets me up nicely for an AF attack. Do any of the other ladies on the board feel they are more prone to AF at different times of their cycle?

Thanks for listening everyone I'm off to start an argument with some poor unsuspecting soul.

Toni

Toni,

Are you a chocolate lover?

The following web page has an interesting discussion re PMS and magnesium deficiency. Hate to keep beating a dead horse.

http://www.wholehealthmd.com/hk/articles/view/1,1471,718,00.html

This one has a nice discussion on alcohol and hormone fluctuations wrt magnesium
http://www.pampermesoftly.com/indepthns.htm

PC, MD v54 (never bored by anything involving LAF)

I have just completed updating the "play" by entering all the references. Big job, but hopefully useful to anyone wanting to get into the details. Should also be useful if we eventually approach an endocrinologist or "friendly" cardiologist for their comments on our deliberations.

Also, I have just heard from Prof Hochberg in Haifa, the world expert on 11-beta-hydroxysteroid dehydrogenase. He does not know of any other dietary, environmental or psychological factors which might inhibit Beta. This, of course, does not mean that there aren't any, just that medical science has not discovered them yet.

Hans

Sorry to bang on about this but I think there is a great opportunity to get some real objective data here. The saliva test is, I understand, accurate and easy as well as being relatively economic. If we could find 10 (say) vagal Afibbers with similar symptoms and 10 controls, we could then do the test 4 times a day for perhaps 10 days. This might show up some statistically significant differences.

One of the companies offering the test might be persuaded to offer a job lot price. What do you think?

Bill

Bill,

What specifically were you thinking of measuring in the saliva?

PC, MD v54

Fellow fibbers,

Before the topic of LAF and the Hormone Connection is relegated to the Proceedings and disappears from the Conference Room altogether I'd like to contribute the following anecdotal experience on the hormone connection.

Last night I went into AF again. ARGHHHHHH!!! I have been experimenting with limiting fluid intake during my VMAF episodes in an attempt to hasten the onset of increased sympathetic tone (the body reacts to dehydration by constricting blood vessels through renin/angiotensin and retaining water through ADH and aldosterone) and termination of the episode. This has resulted in an approximately 50% drop in duration time over the previous three episodes of AF. Last night just after going to bed I went into AF after a short burst of bigeminy. I assiduously avoided all fluid intake during the episode and took 500 mg of potassium gluconate at the four hour mark. At 5 AM (the 8 hour mark) I reverted to NSR. Episodes for me usually last 18- 22 hours. This episode occurred despite being at my MTD (maximum tolerated dose) of Mg. However, I continually monitor my ability to induce a leg cramp and they were definitely easier to induce yesterday morning (vs previous mornings). I do this while lying in bed and forming a figure 4 with my legs and then vigorously tensing the calf muscle on the bent leg. Both Mg and K deficiency have been associated with leg cramps and it would appear that my leg cramps are mediated by transient K

deficiency. Upon arising in the AM in NSR my leg cramps were still easily induced. Five hundred mg more K made them more difficult to induce.

Therefore, I would like to suggest to some of you that you might:

1) try monitoring your intracellular K and Mg levels by this crude test each morning to guide you in adjusting that day's Mg and K intake (I take plenty of Mg, so I just only adjust my K supplements accordingly).

2) curtail all fluid intake during an episode of AF to hasten the onset of sympathetic tone (probably only applicable in VMAF). ANP is favorably rebalancing the Na/K ratios during the episode via renal retention of K at the expense of Na and drinking more fluid (K rich, Na poor) would probably enhance this rebalancing. However this fluid might prolong the AF episode, since it would take more diuresis to reach dehydration. This latter could effectively be addressed with K supplements and plenty of Mg water after termination. However, this would probably be more difficult because aldosterone is king in the immediate post AF episode time period. And, as you all know, aldo retains Na at the expense of K.

I've always noticed that my VMAF tends to occur on days that I've skipped my workout. As Hans has pointed out in "the play", ANP is secreted during exercise. Additionally there is more loss of Na (vs K) in sweat, further enhancing this favorable rebalancing of intracellular Na/K. I've also noticed that my episodes tend to occur on days that I've been naughty, e.g., a piece of chocolate at the end of a meal or a cup of Starbuck's hot chocolate, or when I took a drink of some "sweet beverage", e.g., OJ during a high vagal tone time of the day without benefit of low glycemic companion food. Entry of glucose from these high glycemic foods into the blood stream stimulates release of insulin, which then ties up valuable plasma K. This leads me to suspect that my defective substrate is possibly in some way related to impaired glucose tolerance.
I think Jerry has pointed out a very important player in Na. Too much intake of Na and you'll struggle with urinary K wasting. Is this where the LAF hormone connection lies? Is the kidney the defective substrate? This is precisely what makes judicious use of small doses of spironolactone (a potassium sparing diuretic) so titillating. Taking it during an episode would not only hasten the dehydration but also would aid ANP in its favorable rebalancing of intracellular Na/K. After all, Hans has pointed out that higher levels of ANP during AF are associated with shorter episodes. Taking it sporadically during the interval between AF episodes on days when leg cramps were easily induced might remove one from harm's way wrt an impending episode of AF.

Just some more thoughts for you to consider.

PC, MD v54

PC...Sorry to hear of your experience. I find your post absolutely fascinating, and I commend you for the insight you've brought to the experience, and to our understanding of the process. I think you may have something there, in the sense that you continue to cone down the elements, bringing us closer to the kidneys and their role in endocrine function. I really believe that we're closer than ever to the core cause, and that we will be led to endocrine function and ion exchange, membrane integrity...the things we've recently been focusing on. Thanks for your scientific diligence, and I'm delighted to hear that you've cut duration in half. I have to add that my theory of fluid replacement was shot in the butt, since you remained dehydrated and cut duration. Unless you're the odd anecdote, my theory probably doesn't hold water (if you'll pardon my deliberate pun).

Hang in there. Eager to hear more from you.

Jerry

Jerry,

Thank you for reading my post and for your comments. I believe your successful low salt approach is further evidence of the hormone connection. Perhaps the defective substrate is our adrenals (too much aldosterone ?beta defect). But you don't have to understand the process perfectly in order to make pragmatic headway. I just read an article today about a new drug (eplerenone) that does the same thing as spironolactone but without any of the adverse side effects sometimes seen with extended use, e.g., male breasts and irregular menses in women.
http://www.medscape.com/viewarticle/446495
So the beat goes on. I continue to be quite upbeat and confident, like you, that many LAFers need not live in misery and despair.

PC, MD v54

The idea of the endocrine system being directly involved in the pathogenesis of a-fib via the kidneys and the adrenal glands has a lot of merit as far as I am concerned. Here's for why for what it's worth. As I've banged on about previously on the bulletin board, I had a highly traumatic and violent childhood - particularly between ages 9 and 17 - after which I have remained to this day (age 41) a highly anxious individual who has been diagnosed with GAD and OCD. I remember reading on Dr Abraham Hoffer's (sp?) Internet site that one's hypothalamus can during a childhood/adolescence such as my own become chronically stressed (in which state it presumably remains when one is an adult). Such stress in the hypothalamus results over time in an ongoing over-production of Corticotropin Releasing Hormone (CRH) which in turn makes the pituitary over-produce Adrenocorticotropic hormone (ACTH) which in turn BURNS the ADRENAL cortex OUT by over-stimulating the production of cortisol. Some here will be interested to learn that there is an International Symposium on Aldosterone here in London England in 2003 (http://www.bioscientifica.com/aldo03/), such is the current interest in aldosterone and its effects on the cardiovascular system. Perhaps PC could also have a look at http://www.medscape.com/viewprogram/1004 if he hasn't already (-: (I'm assuming he is already a member as is required to read (and fully understand!) the article available).

Of further interest as regards my own history, the adrenal cortex is also responsible for the production of Dehydroepiandrosterone (DHEA) AND TESTOSTERONE. Cortisol, DHEA, and Testosterone ALL compete for the hormone precursor Pregnenolone: if as in my case one was chronically stressed as a child, most of the available pregnenolone is used up for cortisol production with the result being that DHEA and Testosterone can be in short supply. In my case such a shortage of testosterone actually resulted in the onset of puberty being delayed until I was 16 1/2 yrs old. This also added considerably to my anxiety burden as you can imagine. I cannot help but feel that my chronic stress and resultant hormone problems as a child and an adolescent played a highly significant role in predisposing me as an adult not only to GAD etc. but also to palpitations/a-fib via imbalances in my endocrine system - all of which has its roots in my childhood and adolescence. I wonder; has all the afore-mentioned resulted in me over-producing aldosterone today?

Mike F.

Mike F

I think you are absolutely right about the possibility of a traumatic childhood connection. I wrote a bit about it my book (pages 141-144 with lots of references), but you have further elucidated the concept and related it to the hormone connection. I don't believe it is the underlying problem for most afibbers though. The latest LAF Survey specifically asked about childhood abuse and a dysfunctional upbringing - only 25% of 104 respondents stated that they had been brought up in a dysfunctional home.

Hans

Mike...Brilliant, mate. You've added much more evidence to the belief that ALL of these things are tied together. At this point, i have to tell you that I would be looking for someone to show me how the endocrine system is NOT involved in our cardiac disorder. No matter how one analyzes evidence such as yours, it all turns on the hormonal axis.

Very courageous of you to share your background, and I commend you for it.

Hang in there. We WILL suss this out, and solve it! All the best...

Jerry

Hans:

I read your response to Mike re: childhood traumas and abuse. Although I understand what leads you to write that "only 25%" of your survey respondents indicated that they'd suffered such traumas. It would seem that you had hoped to have a far higher percentage acknowledge such problems, if only to eliminate any possibility of naysayers stepping up to say that such early traumas play no part in LAF/AF.

But 25 PERCENT, Hans! My God, that's an ENORMOUS percentage of people, and it is statistically significant, in my opinion. Whenever 25% of people share a common problem within the context of a scientific study, that seems to be very important.

My thoughts, for what they're worth.

Jerry

Jerry,

You are right, 25% is a fair whack of people. However, what I was doing in that particular survey was to try to establish what set afibbers apart from "normal" people. I was unfortunately not able to find any hard data on what the incidence of dysfunctional upbringing is among "normal" people. However, it seems to me that 25% is probably not out of line so I don't believe afibbers are particularly likely to have been brought up in a dysfunctional home. However, if anybody has data that says that the overall incidence of dysfunctional upbringing is way lower than 25% I'll certainly reconsider my opinion.

Hans

PS. The same survey also showed that afibbers were no more likely to have IBS or GERD than are "normal" people.

And just to go sideways, I thought I would post this newsletter, which although does not mention AF, acknowledges the problem of eating intensively farmed meat and fish and the hormonal problems they bring. To me it is sound to try and combat the problem of unbalanced hormones, but if you can source why the problem has come about, then it is better to stop it in its tracks. So for many on high protein diets this should be worth noting. I know intensively farmed meat and fish will bring on AF in me.

Fran

From Dr Berg

If you have ever been to Europe you'll notice that people are not as fat as Americans. Why, you ask? Is it that they eat less fatty food? Do they eat fewer calories? Is it the food combining or the quality?

I've made an interesting observation over the last five years with two things. There seems to be an increasing number of patients coming in my office with thyroid problems, which include fatigue, weight gain, brittle nails, cold intolerance and hair loss. I've also noticed something interesting upon questioning my European patients, upon arriving to American their weight not only dramatically increased but their overall health decreased. They started losing hair, feeling sluggish, developing digestive problems and noticed that their skin worsened.

This interested me. What was the biggest factor that could cause this? I began to dig into this and found that every single one of these patients noticed that the food had no flavor in America. They also told me that everything in America was bigger chickens, turkeys, cows, the Big Gulp at 7-11. When they first arrive to America it was very difficult digesting these foods.

I wanted to isolate factors that could be responsible for these changes. I found some interesting distinctions. Number one Europeans won't buy or accept America's animal products (meats) because they are grown with growth hormones and antibiotics. In fact, these growth hormones given to animals are used for one purpose to increase more weight as fat, which means more profits. Several hormones are used: estrogen insulin-like hormones and growth hormone. Is it possible that those hormones that were injected into animals could somehow go into your body when you eat them? A commercial chicken can be grown in six weeks. You can grow these animals on hormones faster than you can on foods.

The old theory was that eating fat caused you to become fat. Well, Europeans eat more fatty foods than Americans and they're not as fat as Americans. And if hormones make animals grow big and fat, could it also then make you grow big and fat?

And you might say that the hormones in these animal products are in such small quantities that they couldn't affect your human body. This is not true. The Environmental Protection Agency (EPA) even has a subcommittee that studies how our hormones are affected by environmental toxins. These are called endocrine disruptors, which include pesticides, insecticides, growth hormones, etc.. In her book, Hormone Deception, Dr. Berkson states, "The endocrine system responds to tiny quantities of hormone messengers: minute amounts of endocrine disruptors (growth hormones are a big one) can elicit a response and cause changes".

In a recent article in The Wall Street Journal, Perchlorate (a chemical in our water supply) was shown to block the thyroid gland. The thyroid is the main gland that controls your metabolism. So

here you are trying to lose weight with exercise and diet with very little success. Why? Because it is the hormones that are stimulated from the exercise that really trigger weight loss. The principle of the Atkins diet eating protein to lose weight is base on this hormone factor. Protein triggers hormones that dissolve fat. Even drinking coffee with caffeine stimulated hormones that make you feel awake mentally. It's the hormones that are creating the effect.

If you had been eating meats, eggs cheese contaminated with these hormones over the years, your body has been accumulating these hormones. They actually get stored in your fat cells. And at some point they start to wreak havoc on your hormone system.

What can you do? Start to eat more organic foods, especially meats, eggs and even fish. Farm-fed fish are even grown with hormones nowadays. You could even find a healthcare practitioner who can detoxify these chemicals from your glands. The Body Restoration Technique was developed to do this. For more information go to www.bodyrt.com.

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Thanks for the response/comments. Another thing of note which I forgot to add to my posting was that once I emerged from puberty at age 17 1/2 yrs, I developed a horrendous under-arm sweating problem which lasted for approx. one year. Not smelly or anything, just a massive out-pouring of watery sweat which - rather embarrassingly - SOAKED its way through all my clothes in summer OR WINTER - even thro a leather bomber jacket (I can still remember huge white salty circles manifesting themselves on the outside of the leather jacket which I used to have to repeatedly wash off). I got some special stuff from the doc to rub under my arms - it made little difference, but the problem seemed to resolve on its own at a later stage anyway. I'm mentioning this since I believe it once more dovetails in quite nicely with the overall hormonal/endo imbalance scenario of my late teens. Ironically, having had such a delayed onset in puberty, I now find myself as hairy as a bear!! From one extreme to the other. I also show some male pattern baldness - not as much as I thought I would be showing by age 41 given how badly my hair used to fall out when I was in my early 20s. I used to wake up with a load of hair on my pillow when I was 22-23-ish, and am amazed that the situation arrested slowly as further years went by with the result that I still have ANY hair left on my head today! I guess that once my testosterone (aldosterone) production DID kick in at age 16-18, it REALLY kicked in.....

I wonder if my hirsuteness today is a continuing manifestation of that same over-compensatory hormone production?? Whilst I know all of the contents of this post and the before all relate to me specifically as opposed to a-fibbers in general, I still think that my words are of significance to us all here as regards how hormonal imbalances can so drastically affect one's physical functions in general. I still cannot help but think that my own problematic childhood and adolescence set me up not only for drastic endo imbalances at the time, but also more subtle ones for my later future as an adult. I wonder, does anyone reading agree (or have read (or are aware of) any evidence suggesting) that a swing from under-producing to over-producing hormones could have left me with a resultant and subsisting aldosterone problem today??

Mike F.

Yes, to your last question, Mike. But only a true physician would be able to say for certain. As to the pattern baldness, that comes about when testosterone breaks down to dihydrotestosterone (DHT). You can do yourself, and your prostate, a favor by taking a daily dose of the following:

* 160-320 mg of standardized extract of Saw Palmetto [NO BERRIES!]

* 100 mcg of Selenium [yeast-based, not the selenite]

* Continue with your Vitamin E (200-400 IU]

* 10-15 mg of Lycopene [stronger antioxidant than beta carotene]

* You can get wonderful lycopene content from a 1/2 cup of cooked tomato products, such as pasta sauce, tomato paste, even from tomato juice.

Every day for the rest of our lives, mate.

Jerry

Mike F.....I appreciated your post regarding your childhood difficulties and your present situation. They sound very familiar to me.

I also had a rough childhood and my onset of puberty was delayed later than everyone else. Fascinating and you're sure right about that itself being a major cause of anxiety!

I have not been diagnosed with GAD, but feel like I could be. I have adrenergic type LAF and wonder if many of us would have similar situations-the 25% from the survey.

Rick S.

If aldosterone is the villain, why are not ACE inhibitors and/or ARB's the hero? Is it because afibbers (LAF's) do not see themselves as having a (very early stage) hypertension problem. During a physical, I admitted to the doctor that I had a low-grade hypertension problem (even though my blood pressure was very healthy by his measurement at the time) and that I had episodes of irregularly irregular beats. He put me on Diovan for the hypertension – my hypertension is now well-controlled -- and I have not had another episode of afib since and the PACs have gone away for 2.5 months and counting. Diovan is the only drug that I have ever taken for heart issues so I am a relatively naive subject. I am fairly certain that my low-grade hypertension is a response to work-related stress. I also modified my behaviour (no alcohol, no coffee and no more than 30 minutes of exercise at a time). I am 52 years old.

Tim C

Tim C.,

Thank you for sharing your experience with Diovan (valsartan). This may add a very important piece to the LAF puzzle. As you know from "the play", I believe excessive and persistent aldosterone levels could be the underlying cause of LAF. The fact that you have experienced no LAF episodes for 2.5 months while on valsartan would tend to support this hypothesis.

Valsartan acts selectively on AT1, the receptor subtype that mediates the known cardiovascular actions of angiotensin II, the primary vasoactive hormone of the renin-angiotensin system.

Valsartan blocks the physiologic actions of angiotensin II, including the narrowing (constriction) of blood vessels and the secretion of aldosterone in both the adrenals and heart tissue. Valsartan also helps prevent potassium wasting.

Clearly, valsartan fits the profile of a drug that may be helpful in combating the "villain in the play" and your experience shows this might indeed be so. Now the big question is, "Has anyone else out there tried valsartan (Diovan)"?

Hans

Hi Hans

I just did a search in my database (http://www.dialsolutions.com/af/database/index.html)

6 out of 324 people (<2%) have tried it - none reported anything positive about it and there are at least 2 negatives, though I'm not sure much can be read into this given the small numbers.

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James D

Tim,

Can't thank you enough for your excellent post on ACE inhibitors/ARB's and their nomination as "heroes".

First of all, this need not be an all or none proposition. ACEIs/ARBs are heroes to many, as is spironolactone et al.

Second of all, angiotensin is not required for all aldosterone activity. There are other pathways. See page 8 of Mike's fabulous find (http://www.medscape.com/viewarticle/422919_8).

Thirdly, that same article (last three pages) shows several very pertinent graphs detailing with what happens when eplerenone is added to either ACEIs or ARBs. There is a definite improvement in results wrt lowering blood pressure in both cases (http://www.medscape.com/viewarticle/422919_16).

Fourthly, I'm still voting for ANP or another K sparing diuretic (?eplerenone), because of the absence of adverse reactions/side effects in eplerenone. As James indicated, the ACEIs and ARBs are fraught with difficulty in this area.

PC, MD v54

I was one of the 25% in the survey. I had vagal AF. I actually had early onset puberty (9). I thought I might have had GAD but Dr's would not accept it. They told me that I was mixing up anxiety with depression (absolutely wasn't). I suppose early onset puberty could have as much impact as late onset. Don't know really, but feel that early childhood trauma certainly has a role to play on stress and resulting hormonal imbalances. But really feel that the food we eat has just as big an impact as it can only make hormones etc. from the fuel we put in, and if it is not balanced or we cannot digest it then.....

Fran