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<http://www.afibbers.org>

## **VIRTUAL LAF CONFERENCE**

Proceedings of 59<sup>th</sup> Session  
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### **SUBJECT: Dysautonomia and LAF**

The autonomic nervous system (ANS) controls the body's internal organs including the heart and digestive system and is responsible for regulating blood pressure. It has its origin in the hypothalamus region of the brain from where it divides into two branches – the sympathetic (adrenergic) branch and the parasympathetic (vagal) branch. An imbalance in the ANS is termed dysautonomia. Dysautonomia can manifest itself as chronic fatigue syndrome, irritable bowel syndrome, panic attacks, inappropriate sinus tachycardia (elevated heart rate not caused by exertion), fibromyalgia and vasovagal syncope.

The late Dr. Philippe Coumel of the Lariboisiere Hospital in Paris discovered in 1982 that a dysfunction of the autonomic nervous system also plays a major role in lone atrial fibrillation. He concluded that lone atrial fibrillation only develops when three conditions are met:

1. The autonomic nervous system is dysfunctional (dysautonomia)
2. The heart tissue is abnormally sensitive and capable of being triggered into and sustaining an afib episode
3. A trigger or precipitating cause capable of initiating an afib episode is present.

The cause of dysautonomia is most often unknown, but the condition can be inherited or can be precipitated by viral illness, trauma involving the ANS, or exposure to certain chemicals. There is no known cure for dysautonomia, but anti-depressants and anti-anxiety drugs may sometimes be helpful in controlling the condition.

The above pretty well sums up the current knowledge about dysautonomia. More details can be found at:

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

and (courtesy of Ella)

<http://heartdisease.about.com/cs/womensissues/a/dysautonomia.htm>

It is clear that dysautonomia plays a major role in lone atrial fibrillation. What is not clear is what causes the majority of cases of LAF. Early surveys have established that it is not viral illness, exposure to chemicals or trauma. So what is it?

Another important question of course is, what practical measures can be taken to eliminate or at least control the dysautonomia underlying afib?

With these two questions I would like to start our 59th conference session on "Dysautonomia and LAF".

**Hans**

Thanks for the topic Hans - just to play devils advocate right from the start :) ....

The conundrum I've always had is that, whilst I agree with Coumel's 3 points, I believe AF can also occur when only points 2 and 3 are true. (i.e. if points 2 and 3 are met you can go into AF with a perfectly normal autonomic system.)

I'm still of the (unpopular) opinion that many of us who describe our AF as vagal probably don't have an abnormal ANS - just that a normally slow heart rate (e.g. 50 bpm resting/sleeping) is enough to produce an ectopic to kick start AF. Figuring out whether the ectopic is due to abnormal quantities of acetylcholine or norepinephrine or due to some abnormal cells is beyond me. The problem is of course made harder in the moderately fit since vagal tone can be higher but I believe would still be considered 'healthy normal' in all but the extremely athletic.

Assuming that AF can exist in the presence of a healthy ANS as well as in the presence of an abnormal one what can we do to distinguish the two groups? The reason I believe it's important to distinguish the two groups is of course to do with which bit our body's we need to fix. If you have an abnormal ANS it's a good idea to take steps to try fix it but if you have a normal or moderately fit persons ANS should we be doing anything with it?

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[James D](#)

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This site below is from the National Dysautonomia Research Foundation and has a heap of info on the subject. It is especially useful to educate yourself about Dysautonomia's causes and symptoms.

<http://www.ndrf.org/NDRFHandbook.htm>

I should have added the home website link above for the National Dysautonomia Research Foundation as follows:

<http://www.ndrf.org/index.htm>

I never knew that mitral valve prolapse was a dysautonomia.

Also scoliosis (slightly twisted and offset spine) that I and some other afibbers have been diagnosed with is also a dysautonomia. Scoliosis was discussed in the Conference Room topic on height and chest measurements that PC initiated.

***Dean***

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Hi Hans,

You've chosen another rather provocative topic.

I have a few thoughts FWIW. With all due respect to Prof Coumel, I agree with James in that points 2 and 3 seem sufficient to initiate AF.

Both pathologic and physiologic AF require triggering PACs, less for the former and more for the latter. However, in both they appear to arise predominantly in the PVs as they enter the left atrium. Otherwise, PVI would not be effective in both.

However, in pathologic AF the maintenance substrate appears to be irreversible microfibrosis, whereas in LAF it appears to be reversible autonomic tone and attendant changes in refractory period.

IMHO the dysautonomia is more a consequence and than a cause. Many studies have demonstrated increased natriuretic peptides during NSR in LAF.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=16715186&query\\_hl=2](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16715186&query_hl=2)

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=15629379&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15629379&dopt=Abstract)

These hormones cause urinary sodium (and water) wasting (not to mention magnesium wasting). This results in chronic hypovolemia (low blood volume). Because of the latter, there is a compensatory increase in sensitivity to catecholamines to maintain blood pressure. This leads to the dysautonomia - panic attacks, anxiety disorders, etc.

Mitral valve prolapse also causes an increase in secretion of natriuretic peptides => dysautonomia via the same mechanism.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2952778&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2952778&dopt=Abstract)

In summary IMHO increased vagal tone contributes to creation of the reversible maintenance substrate. The trigger substrate (dilated PVs) is created by atrial distention due to hypertension in pathologic AF and to MVP/mild mitral regurgitation in LAF.

<http://www.atrial-fibrillation.org/showabstract.php?pmid=12154327>

Vagal tone alone cannot explain the increase in PACs during vagal maneuvers. Increased left atrial and PV stretch caused by gravitational changes during such maneuvers can. PACs are more frequent because LAFers are more sensitive to adrenergic stimulation (?dysautonomia) => enhanced automaticity.

## **PC**

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To approach this topic anecdotally, I should report that I never experienced "panic attacks" or "anxiety" before my ablation - even over fifteen years of enduring many hours of afib. However, they came on full force along with syncope AFTER my ablation. The symptoms were disabling. "Anxiety" or "panic attacks" could be brought on by any loud and noisy situations, crowds of people and demanding social situations. Sometimes they occurred without any apparent cause. There was a feeling of being overwhelmed, diaphragm restriction and not being able to breath. The syncope (fainting) hit without warning - "out of the blue."

My GP attributed this to a disturbance of the ANS (dysautonomia) caused by ablating nerves. My electrophysiologist prescribed Cylexa, to see if it would rebalance my ANS, but several doses of that threw me into a profound depression. Fortunately, when I stopped that drug, I came out of that quickly.

Fortunately, the symptoms I have described disappeared last November. Occasionally I feel "off" and "shaky," but usually something simple like drinking a lot of water (dehydration) or eating something salty seems to help rebalance my system.

## **Carol**

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James,

You raise an interesting point and I agree that it may be possible that points 2. and 3. are enough to start an afib episode; however, I am not aware of any medical evidence to that effect as far as lone atrial fibrillation is concerned. On the other hand, there is considerable evidence that most afib episodes are preceded by a change in the balance between adrenergic and vagal branches of the ANS. If the ANS is unable to cope with changes in the balance without precipitating an afib episode then I would suggest that it is dysfunctional (dysautonomia).

I discussed the ANS imbalance preceding an episode on pages 19-21 of my first book. Here is a sample quote:

"Swiss researchers recently reported that vagal afibbers whose AF originates from foci in the pulmonary veins experience an increase in adrenergic tone about 15 minutes prior to the onset of an episode. However, with time, the adrenergic response diminishes and just before fibrillation begins, the vagal branch becomes dominant."

## **Hans**

Hello PC,

I think your statement: "IMHO dysautonomia is more a consequence than a cause" is profound. I am not sure what can be done about reducing the level of natriuretic peptides in afibbers, but if a way could be found then it would seem that that might be effective in managing afib episodes involving dysautonomia, not to mention the potential in dealing with panic attacks, IBS and related conditions.

### **Hans**

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IBS. Please will somebody relate IBS to dysautonomia for me, who am something of an ignoramus? What do IBS and afib have in common? There must be something, because so many afibbers have IBS too. Hans, is your IBS better since your ablation?

### **PeggyM**

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The typical episode of LAF is preceded by increasing PACs (?increasing sympathetic tone due to stress, dehydration, ...) followed by a vagal maneuver that seems to trigger the attack. This would certainly fit with the Swiss article referenced by Hans' in his book.

However, autonomic tone preceding episodes of LAF may manifest either increasing sympathetic tone or increasing vagal predominance.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=10353133&query\\_hl=20](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10353133&query_hl=20)

"Moreover, sympathetic and vagal activity do not exclude one another; both may be active at the same time. In fact, vagal effects are more pronounced in the presence of high sympathetic tone and vice versa ("accentuated antagonism") (Levy 1971).

Furthermore, autonomic considerations are not limited to LAF. They are also important in pathologic AF. However, only sympathetic tone appears to play a role here.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=9874080&query\\_hl=20](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9874080&query_hl=20)

As to the question of whether LAFers and those without LAF are innately different wrt some level of autonomic dysfunction, this is far from clear.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=14522493](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14522493)

IMHO it may not be the autonomic tone itself that wreaks the havoc, but the nonhomogeneous distribution of autonomic nerve fibers around the PVs and atria. Is this dysautonomia? Is this genetic? Is this latent from birth, awaiting sufficient PACs to trigger LAF later in life?

How to counter the deleterious effects of natriuretic peptides?

The heart has been tricked (? by a mischievous mitral valve) into thinking that it is experiencing heart failure (backup in the plumbing). The resulting stretch of heart cells causes secretion of natriuretic peptides. Theoretically if one were to neutralize these peptides, adrenergic hypersensitivity (?dysautonomia) might disappear and with it our PACs and ?LAF. In pathologic AF this might be counterproductive and worsen their organic heart disease.

### **PC**

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I think an explanation on how the autonomous nervous system interacts with the heart is in place. The following is taken from a synopsis of chapter 3 from the book: Investigative Electrocardiography in Epidemiological Studies and Clinical Trials. Section 3.5

[http://www.springer.com/cda/content/document/cda\\_downloaddocument/9781846284656-c3.pdf?SGWID=0-0-45-335294-p165266125](http://www.springer.com/cda/content/document/cda_downloaddocument/9781846284656-c3.pdf?SGWID=0-0-45-335294-p165266125)

### 3.5 Neurohormones and other Receptor Stimulating Agents

The heart responds to demands for increased cardiac output during stress by increasing the heart rate and contractility. This occurs as a response to adrenergic neurohormones released at postsynaptic nerve terminals. A complex of proteins within the cardiac sarcolemmal membrane, including adrenergic receptors and an effector enzyme, adenylyl cyclase, initiate a series of biochemical processes. Among these processes as the end result of positive inotropic and chronotropic response is the synthesis of an intracellular second messenger cAMP and phosphorylation of protein kinase (PKA).

The receptors, categorized as alfa- and beta-adrenergic, muscarinic, and purinergic types, modify the functions of various ionic channels and pumps through receptor–effector coupling systems. Activation of one type of receptor can also influence other receptor types. For instance, beta-1-adrenoreceptors and M2 muscarinic receptors have antagonistic features in their actions.

The autonomic nervous system, acting on the receptors, modulates cardiac rhythm and may contribute to the effects of antiarrhythmic or proarrhythmic agents. Modified receptor functions can influence impulse formation and initiation and propagation of action potentials.

#### 3.5.1 Beta-adrenergic Receptor Stimulation

Beta-adrenergic receptor stimulation acts on various potassium channels only IK1 is apparently not affected), on ICa-LL, ICl, If (also sodium channels under some conditions), and it can enhance Na/K pump activity. Beta- adrenergic stimulation or agonist action can thus be expected to have a variety of manifestations under different conditions. Shift of the If activation curve towards a more positive potential produces a chronotropic effect in the SA node and enhances latent pacemaker activity at ectopic atrial and ventricular sites. Increased L-type Ca<sup>2+</sup> current enhances contractility (increased intracellular Ca<sup>2+</sup>) and it could also induce triggered activity due to early as well as late afterdepolarizations.

The effect of b-adrenergic receptor stimulation on potassium channels can be expected to shorten the refractory period. Spatial heterogeneity in the distribution of Ito channels (present in subepicardial and M cell regions only) could conceivably induce increased dispersion of the end of the refractory period. In the AV node, combined Ca<sup>2+</sup> and K<sup>+</sup> effect may shorten AV node refractoriness and speed up AV conduction. In a healthy heart the conglomerate of the above actions will produce shortening of the QT interval, sinus- and at times ectopic supraventricular tachycardias.

Of the several subtypes of alfa-adrenergic receptor–effector coupling systems, subtypes of alfa-1-receptor are linked to effector systems that modulate impulse initiation and APD. Their stimulation effect on the Na/K pump may suppress the tendency to ectopic pacemaker-type activity in the atria. The potential role of beta-adrenergic receptors (I think this is a misprint. Should be: alfa-1-adrenergic Gunnar) in arrhythmogenic mechanisms in humans is unclear.

#### 3.5.2 Muscarinic Cholinergic Receptor Stimulation

The M2 muscarinic receptor is the main cardiac muscarinic receptor. It is particularly important in the atria where its density is five times higher than in the ventricles. Whereas the ventricles are dominantly under beta-adrenergic control, the atria are strongly under vagal control. Vagal stimulation, muscarinic activation, and muscarinic agonist action (digoxin) have antagonistic adrenergic effects. Muscarinic effect is blocked by atropine. In the atria, muscarinic activation effects include a decrease in If and suppression of the SA node through increased conductance of the muscarinic K<sup>+</sup> channel, thus slowing down the heart rate. An increase in IK(ACh) hyperpolarizes atrial myocytes and shortens atrial APD. A decrease of the SA node impulse rate increases atrial APD in linear proportion, and the direct vagal effect has a simultaneous opposite effect by shortening atrial APD.

At the level of the AV node, the antiadrenergic effect of muscarinic activation on Ca<sup>2+</sup> and K<sup>+</sup> currents contributes to decreased conduction. Muscarinic activation can be expected to be effective in supraventricular arrhythmias and arrhythmias involving the AV node. In humans, an antiarrhythmic effect at the ventricular level has not been documented.

### 3.5.3 A1-purinergic Receptor Stimulation

The cardiac purinergic (adenosine) receptor–effector coupling system is called A1. It apparently has the same effector coupling pathway as the muscarinic receptor. Adenosine is effective in terminating tachycardias where the AV node is in the re-entrant pathway. Adenosine A1-receptor agonists increase the resilience of ventricular myocardium to ischemic injury even several hours after experimental coronary occlusion and reperfusion.

#### ***Gunnar***

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Peggy,

Both atrial fibrillation and IBS (irritable bowel syndrome) involves an imbalance in the autonomic nervous system. See:

<http://cat.inist.fr/?aModele=afficheN&cpsidt=2389314>

I am aware that many afibbers have IBS as well, but my LAF Survey IV did not find the rate (16%) among afibbers higher than the estimated prevalence among the general population (15-20%).

And yes, my IBS has indeed disappeared since my successful ablation. Whether this is due to the ablation or due to my markedly reduced stress level following the "good riddance" of afib is difficult to say.

#### ***Hans***

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I agree that points 2 and 3 are enough to provoke ectopics and AF. I believe that there may be a compounding dysautonomia but it may be similar to "The Perfect Storm" with a combination of low resting pulse, increased vagal stimuli and a burst of sympathetic tone creating a cardiac symptom complex of ectopic cardiac activity.

Prior to the dramatic improvement in symptoms I have had with elevation of the head and thorax when sleeping, I had the classical presentation as described in PC's source documents. I would be deeply asleep and either awakened by something (phone call or need to urinate) or too rapidly change position and I would either develop a brief episode of regular tachycardia or numerous PACs or both. The PACs often being every third or fourth beat and not going away until I would get out of bed and jog in place. My usual resting pulse is 47.

Since I have started consistently sleeping with my upper body above my stomach, I only have symptoms on the occasional night I slip down or eat a large meal immediately before bed and also slip down off the incline. This leads me to believe that the combination of low resting pulse, vagal stimuli accentuated by acid reflux and an episode of sympathetic drive all interplay to create PACs (and AF). The change in my condition for the better and the fact that I can return to my previous condition (of ectopic activity) by merely eating a large meal and sleeping flat, convinces me that attention to factors such as GERD which can enhance vagal stimulation should gain a lot more attention.

It is possible that the heart and the relation of the pulmonary veins to ectopics are all similar to the body's febrile response to some pathogen. In other words fixing the heart or ablating the pathway which allows the ectopic behavior might not be as helpful as going after any cause of excessive vagal tone (similar to treating the pathogen rather than the fever in infectious diseases), particularly in those who have a low heart rate to begin with. I think what confuses the picture is that the symptom begets more symptoms or the heart gets more irritated the more that it beats irregularly and then the initiating causes need lower and lower thresholds.

What has been particularly rewarding is that the day time PACs have decreased along with the nighttime episodes. I also have been able to reduce my dosage of proton pump inhibitors as the GERD symptoms lessen.

PC, excuse my ignorance but what does "IMHO" stand for?

#### ***Lee***

Hi Lee,

IMHO = in my humble opinion.

FWIW = for what it's worth

Sorry for being so lazy.

**PC**

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Hi Hans, I can accept that

Quote:

"On the other hand, there is considerable evidence that most afib episodes are preceded by a change in the balance between adrenergic and vagal branches of the ANS."

but I guess the point I'm trying to make is in how many LAFers is that change abnormal? I suspect you'd see very similar ANS changes in healthy individuals too - they just wouldn't lead to AF - though in some they may lead to a couple of ectopics. I can even accept that the time when an AFer is most likely to go into AF is during this change in ANS but I've yet to see much evidence that these changes are abnormal in the majority of LAFers (except in a few elite athletes - if my memory is working even one of the recent studies on elite athletes only found about half of them to be 'vagal').

Quote:

"If the ANS is unable to cope with changes in the balance without precipitating an afib episode then I would suggest that it is dysfunctional (dysautonomia)"

If the HEART is unable to cope with normal changes in ANS I'd suggest it wasn't dysautonomia. (i.e. the ANS doesn't need to be fixed)

Maybe the question I'm trying to ask is what qualifies as a dysfunctional ANS and is it really the case that the majority of Lone AFers have one?

Apologies if I'm dragging this thread off topic. I'm still interested to read comments on what can be done for those people who do have dysautonomia (as well as figuring out if we have it).

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[James D](#)

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Dean, thank you for that url to the NDRF Handbook. I would like to recommend that handbook for its primer on the autonomic nervous system. It is written for comprehension by people without a medical background, and it is very, very good. Have not yet made it thru the whole handbook yet [springtime and garden matters are pressing] but am working in that direction.

**PeggyM**

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I'm sorry...I incorrectly posted as a new topic before: Again, just to add to the complexity of ANS & LAF:

#### **[AB47-2] ABLATION OF A CASE OF SPEECH INDUCED ATRIAL FIBRILLATION**

Peter L Gallagher, MD, Julie Griffin, PA, Greg McCloney, PA, Hesselson Aaron, MD, Tomassoni Gery, MD. Central

Baptist Hospital, Lexington, KY

Introduction: Paroxysmal atrial fibrillation (PAF) is frequently initiated from the pulmonary veins (PV). The clinical triggers for PAF are diverse. During RFA, high dose isoproterenol, aggressive atrial burst pacing, neural ganglia stimulation and induction of AF are used to map the initiator sites for PAF. We report the first case of a non-cardiac trigger for PAF (speech), which was mapped and ablated. Methods: N/A Results: The patient is a 68 yr old female librarian. She presented to the arrhythmia clinic with a 2 yr progressive course of intermittent, severe fatigue. Her symptoms were noted to worsen during family gatherings, work meetings, emotional church sermons and while talking on the phone. A routine Holter monitor revealed frequent bursts of rapid PAF. She was initially treated with Propafenone SR with no improvement and could not tolerate Sotalol. While on telemetry for Dofetilide, the patient was noted to have frequent bursts of rapid PAF, only while talking. With one or two words, she would have a 7-8 beat run of PAF, with longer sentences, her PAF could last minutes. An MRI of the chest was normal. Cessation of speech would reliably restore sinus rhythm. After an initial slight improvement on Dofetilide, her symptoms returned. She underwent a diagnostic EP study and RFA for her PAF. She was noted to have a large common LPV ostium and normal appearing RPV's. While in the awake state, the patient repeated the word, "Mississippi". Using remote-magnetic navigation (4mm Navistar-RMT, Biosense-Webster) and 3D electroanatomic mapping, a detailed 3D reconstruction of the left atrium and the PV's was created while mapping the trigger beat. The source of the speech-induced PAF was from the anterior, ostial LSPV. A 3.5 irrigated-tip ablation catheter (Thermacool, Biosense-Webster) was used to isolate the LPV at the antral level. After isolation of the LPV, speech could no longer induce PAF. At 3 and 9 months follow up, the patient has had no more PAF. Conclusions: This is the first reported case of speech initiated PAF. This represents the first non-cardiac trigger successfully mapped and ablated and strongly supports a complex link between neural activation and the PV myocardial sleeves.

## **Peter**

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Hello James,

It seems that we agree that most afib episodes are preceded by a change in the balance between the adrenergic and vagal branches of the ANS. Where we may, if I understand you correctly, have different opinions concerns the question: "Does this imbalance initiate afib?" I believe it does in most cases and I am not alone in this belief. The 2006 Guidelines for the Management of Patients with Atrial Fibrillation contains the following statement: "Autonomic influences play an important role in the initiation of AF." The guidelines also clearly recognize the existence of an adrenergic and a vagal form of AF.

Of course, the initiation of afib also requires a "dysfunctional" heart and this is the second point in the triad I described in my lead-in posting:

2. The heart tissue is abnormally sensitive and capable of being triggered into and sustaining an afib episode.

The third component, triggers, is interesting in that many of the more common ones are known to directly affect ANS balance. Again, if I understand you correctly, your question is: "Does exposure to known triggers affect the extent of ANS imbalance differently in afibbers and non-afibbers?" I am not aware of any research that directly compares the extent of imbalance between the two groups. However, there has been some research as to how various triggers influence HRV. One article that looks like it may be of interest is:

"The role of genetic and environmental influences on heart rate variability in middle-aged men."(1)

I'll take a look at that when time permits and see if it contains concrete HRV data that can be compared to that available for afibbers. Until then, I guess the question remains unanswered.

## **Hans**

(1) Uusitalo AL, Vanninen E, Levalahti E, Battie MC, Videman T, Kaprio J. The role of genetic and environmental influences on heart rate variability in middle-aged men. *Am J Physiol Heart Circ Physiol*. 2007 Mar 30; [Epub ahead of print]

Hi Peter,

That is a most interesting article. However, given the association of swallowing and AF, belching and AF, gastric distention and AF, etc., I'd hardly say this was the first reported case of a non-cardiac trigger associated with AF.

The vagus is of vital importance in speech. This would appear to represent another example of 'innocent bystander' effect (v. inflammation) in triggering AF.

**PC**

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Hi Hans,

It appears from reading the abstract of the article to which you referred that genetics is more important than environment in dictating HRV. The exact interpretation depends on what they mean by "unique environment effects."

If this is true and if one takes HRV as a proxy for vagal tone, then VMAFers may represent latent dysautonomics who subsequently express AF when sufficient trigger substrate (dilated PVs) develops.

One problem with this approach is that it assumes that a certain level of vagal tone/HRV => AF becomes inevitable. Yet we all know that this is not true.

I think that the predominant genetic input to LAF comes on the trigger substrate side and not the maintenance substrate side. As the genetically determined factors that lead to dilatation of the PVs work their 'magic' over the decades, the pre-existing maintenance substrate combines with this trigger substrate that has reached threshold value to express LAF.

Does one define dysautonomia as a condition affecting trigger substrate or as one affecting maintenance substrate? IMHO the dysautonomia (sympathetic) potentiates the trigger substrate but does not create it. Does one include strong vagal tone as an expression of dysautonomia? High HRV is an independent prognosticator of longevity and I consider usage of the term dysautonomia to include high vagal tone as inappropriate, as I do including LAF a form of incipient pathologic AF.

Obviously both substrates are vital. AF can be induced in virtually all dogs by fast pacing or adenosine (a vagotonic) => exaggeration of either trigger substrate or maintenance substrate can create AF. Perhaps in extreme cases only one of the three conditions need exist to initiate AF.

**PC**

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Hi Hans, sorry I'm not getting my message across. I think we are all in agreement that a change in the balance between the adrenergic and vagal branches can initiate AFib. You're calling this change an "imbalance" but I'm saying these changes happen all the time in everyone and are perfectly normal. The question is in how many LAFers are these changes out of the ordinary. (Only at that point would I call it dysautonomia).

PC is asking some interesting questions - surely we can't call something a dysautonomia because of the way a substrate responds to the ANS? Only when the ANS is itself malfunctioning is the label useful.(i.e. when "1. The autonomic nervous system is dysfunctional (dysautonomia)") If something is responding badly to a normal ANS then we should attach a label to the response rather than to the ANS. Otherwise, how does this help the diagnosis - it feels about as useful as labelling something as idiopathic.

I've just pictured a yellow post-it note stuck on the heart that reads 'fix this'. I imagine that as well as the heart you are wanting to stick a post-it note somewhere on the ANS? (I'm not convinced many LAFers will need it on the ANS)

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**James D**

James,

I agree with you 100%. I think it is generally normal variations in ANS applied to a heart with substrate issues.

An example is described in my recent post: <http://www.afibbers.net/forum/read.php?f=6&i=8468&t=8468>. It was the post roll in the hay vagal tone increase applied to a heart with an irritated substrate due to electrolyte issues and my recent lack of electrolyte intake that caused afib.

### **George**

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Can a form of dysautonomia occur as a result of prolonged exposure to stress?

I can imagine that after a long stress bout (several years) the sympathetic branch of the ANS would tend to dominate the ANS. If so, could the ANS be restored to balance after the stress is removed?

I asked these questions based on some personal history.

When in my very early 20's, I had what I now recognize as several short episodes of AF. They only lasted from seconds to about 10 minutes. At the time I was under a lot of stress. I was not sleeping well, emotional and full of fear and doubt.

Segue to my 30's. I am confident, enjoying success in life and work. Everything is the exact opposite of my 20's. I start a fitness campaign and quickly improve my fitness level. No AF episodes at all.

Everything is peachy keen until my youngest daughter turns about 14 (I am then about 55) and all hell breaks loose. She has our house in a constant uproar and stress with all the symptoms creeps back into my life. After about 2 years of this stress environment, AF comes back.

I recognize that everyone agrees that stress is a trigger but in keeping with points made by James D. and PC, without some type of substrate issue, a trigger should not produce sustained AF. However, when I was 21, I doubt if I had any substrate issues and I had several bouts (albeit short) of AF. Also after I started fitness running in my early 30's, surely my heart chambers enlarged, vagal tone increased, etc. and this did not cause any AF at that time.

Now that I am 60, I can believe that I have some less than ideal substrate and my AF episodes now last longer than the 10 minutes typical of my 20's.

I guess my point is that I would tend to agree with Dr. Coumel's 3 requirements list for AF. My primary question is can the ANS be rebalanced?

### **Larry Zajdel**

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Could ingested minerals, either as food or supplements, affect the nerve cells of the autonomic nervous system in a manner similar to how they are believed to affect heart cells? Could this be a way that potassium and magnesium supplements affect afib, i.e. through their effect on the ANS?

### **Bob K.**

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To Hans and all~

Thanks for this discussion opportunity. In previous BB posts, each time dysautonomia was mentioned, I was always puzzled as to what exactly that meant in terms of afib rather than the obvious definition of dysautonomia. When I began reading for relevancy, I found quite a bit linking dysautonomia to genetics and auto-immune disorders. Perhaps, the latter is a link worth following to see how many have been tested. Dysautonomia has also been mentioned in discussions of oxidative damage to endothelial tissues and in neuropathies associated with diabetes and it probably

also occurs in the early pre-diabetic stages known as Metabolic Syndrome.

Humor me a bit while I offer some musings...

When the term 'substrate' is mentioned...(I didn't see a definition in Hans' glossary)...I'm not sure what that means. I'd like to see a collective opinion from our brain trust here as to exactly what that references when we use it in terms of atrial fibrillation. The medical dictionary indicates:

Substrate: <chemistry> A substance upon which an enzyme acts. Origin: L. Stratum = layer

[I worked ten years for a chemical company that produced 'substrate treatments for metal prior to painting' and in that frame of reference, I see it as another chemical layer or in the case of that product, a solution used in a process that actually formed a chemical bond with the metal and thereby gave it 'tooth' for paint adherence.]

But for atrial fibrillation, I'm having a difficult time with the use of the word substrate and I'd like some help to get this straight in my mind as to what 'layer' we are referencing and where that may occur.

Thanks for you indulgences. Since my research went far and wide on the topic, following are a few studies that may be of interest if readers have not seen them on the variety of circumstances where dysautonomia is mentioned.

Healthy regards to all,

**Jackie**

Subject: dysautonomia

<http://neurology.jwatch.org/cgi/content/full/2003/905/3>

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list\\_uids=12783421&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=retrieve&db=pubmed&list_uids=12783421&dopt=Abstract)

Comment:

So-called acute and subacute dysautonomias have long been suspected to be autoimmune disorders, but chronic dysautonomia is believed to be a degenerative disorder similar to Parkinson disease with accumulation of -synuclein in peripheral autonomic nerves (Neurology 2001; 56:980).

However, the current report strongly suggests that chronic dysautonomia can in some cases be an autoimmune disorder caused by nAChR autoantibodies. The correlation between antibody titers and symptoms of impaired cholinergic neurotransmission in this study supports a pathogenic role for these antibodies. Alternatively, a degenerative disorder of autonomic nerves may expose the antigen and lead to secondary generation of autoantibodies. Patients with autonomic failure -- particularly those with prominent cholinergic impairment, no evidence of a sensory or motor neuropathy, and no symptoms of CNS dysfunction -- should be tested for the presence of nAChR antibodies in serum.

The results may have diagnostic and potentially therapeutic implications, as preliminary reports indicate that acute, presumably autoimmune, dysautonomias have been successfully treated with intravenous immunoglobulin.

— Horacio Kaufmann, MD - Dr. Kaufmann is Associate Professor, Mount Sinai School of Medicine, New York City.

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*Ann Neurol.* 2003 Jun;53(6):752-8.

*The spectrum of autoimmune autonomic neuropathies.*

Klein CM, Vernino S, Lennon VA, Sandroni P, Fealey RD, Benrud-Larson L, Sletten D, Low PA.

Department of Neurology, Medical University of South Carolina, Charleston, SC, USA.

We analyzed the clinical characteristics of 18 patients (13 female, 5 male) who had autoimmune autonomic neuropathy (AAN) and ganglionic acetylcholine receptor (AChR) autoantibodies. Mean age was 61.4 years (standard deviation, 12.0 years). Ten patients had subacute symptom onset, six with an antecedent event. Eight patients had chronic AAN, characterized by insidious symptom onset, without antecedent event, and gradual progression.

A majority of patients with high antibody values (>1.00 nmol/L) had a combination of sicca complex (marked dry eyes and dry mouth), abnormal pupillary light response, upper gastrointestinal symptoms, and neurogenic bladder. Chronic AAN segregated into two subgroups. One subgroup (N = 4) had low antibody titer (0.09 +/- 0.01 nmol/L) and a paucity of cholinergic symptoms. It was indistinguishable from pure autonomic failure. The other subgroup (N = 4) had high antibody titer (11.6 +/- 2.08 nmol/L), sicca complex, abnormal pupils, and neurogenic bladder; three had severe upper gastrointestinal dysfunction. Higher antibody titers correlated with greater autonomic dysfunction and more frequent cholinergic dysautonomia.

These observations expand the clinical spectrum of AAN to include chronic cases, some being indistinguishable from pure autonomic failure, and support the concept that ganglionic AChR antibodies are important diagnostically and pathophysiologically in acquired dysautonomia.

PMID: 12783421 [PubMed - indexed for MEDLINE]

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*J Cardiovasc Electrophysiol.* 2007 May;18(5):534-41. Epub 2007 Feb 21.

*Mechanism of the conversion of a pulmonary vein tachycardia to atrial fibrillation in normal canine hearts: role of autonomic nerve stimulation.*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17313531&query hl=6&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17313531&query hl=6&itool=pubmed_docsum)

*Department of Cardiovascular Medicine, Tokyo Medical and Dental University, Tokyo, Japan.*

**INTRODUCTION:** The role of the autonomic nervous system in inducing pulmonary vein (PV)-triggered atrial fibrillation (AF) and the termination mechanism of the AF are unknown. The purpose of this study was to elucidate the mechanism of the conversion of a tachycardia within a PV into AF under autonomic stimulation and the termination mechanism of the AF in normal canine hearts.

**CONCLUSIONS:** These findings indicate that the vagal effects affecting the PVT and atria facilitate the onset and maintenance of PV-triggered AF in normal canine hearts.

PMID: 17313531 [PubMed - indexed for MEDLINE]

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*Curr Opin Cardiol.* 2004 Jan;19(1):2-11.

*Autonomic aspects of arrhythmogenesis: the enduring and the new.*

*Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA.*

**PURPOSE OF REVIEW:** Recent progress in understanding the role of the autonomic nervous system in the development of cardiac arrhythmias is reviewed. The focus is on the translation of basic principles of neural control of heart rhythm that have emerged from experimental studies to clinical applications.

**RECENT FINDINGS:** Recent studies have made significant strides in defining the function of intrinsic cardiac innervation and the importance of nerve sprouting in electrical remodeling. A recurring theme is that heterogeneity of sympathetic innervation in response to injury is highly arrhythmogenic. In addition, both sympathetic and parasympathetic influences on ion channel activity have been found to accentuate electrical heterogeneities and thus to contribute to arrhythmogenesis in the long QT and Brugada syndromes. In the clinic, heart rate variability continues to be a useful tool in delineating pathophysiologic changes that result from the progression of heart disease and the impact of diabetic neuropathy. Heart rate turbulence, a noninvasive indicator of baroreceptor sensitivity, has emerged as a simple, practical tool to assess risk for cardiovascular mortality in patients with ischemic heart disease and heart failure. Evidence of the proarrhythmic influence of behavioral stress has been further bolstered by defibrillator discharge studies and ambulatory ECG-based T-wave alternans measurement.

**SUMMARY:** The results of recent investigations underscore the importance of the autonomic influences as triggers of arrhythmia and provide important mechanistic insights into the ionic and cellular mechanisms involved.

PMID: 14688627 [PubMed - indexed for MEDLINE]

*J Cardiovasc Electrophysiol.* 2007 Jan;18(1):83-90.

Comment in: *J Cardiovasc Electrophysiol.* 2007 Jan;18(1):91-2.

Gradients of atrial refractoriness and inducibility of atrial fibrillation due to stimulation of ganglionated plexi.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17229305&query\\_hl=6&itool=pubmed\\_DocSum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17229305&query_hl=6&itool=pubmed_DocSum)

Department of Cardiology, First Hospital of Peking University, Beijing, China.

**INTRODUCTION:** The mechanism(s) whereby atrial ectopy induces atrial fibrillation (AF) is still poorly understood. **METHODS AND RESULTS:** In 12 dogs, we determined the refractory period (RP) along the right atrium (RA) and right superior pulmonary vein (RSPV), and AF inducibility with and without concurrent stimulation of the anterior right ganglionated plexi (ARGP) at the base of the RSPV. Multielectrode catheters were attached to the RSPV and RA with the distal electrodes close to ARGP. The RP and window of vulnerability (WOV), i.e., the longest S1-S2 minus the shortest S1-S2 at which AF was induced, were measured before and during incremental levels of ARGP stimulation. Mapping of the onset of AF was performed using the EnSite mapping system (St. Jude Medical, St. Paul, MN, USA) positioned in the RA. A single premature depolarization (PD) from the RSPV that did not induce AF without ARGP stimulation could do so with ARGP stimulation. The onset of AF consistently arose at the myocardium subtending the ARGP. With GP stimulation, the average WOVS at the RSPV-atrial junction was significantly wider than at the RA appendage (65 +/- 27 vs. 8 +/- 17 msec,  $P < 0.05$ ) or further along the RSPV sleeve (48 +/- 39 vs. 10 +/- 20 msec,  $P < 0.05$ ). Even without GP stimulation, high intensity (10-20 mA) premature stimuli delivered at the RA appendage induced AF, originating from atrial tissue subtending the ARGP, presumably due to axonal conduction that activated the ARGP.

**CONCLUSION:** GP stimulation, subthreshold for atrial excitation, converts isolated PDs into AF-inducing PDs, suggesting that autonomic tone may play a critical role in the initiation of paroxysmal AF.

PMID: 17229305 [PubMed - indexed for MEDLINE]

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*Brain.* 2005 Jan;128(Pt 1):75-85. Epub 2004 Oct 20.

Mental stress and sudden cardiac death: asymmetric midbrain activity as a linking mechanism.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list\\_uids=15496434](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list_uids=15496434)

Wellcome Department of Imaging Neuroscience, Institute of Neurology, University College London, London WC1N 3BG, UK. [h.critchley@fil.ion.ucl.ac.uk](mailto:h.critchley@fil.ion.ucl.ac.uk)

Patients with specific neurological, psychiatric or cardiovascular conditions are at enhanced risk of cardiac arrhythmia and sudden death. The neurogenic mechanisms are poorly understood. However, in many cases, stress may precipitate cardiac arrhythmia and sudden death in vulnerable patients, presumably via centrally driven autonomic nervous system responses.

From a cardiological perspective, the likelihood of arrhythmia is strongly associated with abnormalities in electrical repolarization (recovery) of the heart muscle after each contraction. Inhomogeneous and asymmetric repolarization, reflected in ECG T-wave abnormalities, is associated with a greatly increased risk of arrhythmia, i.e. a proarrhythmic state. We therefore undertook a study to identify the brain mechanisms by which stress can induce cardiac arrhythmia through efferent autonomic drive. We recruited a typical group of 10 out-patients attending a cardiological clinic. We simultaneously measured brain activity, using H2(15)O PET, and the proarrhythmic state of the heart, using ECG, during mental and physical stress challenges and corresponding control conditions.

Proarrhythmic changes in the heart were quantified from two ECG-derived measures of repolarization inhomogeneity and were related to changes in magnitude and lateralization of regional brain activity reflected in regional cerebral blood flow. Across the patient group, we observed a robust positive relationship between right-lateralized asymmetry in midbrain activity and proarrhythmic abnormalities of cardiac repolarization (apparent in two independent ECG measures) during stress.

This association between stress-induced lateralization of midbrain activity and enhanced arrhythmic vulnerability provides empirical support for a putative mechanism for stress-induced sudden death, wherein lateralization of central autonomic drive during stress results in imbalanced activity in right and left cardiac sympathetic nerves. A right-left asymmetry in sympathetic drive across the surface of the heart disrupts the electrophysiological homogeneity of ventricular repolarization, predisposing to arrhythmia. Our findings highlight a proximal brain basis for stress-induced cardiac arrhythmic vulnerability.

PMID: 15496434 [PubMed - indexed for MEDLINE]

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*Heart Rhythm. 2007 Mar;4(3 Suppl):S61-4. Epub 2006 Dec 15.*

*Autonomic nerve activity and atrial fibrillation*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17336887&query\\_hl=6&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17336887&query_hl=6&itool=pubmed_docsum)

*Division of Cardiology, Department of Medicine, Cedars-Sinai Medical Center and David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA. chenpp@iupui.edu*

This review focuses on the importance of autonomic nervous system (ANS) activity in the induction of paroxysmal atrial fibrillation (PAF). Clinical studies suggest that both sympathetic and parasympathetic nervous systems are important in mediating PAF.

Consistent with that hypothesis, heart rate variability analyses showed that sympathovagal imbalance is present before the onset of PAF episodes. The importance of the ANS in PAF is further supported by animal experiments and recent clinical studies showing that vagal denervation enhances the efficacy of circumferential pulmonary vein ablation in preventing AF recurrence. In vitro studies show that ANS activation facilitates early afterdepolarization and triggered activity by simultaneously prolonging the intracellular calcium (Ca(i)) transient (sympathetic effect) and shortening the action potential duration (parasympathetic effect). By simultaneously mapping the membrane potential and Ca(i) transient in canine pulmonary vein during sympathetic stimulation, we demonstrated that spontaneous (voltage-independent) sarcoplasmic reticulum calcium release underlies the mechanisms of focal discharges. We developed and studied canine models of PAF induced by electrical, structural, and neural remodeling. We also have developed methods for long-term continuous recording of sympathetic and vagal nerve activity in ambulatory dogs.

Preliminary results show that simultaneous sympathovagal discharges precede the onset of PAF in these dogs. ANS activity and Ca(i) transient dynamics are important in the development of PAF. These studies suggest that new methods or drugs aimed at modification of cardiac ANS activity may lead to new opportunities for AF control.

PMID: 17336887 [PubMed - indexed for MEDLINE]

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*Heart Rhythm. 2007 Mar;4(3 Suppl):S57-60. Epub 2006 Dec 15.*

*Autonomic nerves in pulmonary veins.*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17336886&query\\_hl=6&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17336886&query_hl=6&itool=pubmed_docsum)

*Division of Cardiology, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California, USA.*

Rapid repetitive activities arising from pulmonary veins may initiate atrial fibrillation. The basis of these rapid repetitive activities remains unclear, but recent evidence suggests that the autonomic nervous system plays an important role in their formation. Pulmonary veins and the adjoining left atrium are highly innervated structures. This review summarizes recent developments in the understanding of the anatomy of autonomic nerves in and around pulmonary veins and their implications for atrial fibrillation.

PMID: 17336886 [PubMed - indexed for MEDLINE]

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*Circulation*. 2000 Nov 28;102(22):2774-80. Links

Catheter ablation of cardiac autonomic nerves for prevention of vagal atrial fibrillation.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list\\_uids=11094046](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list_uids=11094046)

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**BACKGROUND:** Vagal stimulation shortens the atrial effective refractory period (AERP) and maintains atrial fibrillation (AF). This study investigated whether the parasympathetic pathways that innervate the atria can be identified and ablated by use of transvenous catheter stimulation and radiofrequency current catheter ablation (RFCA) techniques.

**CONCLUSIONS:** Transvascular atrial parasympathetic nerve system modification by RFCA abolishes vagally mediated AF. This antifibrillatory procedure may provide a foundation for investigating the usefulness of neural ablation in chronic animal models of AF and eventually in patients with AF and high vagal tone.

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*Lancet*. 2005 Apr 2-8;365(9466):1259-70. Links

Autonomic peripheral neuropathy.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list\\_uids=15811460](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?itool=abstractplus&db=pubmed&cmd=Retrieve&dopt=abstractplus&list_uids=15811460)

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The autonomic neuropathies are a group of disorders in which the small, lightly myelinated and unmyelinated autonomic nerve fibres are selectively targeted.

Autonomic features, which involve the cardiovascular, gastrointestinal, urogenital, sudomotor, and pupillomotor systems, occur in varying combination in these disorders. Diabetes is the most common cause of autonomic neuropathy in more developed countries. Autonomic neuropathies can also occur as a result of amyloid deposition, after acute infection, as part of a paraneoplastic syndrome, and after exposure to neurotoxins including therapeutic drugs. Certain antibodies (eg, anti-Hu and those directed against neuronal nicotinic acetylcholine receptor) are associated with autonomic signs and symptoms. There are several familial autonomic neuropathies with autosomal dominant, autosomal recessive, or X-linked patterns of inheritance. Autonomic dysfunction can occur in association with specific infections. The availability of sensitive and reproducible measures of autonomic function has improved physicians' ability to diagnose these disorders.

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## **AUTONOMIC NEUROPATHY**

- Cardiovascular - Orthostatic onset of palpitations, nausea, tremulousness, presyncope with light-headedness, visual blurring, tinnitus, and even chest pain and shortness of breath
- Orthostatic hypotension may follow and is often associated with postprandial state, alcohol, exercise, or temperature-induced exacerbation of hypotension.
- Supine hypertension and a loss of diurnal variation in blood pressure may occur later.
- Micturition and defecation may induce presyncope.
- With worsening symptoms, episodes of syncope with complete loss of consciousness after standing may occur.
- In the most severe of autonomic neuropathies, orthostatic tolerance loss with inability to stand because of immediate syncope may occur.
- Episodes of palpitations, angina, dyspnea, and syncope may relate to cardiac arrhythmias as well.

<http://www.emedicine.com/neuro/topic720.htm>

## The Neuropathic Postural Tachycardia Syndrome

### ABSTRACT

Background The postural tachycardia syndrome is a common disorder that is characterized by chronic orthostatic symptoms and a dramatic increase in heart rate on standing, but that does not involve orthostatic hypotension. Several lines of evidence indicate that this disorder may result from sympathetic denervation of the legs.

<http://www.emedicine.com/neuro/topic720.htm>

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### More Evidence for Autonomic Neuropathy in Postural Tachycardia Syndrome

Comment:

The strengths of this study include the well-characterized autonomic status of the patients and the measurements of NE spillover and clearance both systemically and locally (leg vs. arm). These findings are strongly suggestive of a denervation of the legs with relative sparing of the arms. The data would have been more definitive if a reduction of the intraneuronal metabolite dihydroxyphenylglycol had been demonstrated in the leg. Jacob G et al. The neuropathic postural tachycardia syndrome. *N Engl J Med* 2000 Oct 05 343 1008 -1014. Published in *Journal Watch Neurology* November 22, 2000 <http://neurology.jwatch.org/cgi/content/full/2000/1122/4>

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*Proc Natl Acad Sci U S A.* 2007 Apr 17;104(16):6818-23. Epub 2007 Apr 9

*Cortical potential reflecting cardiac function.*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17420478&query\\_hl=6&itool=pubmed\\_docsum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17420478&query_hl=6&itool=pubmed_docsum)

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Emotional trauma and psychological stress can precipitate cardiac arrhythmia and sudden death through arrhythmogenic effects of efferent sympathetic drive. Patients with preexisting heart disease are particularly at risk.

Moreover, generation of proarrhythmic activity patterns within cerebral autonomic centers may be amplified by afferent feedback from a dysfunctional myocardium. An electrocortical potential reflecting afferent cardiac information has been described, reflecting individual differences in interoceptive sensitivity (awareness of one's own heartbeats). To inform our understanding of mechanisms underlying arrhythmogenesis, we extended this approach, identifying electrocortical potentials corresponding to the cortical expression of afferent information about the integrity of myocardial function during stress.

We measured changes in cardiac response simultaneously with electroencephalography in patients with established ventricular dysfunction. Experimentally induced mental stress enhanced cardiovascular indices of sympathetic activity (systolic blood pressure, heart rate, ventricular ejection fraction, and skin conductance) across all patients. However, the functional response of the myocardium varied; some patients increased, whereas others decreased, cardiac output during stress. Across patients, heartbeat-evoked potential amplitude at left temporal and lateral frontal electrode locations correlated with stress-induced changes in cardiac output, consistent with an afferent cortical representation of myocardial function during stress.

Moreover, the amplitude of the heartbeat-evoked potential in the left temporal region reflected the proarrhythmic status of the heart (inhomogeneity of left ventricular repolarization). These observations delineate a cortical representation of cardiac function predictive of proarrhythmic abnormalities in cardiac repolarization.

Our findings highlight the dynamic interaction of heart and brain in stress-induced cardiovascular morbidity.

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*Diabetes Metab. 2006 Sep;32 Spec No2:2S37-41.*

*Hemodynamic changes in postprandial state.*

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Several experimental data suggest that single sugar intake may induce heart rate acceleration and blood pressure elevation as a result of sympathetic activation secondary to insulin response and from alterations in endothelial function due to activation of oxidative stress.

These hemodynamic effects might be more marked in patients with arterial hypertension or metabolic disorders, in particular in hypertensive patients with diabetes. A high-fat load may also induce activation of oxidative stress and endothelial dysfunction. However, the long-term effect of repeated intake of single sugar and fat on blood pressure, oxidative stress, and endothelial function should be tested in controlled trials. On the contrary, a balanced mixed meal (50% carbohydrates) does not induce any significant blood pressure changes. Nevertheless, acarbose treatment is able to reduce hypertension incidence in patients with impaired glucose tolerance and to improve endothelial function.

In elderly subjects, in particular with type 2 diabetes or with severe dysautonomia, single sugar intake may account for nonhypoglycemic postprandial dizziness.

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*Psychosom Med. 2004 Mar-Apr;66(2):153-64.*

*Interactions between autonomic nervous system activity and endothelial function: a model for the development of cardiovascular disease.*

*Department of Psychology, University of Pittsburgh, Pittsburgh, PA, USA.*

**OBJECTIVES:** Endothelial dysfunction is a new pathway in cardiovascular disease (CVD) development. Psychosocial factors have been little studied in relation to endothelial function, although they may interact via associations with the autonomic nervous system (ANS). The purpose of this review is to propose a model by which psychosocial factors are related to CVD development through interactions between the ANS and vascular endothelium.

**METHODS:** The literature supporting an interaction between the ANS and endothelium in healthy and disease states is reviewed. Potential mechanisms linking the two systems are explored as a pathway for CVD development.

**RESULTS:** Endothelial dysfunction and impaired cardiovascular ANS regulation are both markers for increased CVD risk. Sympathetic nerves and vascular endothelial cells share a functional antagonism in healthy states to maintain appropriate blood vessel tone. Alterations in sympathetic activity and endothelial cell function are both observed early in the development of CVD and may result from an inability to maintain the functional antagonism. Impairments in either ANS regulation or endothelial function may contribute to further disease development by evoking maladaptive changes in the opposing system.

**CONCLUSIONS:** Although interactions between cardiovascular ANS regulation and endothelial function are likely involved in CVD development, further research is needed to determine whether ANS and endothelium interactions are a plausible pathway linking psychosocial factors with increased CVD risk.

PMID: 15039499 [PubMed - indexed for MEDLINE]

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*Nippon Rinsho. 2005 Jun;63(6):973-7.*

*Aging of the autonomic nervous system*

*Department of Neurology, Saitama Medical School.*

Aging is associated with structural and functional changes in the autonomic nervous system (ANS), which innervates the whole body, and its altered function may influence almost all body systems. Changes related to aging are found in autonomic nerves and ganglia, and ANS controlled functions including cardiovascular functions.

Much of the current knowledge about age-related changes in sympathetic nervous function is derived from studies of circulating catecholamine levels, norepinephrine kinetics and microneurographic recordings from sympathetic nerves of skeletal muscle.

Significant evidence suggests that basal plasma noradrenaline levels increase with age. These data indicates that healthy aging is associated with elevated basal sympathetic nervous activity. In contrast, the reactivity of the sympathetic and the parasympathetic nervous activity are reduced with aging.

PMID: 15948378 [PubMed - indexed for MEDLINE]

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*Int J Cardiol. 2001 Dec;81(2-3):175-80*

*Impaired autonomic function predicts dizziness at onset of paroxysmal atrial fibrillation.*

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**BACKGROUND:** Paroxysmal atrial fibrillation is associated with various symptoms, including dizziness, which presumably reflects hemodynamic deterioration. Given the importance of the autonomic nervous system in mitigating the hemodynamic effect of atrial fibrillation, we hypothesized that autonomic function would be predictive of the severity of dizziness.

**METHODS:** The study group comprised 73 patients with paroxysmal atrial fibrillation (mean age 54.1 years, 51 males). Forty-three (59%) patients had lone atrial fibrillation. Mean ventricular rate during atrial fibrillation was 99+/-16 beats/min. On average, patients had a 3-year history of one paroxysm per week lasting 2 h.

Autonomic function was assessed using autonomic function tests, including noninvasive measurement of baroreflex sensitivity. Head up tilting was used to test vasovagal reactivity. Severity of dizziness at onset of atrial fibrillation was quantified by the patients using a five-point scale (1=none; 2=light; 3=mild; 4=moderate; and 5=severe). Multivariate analysis was performed to identify the independent predictors of the severity of dizziness.

**RESULTS:** Mean severity of dizziness was 3.36+/-1.65. Multivariate predictors of moderate-to-severe dizziness as opposed to none-to-mild dizziness were a low 30-15 ratio after standing up and low baroreflex sensitivity. Though syncope was never reported nine patients showed a full vasovagal response during head up tilting.

**CONCLUSIONS:** It is concluded that dizziness in patients with "treated" atrial fibrillation in the setting of none to mild structural heart disease is predicted by impaired autonomic function. Vasovagal reactivity appears not to be involved in this connection.

PMID: 11744134 [PubMed - indexed for MEDLINE]

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Hi Bob,

"Could this be a way that potassium and magnesium supplements affect afib, i.e. through their effect on the ANS?"

If I assume my heart rate during meditation is a proxy for my ANS balance, I would say no. I looked at several HR series during morning meditation during the recent time when I slacked off on supps. My average HR was 55 BPM. I resumed my full supp program several days ago. This morning I had a 30 minute segment at 48 BPM. I also looked back 3 or so months ago and my average would have been ~50 to 51 then. Of course there are other variables - the quality of my sleep the night before, how hard I exercised the day before & etc. However, I don't think the supps are modifying the ANS.

There may be exceptions, but very much agree with James that the heart is responding abnormally to normal variations in ANS.

**George**

I've probably brought the issue up of Dysautonomia more than anyone on this board. I do not speculate that it is the cause of AFib, I know it is! All you people need to do, is seriously examine your life's history. You'll see issues of having too much "flight or fight" response, or too much "feed or Breed" response in your personal history.

My own history succinctly put, is one of always having a fight or flight dominance. Then, in my twenties, I over did the exercise while under great stress in the first year of law school. Had short bouts of what I now know as AFIB. Backed off the exercise, reeled all in, and tried to mellow out. AFIB and pac's went away. As far back as high school I can remember pac's, but only upon starting an exercise (aerobic) program. Backed off, ANS came back into balance.

In my late 30's I went through a partnership dissolution, and was using the Jacuzzi spa at nights sipping a few beers on a regular basis. Pac's and afib the result. Now in my mid forties. I've learned to walk a couple miles a day in an easy rhythmic exercise. Cut my stress levels by job modifications and workloads. I now have a few pac's and very reduced runs of afib.

My theory is that after so many years of dominance, the sympathetic just sort of weakens, thus allowing an exaggerated parasympathetic to remain abnormally high,(e.g., it got high by balancing the sympathetic for all those years, and now is predominate). I'm very vagal (you all know the drill of symptoms).

My past is one of muscle twitches, IBS, Panic attacks, anxiety, and yes, mild MVP. (MVP is a marker, not the cause) This is when I was cross training, under job stress, and on some stupid self imposed diet of basically no fat and all carbs (lost a lot of weight.) Being trained to follow the facts/evidence and apply it to the law, in this case, the medical doctrine, I now see that:

- 1) My mother had migraines and severe allergies. When I was conceived, she was taking a medicine called Tedryl (ephinephrine and benedryl). The ANS forms in the fetus at about six weeks.
- 2) At age 4, I suffered left eye trauma, and was put under a few times for operations. Anesthesia effect the ANS.
- 3) Wouldn't doubt some genetics at work. (see above about mother, and guess what, Dad is 83 with AFib, and was an avid long distance runner for many years )
- 4) Family law attorney, (i.e, trials and hearings galore, fighting over peoples stupid choices)

Add it up people. The body cannot be "compartmentalized" as the medical establishment has it organized. Events and choices DO MATTER.

I'm presently moving forward with a cardiologist who utilizes ANSAR technology to help pinpoint, and rebalance the ANS. One other poster here has successfully treated his pac's and Afib utilizing this approach. He has not re-posted in a long time, but I keep in touch.

As for the heart being overly sensitive to "normal" variations in the ANS, I say we lone afibbers have never had a normal ANS. Its effect over time, is to slowly make the receptor cells, and ganglia in the heart more susceptible to the stimuli--and unfortunately, we have a lot of stimuli.

THE ANS IS THE DRIVER!!! Wake up.

***DGM***

---

I decided to randomly sample 8 of my stored HR series over 3 months. All of these are early morning series, during meditation, and after morning yoga. I've shown min and max for a number of HRV metrics. As you can see, the variability these metrics is quite large.

Max Min Units Item

61.8 51.2 bpm Average R-R Interval

138.2 62.5 ms Standard Deviation

10.8 3.3 % pNN50 (% of beats where the difference in beat length from one beat to the next is greater than 50 ms)

power spectral density (PSD)

80374.97 47232.73 ms Total power (0.00 - 0.40 Hz)

75597.86 43987.1 ms VLF (0.00 - 0.04 Hz)

2322.2 1492.18 ms LF (0.04 - 0.15 Hz) - adrenergic

2454.91 611.68 ms HF (0.15 - 0.40 Hz) - vagal

371.2 94.6 % LF/HF ratio

Early in my afib career I planned to use this, from p 67 of Hans's first book, "Atrial fibrillation patients with focal ectopy originating from the pulmonary veins experience a significant increase in HF power and a decrease in LF power during the 20 minutes preceding an episode." I wanted to develop real time hardware/software to measure this and predict the onset of an afib episode from this increase in HF power. I hoped to be able to do something to change the ANS balance at that point and head off the episode.

At the time PC discouraged me from this effort. At this point, I believe that he was correct in doing so. I think the ANS balance is too variable and not very predictive.

ANSAR web page: <http://www.ans-hrv.com/>

**George**

---

GeorgeN, In a previous message you wrote, "However I noticed a dramatic increase in heart rate variability (HRV). If I'm not trying to alter it with my breathing, it is typically about 9 beats per minute (BPM) peak to trough with an average heart rate of 55 BPM. The HRV had expanded to about 25 BPM, peak to trough. This must be due to the fasting."

<http://www.afibbers.net/forum/read.php?f=6&i=8277&t=8277>

Could your increase in HRV been from reduced supplement intake which combined with your reduced intake of minerals by fasting?

**Bob K.**

---

Hi Bob,

A more likely suspect is that my insulin levels dropped significantly due to the fasting. The following is from p 67 of Hans's first book.

"The researchers also point out that HRV decreases with age, high insulin levels, physical inactivity, smoking, and rapid and shallow breathing[42].

42. Dekker, Jacqueline M., et al. Low heart rate variability in a 2-minute rhythm strip predicts risk of coronary heart disease and mortality from several causes. *Circulation*, Vol. 102, September 12, 2000, pp. 1239-44"

"Could your increase in HRV been from reduced supplement intake which combined with your reduced intake of minerals by fasting?"

During my fast/prep time, I was very regular with my supplements, as long as I could. I was very concerned that the colonoscopy prep would upset my electrolyte balance, so took my regular supplements until 24 hours before the HRV reading. I also took KCl dissolved in water as part of the "clear fluids" allowed under the prep protocol. So I would give the reduced supplement intake a low probability of being the cause of the increased HRV.

**George**

GeorgeN, Hans' comment that you mentioned referred to a [reference 42](#). And in reference 42, they refer to a [reference 16](#) for supporting their statement about insulin and HRV.

Here is an excerpt from reference 16,

"In individuals not diagnosed as diabetics, serum insulin, and, to a lesser degree, serum glucose were inversely associated with vagal function ... "

Isn't HRV inversely associated with vagal function, i.e. the greater the vagal function the lower the HRV? If so, consider the following.

From the above excerpt from reference 16, in individuals not diagnosed as diabetics, vagal function was associated inversely with serum insulin and hence HRV was associated directly with serum insulin. In other words, the lower the serum insulin in non-diabetics, the lower the HRV.

Thus, reduced insulin levels like those you believed you had during fasting would result in a decrease in HRV, not an increase like you observed. (I am assuming you are not a diabetic.)

If you agree with the above, the question still seems to remain whether reduced supplement intake combined with reduced mineral intake from fasting resulted in your increased HRV.

**Bob K.**

---

GeorgeN, I didn't notice your above message about normal supplementation 24hrs before your prep when I was composing my message. I was going by your previous remarks that seemed to imply that your prep was during a period when your supplement intake was reduced.

However, the main point in my message about low insulin not explaining high HRV still applies.

To clarify, the previous remarks I was referring to were on other threads

<http://www.afibbers.net/forum/read.php?f=6&i=8468&t=8468>

<http://www.afibbers.net/forum/read.php?f=6&i=8277&t=8277>.

**Bob K.**

---

Here is another tidbit:

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11238539&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11238539&dopt=Abstract)

"We conclude that insulin acutely shifts sympathovagal control of HRV toward sympathetic dominance in insulin-sensitive, but not in resistant, subjects."

**George**

---

GeorgeN, Would you consider posting a tutorial on measuring HRV and interpreting the measurements, describing the units used (like ms or ms<sup>2</sup>), etc.?

**Bob K.**

---

Bob,

I will try at some point, but here is a brief explanation: the Polar S810 does it for me.

Ok, here is more. There are several measurements that researchers use. The beat length is measured in milliseconds. So 1000 ms = 1 second. Also heart rate = (1000/beat length) \* 60. So for a beat length of 1100 ms, HR= (1000/1100) \*

60 = 54.5 BPM. Smaller beat length numbers mean a faster heart rate.

You record a series of beat lengths like (this can be also done with an ECG machine).

1100  
1113  
1152  
1050  
...

You then perform fourier analysis on the series.

The results are then broken into various frequency ranges:

Total power (0.00 - 0.40 Hz)  
VLF (0.00 - 0.04 Hz)  
LF (0.04 - 0.15 Hz) - adrenergic  
HF (0.15 - 0.40 Hz) - vagal  
% LF/HF ratio

To get the lower frequencies you need to monitor for longer periods of time.

Other measures include:

Standard Deviation of beat length in ms

% pNN50 (% of beats where the difference in beat length from one beat to the next is greater than 50 ms)

& there are others. I don't have time now to explain fourier analysis as I have a date to go rock climbing, so you'll have to Google it.

**George**

---

Thanks GeorgeN, That was helpful.

Re: "power spectral density (PSD)  
80374.97 47232.73 ms Total power (0.00 - 0.40 Hz)  
75597.86 43987.1 ms VLF (0.00 - 0.04 Hz)  
2322.2 1492.18 ms LF (0.04 - 0.15 Hz) - adrenergic  
2454.91 611.68 ms HF (0.15 - 0.40 Hz) - vagal"

- 1) Is your data the integrated PSD of the R-R interval as a function of time over the various frequency ranges?
- 2) Did you mean  $\text{ms}^2$  instead of ms?
- 3) What are the two numbers at the beginning of each line? For example, the first two numbers in the line:  
2454.91 611.68 ms HF (0.15 - 0.40 Hz) – vagal

Maybe I should clarify my first question by modifying it as follows:

- 1) Is your data the integrated PSD of RR(t) over the respective frequency ranges?

By RR(t) I mean the R-R interval as a function of time.

**Bob K.**

---

Hi Jackie,

There were a couple of good references in those you listed. I was particularly intrigued by the article entitled "Gradients of atrial refractoriness and inducibility of atrial fibrillation due to stimulation of ganglionated plexi."

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list\\_uids=17229305&query\\_hl=6&itool=pubmed\\_DocSum](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17229305&query_hl=6&itool=pubmed_DocSum)

Another recent article reiterates this point

*Autonomic Ganglionated Plexi: Characterization and Effect of Epicardial Microwave Ablation in a Canine Model of Vagally Induced Acute Atrial Fibrillation.*

<http://www.ismics.org/abstracts/2006/18.cgi>

According to Pappone, at 12-month follow-up post ablation, 85% of patients without vagal reflexes were free of symptomatic AF, compared with 99% of patients with vagal reflexes and complete vagal denervation.

[http://www.italheartj.org/pdf\\_files/20050045.pdf](http://www.italheartj.org/pdf_files/20050045.pdf)

According to Haissaguerre, such sites are more frequently encountered in those with persistent (>48 hr duration episodes) v. those with paroxysmal AF. These vagal reflex sites can be found in a few specific areas in the left atrium and seem to be the origin of the DF (dominant focus) that provides the primary rotor for maintaining AF.

Another author with whom I've communicated has called these foci "AF nests" because in his opinion they are the real substrate for AF. They were present in 34/34 drug refractory LAFers (paroxysmal and persistent) v. 1/5 controls. However, in that one control AF was inducible, despite the absence of a history of AF.

A new treatment for atrial fibrillation based on spectral analysis to guide the catheter RF-ablation

<http://europace.oxfordjournals.org/cgi/content/full/6/6/590>

Accordingly, it would appear that the maintenance substrate of LAF is basically a reflex mediated by vagal ganglion cells on the epicardial surface of the heart. They lie dormant during the first few decades of life and then suddenly announce their presence after a certain threshold level of PAC activity has been achieved (via atrial and or PV stretch) in the immediately adjacent tissue.

It is been repeatedly noted during PVI that virtually all individuals with AF have dilated PVs and the source of the ectopic activity is almost always associated with the most dilated PV. It is enticing to imagine ectopic activity, triggered by a gradual increase in circulating catecholamines (?30 imn), causing a micro-reentrant circuit, facilitated by the shortened AERP in the immediately adjacent heart tissue innervated by these vagal ganglia => AF. I believe the phrase in Jackie's article was "myocardium subtending the ganglionated plexus." It doesn't take much of an intellectual leap to envision this happening in an extra-pulmonary vagal reflex site => DF.

I've also been pondering the decrease in BNP post successful ablation and a possible connection between natriuretic peptides and this

"dysautonomia". It appears that this hormone, routinely elevated in LAFers (?due to subclinical ventricular dysfunction caused by recurrent LAF and increased PACs), might be the cause of the low intracellular magnesium levels found in many LAFers, despite proactive supplementation.

If that is the case, then my IC Mg ought to have increased over the past nearly two years. My BP should also have increased. The latter has definitely not occurred (not a bad thing) and I suspect that a repeat test from IC Diagnostics would show no change on the IC Mg++.

This reason (in addition to recurring mild orthostatic hypotension) I suspect this is because I've recently experienced a peculiar phenomenon. Twice

now in the last two months, while refereeing soccer games, I have experienced an acute increase in PACs and bigeminy (fortunately no AF=>?maintenance substrate can no longer support an episode), lasting about an hour.

These arrhythmias appear to be associated with dehydration and/or a potassium shortfall, as they never occur when I'm religious about hydration and supplementing K+. Bigeminy can be due to heart failure, digoxin toxicity or electrolyte imbalance.

Being on my feet for at least 30-45 minutes prior to onset is also important, as is the catecholamine stimulating activity of running wind sprints. The resulting enhanced automaticity => more PACs.

Dehydration can cause functional MR. DGM should like this article as it fits right in with his thoughts on MVP. Those with MVP also exhibit increased plasma renin activity => increased aldosterone.

*"Gender differences in dehydration-induced mitral valve prolapse"*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7817930&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7817930&dopt=Abstract)

In below article it appears that functional MR causes a greater release of BNP than organic MR. And remember BNP is elevated in virtually all LAFers.

*"Association of B-Type Natriuretic Peptide Activation to Left Ventricular End-Systolic Remodeling in Organic and Functional Mitral Regurgitation"*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=16563910&dopt=Citation](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=16563910&dopt=Citation)

So, we are left with a curious scenario. Those with LAF (increased BNP=>decreased blood volume => increased adrenergic sensitivity) may actually further exacerbate their MVP (and mild MR) during dehydration. This then leads to an additional increase in BNP and possibly ANP.

*"Atrial natriuretic factor: a possible link between left atrium, plasma volume, adrenergic control and renin-aldosterone in the mitral valve prolapse syndrome."*

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2952778&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2952778&dopt=Abstract)

In summary, IMHO vagal ganglionated plexi probably represent the real maintenance substrate of AF. However, this "dysautonomia" is more anatomic than physiologic. Most of these plexi are located in the PVs, but as episodes increase in duration and frequency extra-pulmonary foci develop. The ganglion cells were probably always there but an ectopic focus has developed in the "myocardial tissue subtending the plexus." There are probably other extra-pulmonary ectopic foci but their expression is limited to PACs and bigeminy in the absence of an immediately adjacent plexus.

Despite a successful ablation, the cause of the trigger substrate (increased left intra-atrial pressure) remains. In pathologic AF this is predominantly hypertension and in LAF this is predominantly mild MR IMHO. Physical stress, e.g., dehydration, or emotional stress => increased catecholamines => increased automaticity. The increased natriuretic peptides in LAF => low blood volume => hyper-adrenergic state. Also, increased natriuretic peptides (and aldosterone) => electrolyte imbalance.

Close attention to replacement of K, Mg and H2O is especially important, if one is to minimize ectopics. I'm sure George will agree with that advice.

For the next 3 weeks I will be on a walkabout Down Under and will be unable to participate in the ensuing discussion. But there is much food for thought.

**PC**

---

Bob,

1) Is your data the integrated PSD of the R-R interval as a function of time over the various frequency ranges?

Yes

2) Did you mean  $ms^2_{1/2}$  instead of ms?

*ms<sup>2</sup> - the superscript 2 did not survive cut & paste*

3) What are the two numbers at the beginning of each line?

They are the min and max readings of from my 8 random samples of series over 3 months.

You'd probably get a lot more info about HRV with a Google search. When I commented about the increased HRV during a fast, it was a visual observation, not a mathematical one. Also to be consistent one should compare PSD analysis over the same length of time in the sample, something I was not careful about.

**George**

---

Hi PC,

Some excellent thoughts.

"Close attention to replacement of K, Mg and H2O is especially important, if one is to minimize ectopics." and I'd add taurine.

In my case, it appears as long as I'm diligent with the supps. the triggers, vagal or otherwise, don't trigger. If I let down my guard, then the vagally shortened AERP kicks in.

Have fun on your walkabout. Since it will soon be winter in Oz, dehydration should be less of an issue. My wife & daughter are in Oz for three more weeks and are enjoying it immensely.

Mahalo,

**George**

---

PC wrote:

Quote:

*In summary, IMHO vagal ganglionated pexi probably represent the real maintenance substrate of AF. However, this "dysautonomia" is more anatomic than physiologic.*

I'd like to further emphasise that we must consider anatomy as part of the substrate. The PVs, particularly large PVs, are such an ideal spot for driving rotors to exist I'm often amazed at how any heart manages to stay in normal rhythm. To further exacerbate the situation heart cells in these myocardial sleeves go through an abrupt (90 degree) change of orientation making it even easier for conduction to spin round the vein. I believe anatomy plays a massive role in the maintenance of some people's AF.

--

**James D**

(stay hydrated PC but no drinking from the billabong :)

---

James, Re: "To further exacerbate the situation heart cells in these myocardial sleeves go through an abrupt (90 degree) change of orientation making it even easier for conduction to spin round the vein."

I'm not sure what 90° you're referring to but the reentrant currents going around the pulmonary veins (PV) is interesting. If they were going around the PV it seems that they would cause aflutter rather than afib. Maybe the circumference of the PV is too large for this reentrant path?

On second thought, disregard the sentence about aflutter. The topological effects are interesting because a reentrant path around the circumference of a PV may or may not cause aflutter, depending on the heterogeneity of conduction from the PV to the atrium.

**Bob K.**

Hi Bob - I think you are close to the mark when talking about flutter in the PVs - there is some talk of AF actually being more organised than we imagine. I too think of it more like flutter in the PVs but the flutter soon degenerates in to AF as it enters the atria as waves split up. Thinking of static mother rotors as being in stable flutter is entirely reasonable in my opinion (even when the rest of the aria is actually fibrillating in response to this stable rotor)

As you go further up the PVs the cells switch so the longest part of the cell is 90 degrees to the blood flow. (as you know most gap junctions occur at the thin ends of the cells so conduction is predominately in the same direction as the long side)

--

**James D**

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Hi James,

To me the following quote, from one of PC's references, perhaps illustrates your point, "I've just pictured a yellow post-it note stuck on the heart that reads 'fix this'. I imagine that as well as the heart you are wanting to stick a post-it note somewhere on the ANS? (I'm not convinced many LAFers will need it on the ANS)"

PC's reference: <http://europace.oxfordjournals.org/cgi/content/full/6/6/590>

"AF nests were found over the whole left surface of the interatrial septum, but were less frequent on the right. This finding raises the possibility that distension of the atrial myocardium converted the compact into fibrillar myocardium, perhaps by detaching inter-cellular connections. This phenomenon could explain one acquired origin of fibrillar myocardium, caused by the stretching and/or degeneration of compact tissue. Less frequent AF nests were found in the right atrium.

In five control patients we did not find AF nests and could not manage to induce AF with atrial stimulation. However, in one control patient (a 22-year-old man) presenting AF nests, sustained AF was induced despite having no AF history."

IMHO, no doubt the ANS is always operative, but if the heart had no AF nests, there would likely be no AF.

As an aside, haven't I read that Natale & Bordeaux ablate the AF nests in addition to the PV's?

**George**

---

James, Re "As you go further up the PVs the cells switch so the longest part of the cell is 90 degrees to the blood flow." That's interesting. I hadn't thought of the cell orientation there before. Now I understand your point, "To further exacerbate the situation heart cells in these myocardial sleeves go through an abrupt (90 degree) change of orientation making it even easier for conduction to spin round the vein."

I seem to recall that there is a case of reentrant aflutter paths about some structure in the right atrium but I can't remember the specifics. That phenomenon in the right atrium may have similarities to the PV case that you are suggesting.

**Bob K.**

---

I've been trying to find some references - I know I've seen a really good picture of the cell orientation in a recent article and I think it was one of the videos posted on this site that talks how organised AF can be in the pulmonary veins before it degenerates into the chaos of AF as activity propagates further into the atria. (I'm guessing the one with Pappone and Camm if that jogs anyone's memory but I'm not 100% sure!)

I've failed on both counts to find the web references but in my hunt I stumbled across this

[Autonomic Innervation and Segmental Muscular Disconnections at the Human Pulmonary Vein-Atrial Junction](#)

which I think highlights just how different individuals can be. (note that the hearts in this article were from people without atrial arrhythmia or cardiovascular problems)

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**James D**

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Since we don't actually have conclusive evidence of what causes some forms of dysautonomia - and apparently there are many forms - dysautonomia was reported to be a symptom/consequence of gluten/gluten sensitivity - Conference Room #54.

**Jackie**

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*Is Vagal Denervation a Good Alternative or Just Adjunctive to Pulmonary Vein Isolation in Catheter Ablation of Atrial Fibrillation?*

<http://content.onlinejacc.org/cgi/content/full/49/12/1349>

and

"The high AF recurrence rate observed during follow-up did not allow us to continue the protocol."

*Selective Atrial Vagal Denervation Guided by Evoked Vagal Reflex to Treat Patients With Paroxysmal Atrial Fibrillation*

<http://circ.ahajournals.org/cgi/content/full/114/9/876?ijkey=690399ae175181eaf92cb18cc35c9cb11f01d365>

My take from this is that you can perform vagal denervation, and it can help, but it doesn't solve the root cause- AF nests.

**George**

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GeorgeN, Re "Also to be consistent one should compare PSD analysis over the same length of time in the sample, something I was not careful about."

If you are referring to the length of time it took to acquire the sample, it isn't necessary to have the same length of time for each sample for comparison since your power calculation is obtained by integrating the PSD in the frequency domain, not the time domain. Perhaps you meant something else.

**Bob K.**

---

Bob,

I was concerned about length of time since the longer the sample, the more numerous very low frequency elements will be. You will not "see" these very low frequency events in a short sample. This was an offhand comment and I haven't tried to quantify it.

**George**

---

A higher than normal (for me) TSH test prompted some research on iodine & thyroid. It occurred to me that there might be correlation between hypothyroidism and dysautonomia. The following response to a *British Medical Journal* popped up:

<http://www.bmj.com/cgi/eletters/314/7088/1175#25519>

" For what it's worth, I was on T-4 only meds beginning in 1985 because of a TSH of 6.25. T-4 brought my TSH down to 2.2, yet for 3 years before treatment, and 17 years during, I had debilitating exercise-induced Dysautonomia. When my TSH (while still on T4 only) rose to a "normal" 3.15 the past year, my dysautonomia became crippling--I couldn't do anything without suffering debilitating consequences. Only when I switched to natural hormones, which raised my T3, did my dysautonomia DISAPPEAR, and I am getting closer to normal as far as energy levels than I've been for over 20

years!!! Measuring my TSH as the only guide for my overall health was foolish in my case."

Jackie's post on iodine:

<http://www.afibbers.net/forum/read.php?f=6&i=943&t=943>

Ann's post on iodine:

<http://www.afibbers.net/forum/read.php?f=4&i=12057&t=11997>

Just a thought -

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### **George**

George - excellent. I've been reading more on the subtle issues presented with iodine deficiency and it would appear there is a significant connection to many conditions and symptoms that are not often thought of in terms of iodine deficiency. It seems to make so much sense- especially in my case as I apparently was hypothyroid for much of my adult life. I also never had any physician/endocrinologist order a test for iodine status. I find that incredibly remarkable.

Just for the record, I'm continuing on with my very minor supplementation of potassium iodide and the flow of saliva continues. It's a wonderful feeling not to have a continual dry mouth. And, while very insignificant but still very important.... no medical people could explain the defect in my fingernail on the longest finger. It resolved completely within 6 weeks of starting the potassium iodide and has not returned.

I'm scheduled for another ultrasound of my thyroid nodules to see if anything has changed there.

While I'm not sorry to be rid of afib, I'm still extremely curious about the potential for a minor amount of supplementation benefits and this link you provide reinforces that curiosity.

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### **Jackie**

James, The structure that I couldn't remember was the tricuspid valve.

<http://circ.ahajournals.org/cgi/content/full/112/22/e334>

"Atrial flutter typically originates from the right atrium and most often involves a large circuit that travels around the area of the tricuspid valve that is between the right atrium and the right ventricle."

On another subject, one question that I carry in the back of my mind is why afib tends to originate in the PV. Thus, whenever I encounter a possible lead to answer that question I take note. I feel that the description of the PV that you mentioned regarding the atrial cells changing orientation from longitudinal to transverse, might be a lead. Perhaps if the transition from longitudinal to transverse doesn't go just right, there may be dysfunctionally firing cells. Just speculation.

---

### **Bob K.**

Thanks Bob - not everyone's PV anatomy is the same and increasing the size of the obstacle by having veins sharing a common ostia (as in Jackie's case) of having abnormally large veins (as in mine and many other cases) increases the chance of arrhythmia.

Of course most normal folk have a tricuspid valve and other obstacles in the heart but don't have arrhythmias. So is a dysautonomia or some poor cell alignment at these boundaries, or both (!), a requirement for AF to appear?

Apologies to Hans for this thread straying a little off topic - I'm still none the wiser on how much a dysfunctional ANS plays a part. (I accept that it does in some Lone AFers but don't have a good feel for how many) Just how many Lone AFers have these abnormalities in structure? and how many of these still require an abnormal ANS to get the AF ball rolling?

--

**James D**

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As long as we're straying a bit -From my ribose collection, note this regarding arrhythmogenesis:

*J Biol Chem. 1999 Jun 18;274(25):17820-7.*

An antagonist of cADP-ribose inhibits arrhythmogenic oscillations of intracellular Ca<sup>2+</sup> in heart cells.

Rakovic S, Cui Y, Iino S, Galione A, Ashamu GA, Potter BV, Terrar DA.

University Department Of Pharmacology, Oxford University Oxford OX1 3QT, United Kingdom.

Oscillations of Ca<sup>2+</sup> in heart cells are a major underlying cause of important cardiac arrhythmias, and it is known that Ca<sup>2+</sup>-induced release of Ca<sup>2+</sup> from intracellular stores (the sarcoplasmic reticulum) is fundamental to the generation of such oscillations.

There is now evidence that cADP-ribose may be an endogenous regulator of the Ca<sup>2+</sup> release channel of the sarcoplasmic reticulum (the ryanodine receptor), raising the possibility that cADP-ribose may influence arrhythmogenic mechanisms in the heart.

8-Amino-cADP-ribose, an antagonist of cADP-ribose, suppressed oscillatory activity associated with overloading of intracellular Ca<sup>2+</sup> stores in cardiac myocytes exposed to high doses of the beta-adrenoreceptor agonist isoproterenol or the Na<sup>+</sup>/K<sup>+</sup>-ATPase inhibitor ouabain. The oscillations suppressed by 8-amino-cADP-ribose included intracellular Ca<sup>2+</sup> waves, spontaneous action potentials, after-depolarizations, and transient inward currents. Another antagonist of cADP-ribose, 8-bromo-cADP-ribose, was also effective in suppressing isoproterenol-induced oscillatory activity.

Furthermore, in the presence of ouabain under conditions in which there was no arrhythmogenesis, exogenous cADP-ribose was found to be capable of triggering spontaneous contractile and electrical activity. Because enzymatic machinery for regulating the cytosolic cADP-ribose concentration is present within the cell, we propose that 8-amino-cADP-ribose and 8-bromo-cADP-ribose suppress cytosolic Ca<sup>2+</sup> oscillations by antagonism of endogenous cADP-ribose, which sensitizes the Ca<sup>2+</sup> release channels of the sarcoplasmic reticulum to Ca<sup>2+</sup>.

PMID: 10364226 [PubMed - indexed for MEDLINE]

**Jackie**

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Do supplements affect the autonomic nervous system?

Regarding a survey here of 153 afibbers Hans wrote, "Vagal afibbers who took supplements had significantly shorter episodes than did vagal afibbers who did not and this effect was independent of age and years of afib. No overall benefits of supplementation were observed for adrenergic and mixed afibbers."

Do supplements have the effect of shifting the balance of the autonomic nervous system more towards the adrenergic side? Could this be why vagal afibbers tended to do better with supplements than adrenergic afibbers in Hans' survey?

**Bob K.**

---

Thanks Jacky, it's another thing that confuses me when the subject of dysautonomia is talked about in relation to the heart because the heart has its own intrinsic ability to contract (myogenic). I understand that this intrinsic ability is extremely influenced by the ANS but would a flaw at the heart cell layer be called a dysautonomia? I see the heart cells as part of the substrate and do not think of a flaw here to be a dysautonomia since the nervous system could be working fine, but what do I know!

--

**James D**

---

Bob,

"Do supplements have the effect of shifting the balance of the autonomic nervous system more towards the adrenergic side?"

My empirical evidence would say no. With 31 months of nearly 2x daily heart rate series, a visual (not quantitative) examination of the data would not indicate a shift towards the adrenergic side, at least as far as resting HR is concerned. At one point I'd remembered a series with an average HR in the low 40's early on. As my resting HR tends to be ~52 +/-5, I thought this might illustrate your hypothesis. However, when I went back & examined the data, it appears that the low 40's series was a one-time anomaly. When looked at in totality, I can see no trends. There is a fair amount of spread to the data anyway. Confounding factors include how hard I worked out the day before (in a morning reading), or how hard I worked out today, in an afternoon reading, what I had to eat, how well I slept & etc.

**George**

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GeorgeN, Thanks for your response. From what I've read in your messages regarding HRV, it seems that the ratio of LF to HF power is the best way to assess your ANS status.

However, I was considering an explanation for the different effect that supplements had in the 153 vagal and adrenergic afibbers in Hans' survey.

**Bob K.**

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Bob,

To be done properly, ectopics have to be excluded from the series, then the metrics calculated. I've done some of this manually and have found a large variability in the outcome. When you read the HRV studies, the supposed differences in their metrics are, in my experience, dwarfed by the variability of the metrics calculated on series from one person (me), captured at essentially the same time on a daily basis.

In other words, I have a hard time getting the same meaning out of the data that the researchers do.

**George**

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Our afib is obviously affected by the ANS. Whether abnormal heart tissue is responding to normal ANS responses or is it normal heart tissue responding to abnormal ANS responses (dysautonomia) or both is an open question.

In any case, people have found relief from their afib by a course of action that limits the ANS response, normal or otherwise. Such courses of action include attacking a GERD problem, changing a diet by, for example, excluding gluten or eating a paleo diet.

I posted about my fasting and a reduction in PAC's here:

[http://www.afibbers.net/forum/read.php?f=6&i=8277&t=8277#reply\\_8277](http://www.afibbers.net/forum/read.php?f=6&i=8277&t=8277#reply_8277).

In a recent email exchange with George Eby, he told me that several years ago he underwent a procedure that required fasting for 5 days. He said, "During those five days, I didn't have any arrhythmias. "

We speak of biochemical individuality when we talk about various solutions to afib, therefore a person could have a diet issue that paleo or gluten avoidance would resolve. It would seem that a fairly quick approach to determine whether diet is an issue for a particular individual would be a several day fast. If the afib (or ectopics) improved during this time, then the person could get to work trying to determine what foods are the culprits. As I posted in the linked, I'm going through a process of blood testing to (hopefully) see what the bad actors are. However a person could just carefully add back in foods, keep a journal & see what happens. The difficulty being that some foods give an IgG response which is delayed.

## **George**

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George - That fasting quote from George Eby reminds me of one that was mentioned in a discussion I heard about food intolerances and allergies.

The doctor speaking mentioned that years back, people with lupus were put on a 5-day fast and their symptoms of lupus disappeared. From that, they determined that it was a gluten sensitivity and those patients were placed on gluten-free diets with great success in returning to almost normal status being free of lupus symptoms.

I'm thinking that gluten/gliaden proteins and the associated casein protein sensitivities that occur in people who do not have celiac disease is very possibly a critical connection to eliminating afib or any of the other many, many symptoms that come up in that list. George could well be one of those as well.

It all is based on the inflammatory response the body generates when offending substances are ingested. The inflammation connection and afib has been established.

## **Jackie**

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Hi Jackie,

I think a fast would be prudent for many afibbers. If they improved, then they'd know that food is an issue and then they could go about determining which ones. The question then is figure this out. Though gluten/gliaden and casein are common culprits, in my wife's case, she is fine with gluten/gliaden, but not with yeast, casein and blueberries. In my daughter's case, grains were fine, but casein is a bad actor, and garlic is the worst offender.

I should note that neither my wife or daughter have afib, I'm only stating the results of their IgE/IgG test. The test appears to have empirical validity as they feel much better when they avoid foods that positive. The point being that without testing, people may make their diets more restrictive than necessary.

## **George**

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George - just to complicate this issue, I just heard a doctor's presentation on food addictions and who does deal with food allergies. He uses the blood marker testing but finds that they are often inconclusive and feels the best testing is yet to be developed. He says it's almost fool-proof to do the fasting and then gradually introduce back in some of the prime suspect foods.... after a couple of months. This would equate, though, to a very lengthy process. I guess just choose the most commonly known foods for sensitivities and branch out from there.

Would probably be a hit or miss thing, but from my own experience over many years, I have a good idea to which foods I most likely have some sensitivities, because of the physical symptoms that come up repeatedly. He also says that people who test negative for gluten may still have an allergy to wheat which I thought was interesting.

On the yeast sensitivity - that probably goes to a candida overgrowth. Was she tested for that?

## **Jackie**

I agree, foods can be the instigator of LAF. In my case, niacin seemed to be the magic bullet. One thing I noticed is that my salt sensitivity (which caused severe arrhythmias (LAF) nearly instantly upon ingestion of sodium chloride) stopped after getting on niacin. Now I can eat salty items without problems. I was really convinced that foods were the cause of my arrhythmias, and I still am convinced. However, other than salt, I have been unable to identify any specific food as the cause of LAF or PACs. Even today, if I am going to have arrhythmias, it will be for a few minutes about an hour after a meal. All I eat is meat, vegetables and fruit. What more can I do. Beats me!

### **George Eby**

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It is really too early to tell, however in the 6 days since I added a couple of mg of K iodide to my daily routine, my resting heart rate seems to have increased significantly (>8 BPM). There are other things that can cause this like illness & exercising too hard. I don't think these are factors, but will have to get more data to see if this correlation holds.

This would be in response to Bob's question about supplements, "Do supplements have the effect of shifting the balance of the autonomic nervous system more towards the adrenergic side?" Possibly yes in the case of potassium iodide.

Ectopic counts seem lower, too. However these also vary and are already pretty low.

### **George**

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GeorgeN - are you really saying milligrams of potassium iodide? Be careful initially in adding too much. There are two very distinct opinions on getting into milligrams of supplemental iodine vs. micrograms.

George Eby - it's totally understandable that if you retain sodium, then your biochemistry allows afib to occur with resulting the depleted potassium status. Do you also retain water (tissue edema) with this sensitivity? Puffy face, around the eyes, ankles? I think your diet sounds great as long as they are whole foods, cooked from scratch and not commercially prepared. If the latter, that's a typically source of too much sodium chloride, as you undoubtedly know.

Best to you.

### **Jackie**

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Jackie,

Yes I'm saying milligrams and have read the arguments on both sides. One of the protocols talks about: " Therapy usually starts at 1 tablet of Prolamine Iodine daily for a week. If no problem arises, the dose increases slowly (every week to 2, 3, 4, 5, and 6 tablets daily)"

Prolamine Iodine has 3 mg iodine in it, so they are talking about daily doses of 6, 9, 12, 15 and 18 mg daily. I'm taking in much less, about 1.8 mg/day, which is admittedly 12x higher than the RDA. In your post, <http://www.afibbers.net/forum/read.php?f=6&i=943&t=943> you stated, "Started out by working up in microgram doses to 2 mg a day of potassium iodide".

The FDA recommends a daily dose of 130 mg KI as a specific blocker of thyroid radioiodine uptake. [http://www.fda.gov/cder/drugprepare/KI\\_Q&A.htm](http://www.fda.gov/cder/drugprepare/KI_Q&A.htm)

Here is their comments regarding side effects of this dose: "9. What are the possible risks and side effects of taking potassium iodide (KI)? Thyroidal side effects of KI at recommended doses rarely occur in iodine-sufficient populations such as the U.S"

I am paying careful attention to ectopics & looking for any other side effects. I will have another discussion with my MD on Friday regarding testing & dosage.

**George**

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Jackie,

I should note that in my post where I said, "The FDA recommends a daily dose of 130 mg KI as a specific blocker of thyroid radioiodine uptake." This is specifically for the purposes of prevention in the case of radioactive fallout. I did not intend to imply the FDA suggests everyone should take 130 mg/daily on a regular basis, as opposed to a nuclear emergency.

Also my resting HR was back down this morning, so it must have been something other than the iodine.

**George**

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Question: Would autonomic dysregulation be the same or similar to dysautonomia?

In Leo Galland's book "Power Healing," (Leo Galland, MD FACN, (Director of Foundation for Integrated Medicine), he uses the term, "autonomic dysregulation" and describes a complicated patient case.

In the physical assessment of the patient, he says a minor congenital anomaly reflects a disturbance in growth during the third month of pregnancy. He says physical signs currently observed in the patient can result during that third month like indented breastbone (pectus excavatum) and mild scoliosis could indicate some fetal distress or disturbance. He then says....

"The part of the nervous system that regulates heart rate, the autonomic nervous system, also undergoes a critical stage of its development during the third month; so do the valves of the fetal heart."

In this patient, he heard mitral valve clicking and she had problem with extreme fatigue and elevated pulse after standing. He says, "all of these associations suggested to me that the speeding of her pulse on standing was not the result of prolonged rest but represented an inborn disturbance in the function of the autonomic nervous system, a condition called autonomic dysregulation.

(pp 80-81)

This all sounds remarkably similar to the post PC did in CR #57 with his entrapment discussion.

Any comments?

**Jackie**

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Hi Jackie,

Sorry for the delay in responding, but I've just returned.

Your above post is rather provocative and yes, I'd classify autonomic dysregulation or dysfunction as the more modern equivalent of dysautonomia, a term that has been around a long time and means many things to many people.

My view of this so-called autonomic dysregulation and LAF is not as a congenital anomaly, at least not in the vast majority of cases. However, I certainly think that MVP (genetic component) can often lead to LAF.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2739055&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2739055&dopt=Abstract)  
MVP is seen in 5% of the population (equal male and female) and predisposes to but does not actually cause LAF. In addition I think the predisposition is structural and not autonomic. Pectus excavatum is part MVP Syndrome.

If you'll recall, virtually all with LAF have slightly elevated BNP during NSR. An elevated BNP is an early warning

indicator of left ventricular dysfunction and this has been IMHO the primary hurdle in getting mainstream medicine to differentiate LAF from pathologic AF.

BNP is an indicator of ventricular stretch, esp. left ventricular stretch (enlargement or dilatation). Such individuals are often hypertensive and usually eventually develop congestive heart failure. BNP is also a biomarker for left ventricular end systolic volume (increased in mitral regurgitation).

However, as we have also shown, those with LAF are taller and thinner than normal (not to mention those with pathologic AF). This means that they have higher vagal tone and lower sympathetic tone => lower HR => greater stroke volume (more blood ejected from the left ventricle with each beat) => more left ventricular stretching => greater baseline BNP.

This situation is further amplified if blood volume is lower, e.g., dehydration or this increased BNP alone. For LAFers with low blood volume and whose HRs are low this means that there is even more left ventricular stretching than otherwise. The left ventricle has to be even more efficient with each stroke => greater stroke volume. Furthermore, a greater stroke volume => greater transient increase in hydrostatic pressure sensed by the carotid sinus in the neck => greater vagal tone.

So, it's kind of a vicious circle for those with LAF. Episodes only make it worse, since ANP is added to the mix. Both conspire to deplete the body's stores of Mg<sup>++</sup>. Perhaps this slow process of depletion is what actually determines the onset of LAF and why "AF begets AF."

IMHO LAF is not due to autonomic dysregulation, although it certainly involves the ANS. Catecholamine hypersensitivity can certainly develop, but that's another kettle of fish.

It would be interesting to know the average % of body volume comprised by blood in LAFers (v. normals), but blood volume is expensive to measure.

**PC**

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