THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 87 **MARCH 2009** **9th YEAR**

In this issue we return to our main mission – that of reporting the latest developments in afib-related research. A team of researchers at the Hartford Hospital in Connecticut has confirmed what we have long suspected – afibbers are deficient in magnesium! Another group of American researchers has confirmed that stress is a hugely important trigger for adrenergic afibbers; simethicone may be a viable approach for preventing or perhaps even terminating certain types of afib episodes; and digoxin has added to its reputation by being implicated in the development of invasive breast cancer.

In light of recent research touting statin drugs as the ultimate inflammation fighters (JUPITER trial), it is encouraging to see a study by highly respected, independent investigators which concludes that vitamin C is just as effective in fighting inflammation and is, of course, much cheaper and completely safe. Another natural remedy, ginger, also has strong anti-inflammatory properties and may even be useful in preventing some vagal afib episodes.

An industry-sponsored study promoting more widespread use of warfarin among paroxysmal afibbers is carefully analyzed and found wanting in scientific merit. All this and more in this March banner issue – enjoy!

Finally, if you need to restock your supplements, please remember that by ordering through my on-line vitamin store you will be helping to defray the cost of maintaining the web site and bulletin board. You can find the store at http://www.afibbers.org/vitamins.htm - your continuing support is truly appreciated.

Wishing you lots of NSR,

Hans

Highlights

Digoxin increases risk of breast cancer

AARHUS, DENMARK. Digoxin (digitalis, Lanoxin), originally an extract from the foxglove plant, has been used since the 18th century to treat congestive heart failure and, more recently, is also being prescribed for rate control in atrial fibrillation patients. Digoxin inhibits the Na^+/K^+ ATPase, which indirectly raises intracellular Ca^{2+} concentration, thus increasing the force of contractility in cardiac myocytes (heart cells). Recent research has clearly shown that digoxin should not be used on a continuous basis in patients with paroxysmal lone atrial fibrillation since it is likely to worsen their condition and result in it eventually becoming permanent.

A team of American and Danish researchers now report that digoxin increases the risk of breast cancer among postmenopausal women. Their study involved 5,565 women diagnosed with invasive breast cancer during the period 1991 to 2007 and 55,650 matched population controls. The researchers found that the use of digoxin for at least a year was associated with a 30% greater risk of being diagnosed with invasive breast cancer. The association did not change when adjusted for age, hormone replacement therapy, other drugs, medical

history (reason for prescribing digoxin), and mammography exposure. The researchers conclude that digoxin treatment increases the risk of invasive breast cancer among postmenopausal women and that this risk increases with increasing duration of treatment.

Ahern, TP, et al. Digoxin treatment is associated with an increased incidence of breast cancer: a population-based case-control study. **Breast cancer Research**, *Vol. 10, No. 6, December 2008*

Editor's comment: This latest finding implicating digoxin in breast cancer further adds to the evidence that this drug is a bad actor indeed and should never be used by lone afibbers. Digoxin poisoning is a leading cause of hospital admissions with anywhere between 10 and 30% of patients on the drug being hospitalized for digoxin intoxication. Digoxin is particularly dangerous for patients over the age of 60 years. In this group the mortality associated with acute digoxin toxicity is almost 60%[1].

Digoxin may cause sinus bradycardia, heart block and ventricular arrhythmias, and interacts with a host of other medications among them amiodarone, propafenone (Rythmol), flecainide (Tambocor), tetracycline, calcium channel blockers, and St. John's wort. As if this is not enough, researchers have also found digoxin can cause visual problems even at dosages normally considered safe, and may significantly aggravate asthma symptoms[2,3].

Digoxin may truly be the medicine from hell and certainly should never be used by people with lone afib. If a medicine is needed for the control of heart rate, then calcium channel blockers such as verapamil or diltiazem, or beta-blockers like bisoprolol or metoprolol would be a better choice.

[1] Roever, C, et al. Comparing the toxicity of digoxin and digitoxin in a geriatric population: should an old drug be rediscovered? Southern Medical Journal
http://www.medscape.com/viewarticle/410488
[2] Butler, VP, et al. Digitalis-induced visual disturbances with therapeutic serum digitalis concentrations. Annals of Internal Medicine, Vol. 123, No. 9, November 1, 1995, pp. 676-80
[3] Ayson, M, et al. A pilot study to investigate the pulmonary effects of digoxin in patients with asthma. New Zealand Medical Journal, Vol. 108, February 9, 1996, pp. 36-37

Simethicone to the rescue!

DUSSELDORF, GERMANY. Many afibbers have reported that their episodes often start with a bout of abdominal gas build-up accompanied by belching. German researchers now report that simethicone (*Gas-X*) may be effective in terminating such episodes. Simethicone (polydimethylsiloxane) is a common anti-flatulent, which effectively reduces gas formation and helps prevent bloating and belching by breaking up large gas bubbles. The drug has no known adverse effects.

The German researchers report the case of a 26-year-old male patient who reported to the emergency room with atrial fibrillation accompanied by extensive belching. The ER physicians gave him 169 mg of Simethicone and shortly after he converted to normal sinus rhythm. Based on further tests, it was concluded that the patient suffered from paroxysmal lone AF. Over the next 12 years the patient experienced 40 more afib episodes, which were all terminated successfully with varying doses of Simethicone. The researchers conclude, "that gastric distension with abdominal flatulence may represent one more possible trigger to initiate AF in otherwise heart healthy patients".

Litmathe, J and Litmathe, AM. Simethicone – another "pill in the packet" in paroxysmal atrial fibrillation? **International Journal of Cardiology**, *December 11, 2008 [Epub ahead of print]*

Editor's comment: I have personally found that gas build-up in the stomach and accompanying burping is a potent initiator of ectopics. I have also found that relieving the gas pressure and breaking up large bubbles with the help of Simethicone brings almost immediate relief. The finding by the German researchers that Simethicone may also be effective in terminating episodes initiated by abdominal gas build-up is intriguing indeed and well worth further investigation by readers of *The AFIB Report.*

Vitamin C is a powerful anti-inflammatory

BERKELEY, CALIFORNIA. There is now ample evidence that atherosclerosis and cardiovascular disease involve a systemic inflammatory process. The extent of the systemic inflammation can be ascertained by measuring the blood level of C-reactive protein (high-sensitivity C-reactive protein or CRP). The American Heart Association has designated a CRP concentration of less than 1.0 mg/L (< 0.1 mg/dL) as representing low risk for cardiovascular disease, a level between 1.0 and 3.0 mg/L indicates average risk, while a level above 3.0 mg/L indicates high risk.

A level above 10.0 mg/L represents acute infection or inflammation and should be disregarded when it comes to evaluating cardiovascular disease risk. There is mounting evidence that a systemic inflammation is involved not only in heart disease, but also in such varied conditions as asthma, rheumatoid arthritis, Crohn's disease, intermittent claudication, diabetes, depression, and most common cancers. There is also a clear association between elevated levels of CRP and atrial fibrillation, but at this point, it is not clear whether afib is caused by inflammation or whether sustained inflammation causes afib. In any case, a systemic inflammation is not a good thing to have and finding ways of eliminating it is clearly crucial.

A group of researchers from the University of California in Berkeley, Montefiore Medical Center in the Bronx, NY and the Children's Hospital in Oakland, CA now report that vitamin C is very effective in reducing elevated levels of CRP. Their clinical trial involved 396 healthy non-smokers who were randomized into 3 groups with group A supplementing with 1000 mg/day of vitamin C (ascorbic acid), group B supplementing with 800 IU/day of natural, mixed tocopherols (mostly alpha-tocopherol), and group C receiving a placebo. At the end of the 2-month trial, there were no statistically significant differences in CRP levels among the 3 groups. However, when a sub-group of 162 participants with an initial CRP level above 1.0 mg/L was studied separately, it became clear that vitamin C supplementation is effective in reducing CRP in people with elevated levels.

The median CRP level in the vitamin C group dropped by 0.25 mg/L or 16.7%, while the median level in the placebo group increased by 0.12 mg/L or 8.6%. The vitamin E group also experienced a slight drop in CRP, but it was not statistically significant. The researchers also observed a strong correlation between increasing BMI (body mass index) and elevated CRP with 75% of obese study participants having a CRP level above 1.0 mg/L.

The researchers point out that several studies have shown that statin drugs also reduce CRP levels. Five years of treatment with pravastatin (Pravachol) was found to reduce CRP by 17.4% in a group of heart attack patients. Lovastatin (Mevacor) was found to reduce CRP by 14.8% after treatment for one year. The more recent JUPITER trial involving rosuvastatin (Crestor) found a CRP reduction of 29% after 2 years when compared with the placebo group. This corresponds to the 25% reduction after 2 months when the vitamin C group is compared to its placebo group. The researchers conclude that the CRP-lowering effect of vitamin C is virtually identical to that of statin drugs.

Block, G, et al. Vitamin C treatment reduces elevated C-reactive protein. **Free Radical Biology & Medicine**, *Vol. 46, 2009, pp. 70-77*

Editor's comment: The finding of the JUPITER trial that reducing CRP also reduces the risk of cardiovascular disease is clearly of huge importance. However, of equal importance is the finding that this CRP reduction can be achieved by simply supplementing with vitamin C rather than by taking expensive and dangerous statin drugs.

Ablation data from Sweden

UMEAA, SWEDEN. Being a highly organized country it should come as no surprise that Sweden actually has a National Catheter Ablation Registry that records the outcome of every single catheter ablation performed in this country of 9.2 million people. In 2007 a total of 2,314 ablations were carried out in 8 specialized centers. Of these, 521 procedures were for atrial fibrillation (AF) and 414 for atrial flutter (AFL). This translates to 57 AF procedures per million inhabitants. Considering that about 90,000 newbies join the ranks of afibbers every year in Sweden (incidence about 1%) and that the total number of afibbers in Sweden is likely close to 500,00 (based on European prevalence of

5.5%), it is clear that only a very small proportion of patients (around one in a thousand) presently receive curative treatment for AF in Sweden. It certainly would be of interest to see comparative numbers for the US, Canada, and the UK, but unfortunately none of these countries have national catheter ablation registries.

The most common procedure (accounting for 25% of overall volume) carried out in 2007 was for supraventricular tachycardia (SVT). Atrial fibrillation ablation accounted for 23% of overall volume and atrial flutter for 18%. Mean procedure time for an AF ablation was about 3.5 hours with an average fluoroscopy exposure of 43 minutes. The most common procedural complication was hemorrhage (requiring treatment) at 1.7% followed by pericardial effusion at 0.4%. Tamponade, valve damage, pulmonary embolus, cerebral embolus, and pseudoaneurysm each accounted for about 0.2% bringing the total complication rate to 2.9%. In contrast, the complication rates for SVT and AFL procedures were 1.8% and 0.7% respectively. The acute success rate for an AF procedure was 89%, but unfortunately, no data are presented for long-term success.

Kesek, M. Ablation procedures in Sweden during 2007: results from the Swedish Catheter Ablation Registry. **Europace**, *Vol. 11, 2009, pp. 152-54*

Ginger benefits cardiovascular system

UMEAA, SWEDEN. Ginger (*Zingiber officinale* Roscoe) has been cultivated for medicinal and culinary purposes for over 2000 years. It is now generating considerable excitement within the cardiology community (more than 1000 scientific articles about ginger are listed on MEDLINE). Recent research has shown that ginger exhibits strong anti-inflammatory and antioxidant effects and effectively inhibits platelet aggregation induced by arachidonic acid. Ginger also has significant fibrinolytic activity and exhibits calcium channel-blocking activity similar to that of verapamil. Of more immediate interest to the afib community, especially a vagal afibber, is the finding that ginger stimulates the release of adrenaline and increases the strength of the heart beat.

Nicoll, R and Henein, MY. Ginger (Zingiber officinale Roscoe): a hot remedy for cardiovascular disease? **International Journal of Cardiology**, *Vol. 131, No. 3, January 2009, pp. 408-09*

Editor's comment: Vagal afibbers often experience their episodes when resting or digesting a heavy meal; in other words, when the parasympathetic (vagal) arm of the autonomic nervous system is dominant. It is conceivable that ingesting ginger (minimum of 5 g) an hour or so before bedtime may increase sympathetic (adrenergic) response through adrenaline release and thus prevent episodes that come on when the "head hits the pillow".

Main factors affecting ablation outcome

BAD KROZINGEN, GERMANY. Being able to predict whether a RF ablation for atrial fibrillation is likely to be successful or not – prior to the actual procedure – would clearly be of great benefit. There is considerable evidence that systemic inflammation and afib are associated, but it is not entirely clear whether inflammation causes afib or afib, particularly persistent and permanent, causes inflammation. A group of German researchers recently set out to determine whether being in an inflammatory state prior to a pulmonary vein isolation (PVI) procedure would affect the long-term outcome of the procedure.

The study involved 72 patients with paroxysmal (64%) or persistent (36%) afib who underwent an acutely successful circumferential PVI (no conduction between isolated area and the rest of the left atrium). The majority (81%) of the patients were male and the average age at ablation was 55 years (46-64 years). The patients had suffered from afib for an average of 5.5 years and only 14% had underlying heart disease, so 86% would be classified as having lone atrial fibrillation (LAF). However, 52% of the group had high cholesterol/triglyceride levels, 22% had diabetes, and 19% had hypertension.

All patients underwent a medical examination on the day prior to the ablation during which baseline blood samples were obtained. NOTE: Patients with left atrial diameters larger than 55 mm were excluded

from the study. All patients underwent 24-hour Holter monitoring 1, 3, 6 and 12 months following the procedure and were also advised to report any afib symptoms during the average 12.5-month follow-up. Any symptomatic or asymptomatic afib episodes observed after the first month post-procedure were classified as a recurrence.

At the end of the study 44 patients (61%) were in normal sinus rhythm without the use of antiarrhythmic drugs. The remaining 28 patients had experienced one or more recurrences with the mean time to relapse being about 10 months. The following variables were found to increase the risk of recurrence:

- Hypertension
- Elevated body mass index
- Diminished left ventricular ejection fraction
- Low left ventricular end-diastolic diameter
- Enlarged left atrium
- High white blood cell (WBC) count
- Elevated C-reactive protein (CRP) level

Age, afib type, years of afib, structural heart disease, medications, and fibrinogen level were not associated with relapse. A Cox multivariate analysis showed that only hypertension (Hazard ratio = 3.1), enlarged left atrium (HR = 1.08) and WBC count (HR = 1.42) were independent predictors of afib recurrence following an initially successful PVI. There was a trend for longer AF duration to be associated with greater risk of failure. The data showed that having a WBC count above about 6280/cubic millimeter (normal range of 4300 – 10800) was a fairly accurate predictor (70.4% sensitivity and 69.8% specificity) of AF recurrence after an initially successful circumferential PVI.

Letsas, KP, et al. Pre-ablative predictors of atrial fibrillation recurrence following pulmonary vein isolation: the potential role of inflammation. **Europace**, *Vol. 11, 2009, pp. 158-63*

Editor's comment: WBC count is a common blood test and it is generally accepted that an elevated level indicates the presence of an infection or inflammation. In light of the above findings, it would seem prudent to have a WBC count, and a CRP level determination a month or two prior to a scheduled PVI. If they indicate the presence of an inflammation, it should be brought under control before the procedure. This can usually be accomplished by supplementing with a natural anti-inflammatory such as *Zyflamend*, ginger, curcumin, vitamin C, beta-sitosterol, boswellia, or *Moducare*.

Afibbers are magnesium-deficient

HARTFORD, CONNECTICUT. Magnesium (Mg) is an enormously important mineral being a cofactor in over 300 enzymatic reactions continuously taking place in the body. Magnesium is also a vital component of the skeletal structure and about 65% of the body's magnesium stores are found in bone, another 34% is found in transcellular fluids, and the remaining 1% is found in extracellular fluids such as blood. It is thus clear that measuring magnesium in blood serum is not likely to be a very accurate measure of the body's overall magnesium status.

There is increasing evidence that magnesium plays a crucial role in preventing and terminating cardiac arrhythmias. A group of cardiologists and pharmacologists at the Hartford Hospital reasoned that a pre-procedure infusion of magnesium might help prevent the acute development of atrial fibrillation following a radiofrequency ablation for this disorder. As a first step in proving or disproving this hypothesis, they decided to do a trial in which half the participants would have saline solution (0.9% sodium chloride) with 4 grams of magnesium sulfate (800 mg elemental magnesium) infused over a 15-minute period just prior to accessing the left atrium in a standard PVI procedure, while the other half would just have a saline solution infusion.

The trial involved 22 patients with paroxysmal or persistent afib. Samples of venous blood (for determination of extracellular Mg concentration) and buccal scrapings (scrapings from inside the cheek) were collected before the start of the procedure, 15 minutes after the completion of the infusion, at the end of the ablation procedure, and at 6 hours after the infusion. The blood samples (serum) were analyzed for extracellular magnesium concentration and the buccal scrapings were analyzed (using the *EXAtest*) for intracellular magnesium concentration as well as for concentrations of calcium, potassium, sodium, chloride, and phosphate. At least one study has shown that there is an excellent correlation between the magnesium (intracellular) content of buccal scrapings and that of myocytes (heart cells). The major findings are as follows:

- None of the study participants were deficient in Mg at baseline when considering blood serum values only. The average serum Mg concentration was 2.08 mg/dL versus the normal lower limit of 1.6 mg/dL.

- The majority (89%) of participants were magnesium-deficient at baseline when considering intracellular (*EXAtest*) values only. The average intracellular Mg concentration was 32.2 mEq/IU versus a normal lower limit of 33.9 mEq/IU. NOTE: The unit is defined as x-ray intensity (peak divided by background) divided by unit cell volume.

- There was no correlation whatsoever between serum magnesium and intracellular magnesium concentrations.

- Serum levels of Mg rose rapidly in the magnesium infusion group 15 minutes post-infusion and, although declining over the 6-hour observation period, remained considerably higher than the level in the placebo group (saline infusion only).

- Intracellular level of Mg increased rapidly in the magnesium infusion group 15 minutes post infusion and continued to rise throughout the 6-hour observation period. Somewhat surprisingly, the intracellular Mg level also increased somewhat (over baseline) in the placebo group over the 6-hour period. The Hartford researchers speculate that the ablation procedure itself, most likely the anaesthesia, facilitates the transfer of magnesium from serum to intracellular space.

- The intracellular calcium concentration increased significantly in the Mg infusion group post infusion, but gradually reverted to baseline over the 6-hour period.

- The intracellular potassium concentration increased by about 50% from baseline to the end of the PVI procedure and then began to drop off at the 6-hour mark.

The authors of the report conclude that future studies are needed to evaluate the electrophysiologic benefits of magnesium repletion and the effects of routine procedures and anaesthesia on intracellular electrolytes.

Shah, SA, et al. The impact of magnesium sulfate on serum magnesium concentrations and intracellular electrolyte concentrations among patients undergoing radio frequency catheter ablation. **Connecticut Medicine**, *Vol. 72, May 2008, pp. 261-65*

Editor's comment: A 2006 LAF Survey (LAFS-11) found that, among a small sample of 7 afibbers who had *EXAtest* results, all 7 were either below or very close to the lower normal limit. The Hartford report provides important additional evidence to support the conclusion that afibbers are likely low in intracellular magnesium even though their blood serum levels may be normal. It is also of interest that replenishing magnesium via an infusion not only increases intracellular Mg concentration, but also increases intracellular potassium levels. This is all good support for our long-held conviction that lone afibbers with normal kidney function are likely to benefit from supplementing with magnesium, potassium, and taurine (facilitates the uptake of Mg and K).

New ablation catheter looks promising

NIEUWEGEIN, THE NETHERLANDS. The Holy Grail of pulmonary vein isolation (PVI) procedures is to consistently achieve complete elimination of afib in one hour or less. Many approaches have been developed and tried to achieve this goal. Electroanatomical (CARTO) mapping, catheters with irrigated tips, mesh catheters, robot-assisted systems (*Stereotaxis* and *Hansen Sensei*), cryoablation, HIFU (high intensity focused ultrasound) powered ablation, and CARTO mapping with CT scan or MRI overlay are some examples of these novel approaches. Unfortunately, none of them have "found" the Holy Grail. Most procedures still take about 3 hours, expose the patient to significant amounts of radiation through the use of fluoroscopy, are sometimes accompanied by complications (1.5 – 6% of cases), and have a long-term success rate of about 50% unless performed by highly skilled and experienced EPs.

A new ablation catheter has now been developed which may well revolutionize the world of PVIs. The catheter, developed by Ablation Frontiers Inc., has several unique features. It is a combined circular

mapping and ablation catheter with 10 independent platinum electrodes of 3 mm length and 3 mm spacing. The nominal diameter of the catheter is 25 mm, but can be varied by simply turning a handle on the catheter control mechanism. The catheter receives radiofrequency power from a unique generator that can deliver either unipolar or bipolar energy to individual electrodes, or to the whole array of electrodes simultaneously. NOTE: *Unipolar energy consists of current flowing from the electrodes at the catheter tip to the dispersive electrodes on the patient's back. Bipolar energy consists of current flowing between adjacent selected pairs of electrodes on the catheter tip. Bipolar current can be applied simultaneously with unipolar current or it can be field sequential.*

A team of American and Dutch electrophysiologists recently carried out a trial of the new ablation system in a group of 98 lone, paroxysmal afibbers (75% male) with a left atrial diameter of less than 45 mm. The ablation was performed using a 4:1 ratio of duty-cycled bipolar/unipolar radiofrequency energy simultaneously at all selected electrode pairs until complete electrical isolation was achieved between the pulmonary veins and the left atrium. NOTE: The lesion line was placed just outside (on the atrium side) the antrum (edge) of the pulmonary veins and encircled each vein with a continuous band of ablated tissue. Average total procedure time was 84 minutes (range of 45 – 180 minutes) and average fluoroscopy exposure was 18 minutes (range of 9 – 45 minutes).

There were no procedural or post-procedural complications and no stenosis was observed at the 3-month follow-up. Al patients were followed up with 7-day Holter monitoring after six months. Among the 53 patients who had gone 6 months or longer following their procedure at the writing of the report, 44 were free of afib without the use of antiarrhythmic drugs. In other words, this is an excellent single procedure success rate of 83%. It is also worth noting that none of the afib episodes observed in the Holter monitoring were asymptomatic. NOTE: Four of the 5 authors of this report have financial ties to Ablation Frontiers, Inc.

Boersma, LVA, et al. Pulmonary vein isolation by duty-cycled bipolar and unipolar radiofrequency energy with multielectrode ablation catheter. **Heart Rhythm**, *Vol. 5, December 2008, pp. 1635-42*

Kistler, PM. Multielectrode ablation for paroxysmal atrial fibrillation: pulmonary vein isolation made easy? **Heart Rhythm**, *Vol. 5, December 2008, pp. 1643-44*

Editor's comment: The results obtained with this new catheter do indeed look promising. It makes sense that the application of bipolar energy would produce better results than the use of unipolar energy, and it also seems reasonable that the capability to apply energy to 10 "catheter tips" simultaneously would shorten procedure time when compared to point-by-point ablation with a single catheter tip. One concern might be that the Ablation Frontiers catheter is non-irrigated; however, the authors of the report specifically point out that no char formation was observed on the electrodes after withdrawal of the catheter.

Real AF burden following ablation

HAMBURG, GERMANY. Routine follow-up following a catheter ablation for atrial fibrillation (AF) is usually based on periodic ECGs, 24-hour Holter monitoring, or the use of 7-day event recorders as well as on the patient's own reporting of symptomatic episodes. It is clear that these protocols could miss some episodes, especially if they are asymptomatic. A group of EPs from the University Heart Centre in Hamburg now report the results of a study to determine the "real" long-term success rate of PVIs.

The study involved 37 afibbers (20 paroxysmal and 17 persistent or permanent). The average age of the patients was 65 years, 20% were male, and 68% had no underlying structural heart disease. All study participants had previously had a pacemaker or ICD (implantable cardioverter defibrillation) implanted for sick-sinus-syndrome (53%), to prevent bradycardia when on sotalol or other drugs (16%), or because of an AV conduction block (13%). The pacemakers all had a built-in Holter monitoring function so that the researchers were able to determine, on a continuous basis, the afib burden (total time spent in afib or episode frequency multiplied by episode duration) prior to and after the ablation.

The researchers found that the mean afib burden among paroxysmal afibbers during the 7 months preceding the ablation was 17.3%; i.e. these afibbers had spent 17.3% of their lives in afib during the preceding 7 months. Among persistent and permanent afibbers, the pre-ablation afib burden averaged 57%. All participants underwent a segmental PVI and a standard right atrial flutter

ablation. Additional linear lesions were created as required in persistent/permanent afibbers, two of whom underwent a follow-up procedure.

The afib burden was tabulated at 3, 6, 9 and 12 months following the procedure. Among paroxysmal afibbers, 17 patients (85%) had experienced no episodes at all during the 112-month follow-up, so had an afib burden of 0%. However, 4 of these patients were still on antiarrhythmics. The average afib burden among the remaining 3 patients had been reduced from 15.5% to 4.3%.

Among the persistent/permanent afibbers, 10 had experienced no episodes (0% post-procedure afib burden), while the remaining 7 patients had reduced their burden from an average 57.4% to 13.9%. It is of considerable interest that all Holter-recorded episodes were symptomatic and coincided fully with episodes observed by the patients themselves. *NOTE: An afib episode was defined as an atrial high-frequency episode of less than 180 bpm lasting longer than 30 seconds.*

Steven, D, et al. What is the real atrial fibrillation burden after catheter ablation of atrial fibrillation? **European Heart Journal**, *Vol. 29, 2008, pp. 1037-42*

Shah, D. Atrial fibrillation burden: a 'hard' indicator of therapeutic efficacy and prognostic marker to boot? **European Heart Journal**, *Vol. 29, 2008, pp. 964-65*

Editor's comment: This study confirms our survey findings that even an unsuccessful ablation usually leads to a better quality of life (reduced afib burden). However, there certainly are exceptions to this – I was one of them. Another important finding is that there were no asymptomatic episodes recorded. This demolishes the argument that life-time warfarin may still be required even after a successful PVI. Nevertheless, it should be kept in mind that all the study participants had highly symptomatic episodes prior to their ablation. If their episodes had been asymptomatic prior to the PVI, might the unlucky few still have experienced asymptomatic episodes following the procedure? The German study does not answer this question.

Stroke risk in paroxysmal AF

STOCKHOLM, SWEDEN. Recent headlines proclaimed that stroke (ischemic) is just as common in paroxysmal atrial fibrillation patients as it is among permanent afibbers. Not surprisingly, the conclusion of the Swedish study was, "*It is therefore important to increase the use of anticoagulants (warfarin) among patients with paroxysmal atrial fibrillation*". Let us look beyond the headlines and abbreviated summary (abstract) of the study and see what it really means for otherwise healthy lone afibbers.

The study involved 855 paroxysmal and 1126 permanent afibbers who were treated for atrial fibrillation (AF) in two Stockholm hospitals during 2002. At the end of the 3.6-year follow-up period, 110 patients had suffered a first ischemic stroke. This corresponds to a stroke incidence of 2.1%/year in paroxysmal and 2.5%/year in permanent afibbers.

Before proceeding any further, it should be pointed out that the study group did not consist of very healthy people. As a matter of fact, more than a third of them died during the follow-up. Almost half (48%) had hypertension, 50% had heart failure (64% in the permanent group), 10% had some sort of valvular defect, 12% had thyroid problems, and 14% had chronic pulmonary disease. Only 4% of the group had lone atrial fibrillation and no strokes, of any kind, occurred in this group during the 3.6 years of follow-up. In contrast, the rate of stroke among patients with heart failure was 9%/year, 14%/year among those who had already had one stroke, 10%/year among those who had experienced a heart attack, and 9%/year among patients diagnosed with hypertension. In other words, 96% of the participants upon which the conclusion of the study are based bear no resemblance whatsoever to a group of otherwise healthy lone afibbers.

The Swedish researchers also evaluated stroke risk based on $CHADS_2$ score where a score of 0 corresponds to no increased risk factors for ischemic stroke and a score of 1 indicates the presence of one risk factor (hypertension, diabetes, heart failure or age over 75 years). Study participants with a $CHADS_2$ score of 0 to 1 had a stroke risk of 1.0%/year if they were paroxysmal and 1.0%/year if they were permanent. A rate of 1.0%/year is exactly what would be expected from an age- and sex-matched sample of the general population. In other words, afibbers with a $CHADS_2$ score of 1 or 0 do not have an increased risk of stroke. The researchers also investigated the relationship between age and stroke risk and found that afibbers below the age of 70 years had an

annual stroke risk of less than 0.5% (less than half of that found in the general population).

The only conclusion that can be reached from this data is that any increased stroke risk that may be associated with AF applies only to very sick, old people. Similarly, it is clear that warfarin therapy only benefits that same group of people. When considering paroxysmal afibbers only, the stroke rate was 1.3%/year among patients on warfarin as compared to 5.3% among those not on warfarin. However, when patients with a prior stroke or TIA (transient ischemic attack) were excluded from the analysis, there was no statistically significant difference in stroke risk between warfarin-treated patients and those not on warfarin. Considering the flip side of this finding, one could certainly be pardoned for concluding that warfarin, like aspirin, really only benefits patients who have already suffered an ischemic stroke or TIA. *NOTE: Two of the authors of this study have financial ties to AstraZeneca, a major Swedish pharmaceutical company.*

Friberg, L, et al. Stroke in paroxysmal atrial fibrillation: report from the Stockholm Cohort of Atrial Fibrillation. **European Heart Journal,** *January 27, 2009 [Epub ahead of print]*

Editor's comment: The results of this study unequivocally confirm that lone, otherwise healthy afibbers have a very low risk of ischemic stroke; as a matter of fact, substantially lower than that of the general population. A more detailed examination of the data presented in the report would also lead one to the inescapable conclusion that afib, as such, is not a risk factor for stroke – rather it is the conditions that often accompany it (heart disease, hypertension, etc) that increase the stroke risk.

American Heart Association
Abstracts from Scientific Sessions 2008
Published in **Circulation**, *Vol. 118, No. 18S, October 28, 2008*

Happiness = no afib

Our very first LAF Survey in February 2001 clearly established that emotional and work-related stress are important triggers for the initial and subsequent afib episodes. A later, considerably larger, survey carried out in June 2001, refined this finding with the observation that emotional stress is predominantly a trigger for adrenergic afibbers where 94% of respondents listed stress as their most important trigger. In contrast, only 29% of vagal afibbers listed stress as an important trigger. Among mixed afibbers, 56% listed stress as an important trigger.

A group of researchers from Yale University and the University of California now confirm our findings. Their 1-year study involved 75 paroxysmal or persistent afibbers with adrenergically mediated afib, 60% of whom were male and 60% of whom were taking beta-blockers. The study participants kept detailed diaries recording their mood states every 30 minutes, as well as at the end of each day. They were also equipped with event monitors which recorded all their afib episodes. Detailed analysis showed that participants (not taking beta-blockers) reporting "feeling happy" in a diary entry were 10 times less likely to experience an afib episode within the next 30 minutes than were those reporting a neutral mood state. On the other hand, those reporting feeling sad were 8 times more likely to experience an episode within 30 minutes of recording this feeling. Anger and worry were other significant triggers, with anger being particularly bad for men and worry being particularly detrimental for women.

Abstract #1036

Bisphosphonates increase risk of afib

There are now several studies linking the use of bisphosphonates such as alendronate (Fosamax) and Zoledronate (Zometa) to an increased risk of atrial fibrillation among postmenopausal women. A group of Chicago-based researchers have just completed a meta-analysis of these studies involving over 26,000 women. They conclude that the use of bisphosphonates is associated with a 52% increased risk of developing afib that requires hospitalization. They speculate that the increased risk may be due to bisphosphonate-induced release of inflammatory cytokines or shifts of calcium within atrial cells. NOTE: Other studies have shown that just taking one packet of bisphosphonate is enough to increase the risk of AF in postmenopausal women.

Abstract #2159

Afib and the autonomic nervous system

In 1982 (27 years ago!) Dr. Philippe Coumel of the Lariboisiere Hospital in Paris discovered that a dysfunction of the autonomic nervous system (ANS) plays a major role in lone atrial fibrillation (LAF). Dr. Coumel coined the terms vagal and adrenergic to describe two types of afib – one associated with an overactive parasympathetic (vagal) branch of the ANS, and the other associated with an overactive sympathetic (adrenergic) branch. For many years, Dr. Coumel's findings were ignored (especially in North America) and cardiologists lumped all cases of afib together as adrenergic with often disastrous results such as prescribing beta-blockers for vagal afibbers.

The tide has now turned with most electrophysiologists and, to a lesser extent, cardiologists recognizing the existence of the two types and adjusting their prescription patterns accordingly. German researchers recently provided additional evidence of the association between the ANS and LAF. From a total of over 20,000 consecutive Holter recordings they identified 715 episodes of paroxysmal afib. They found that 41% were preceded by a run of ectopic beats, 29% were of sudden onset, and 20% were preceded by a change in heart rate (possibly bradycardia as experienced by vagal afibbers whilst at rest). By analyzing heart rate variability (HRV) in 5-minute segments just prior to the onset of an episode, the researchers discovered that sudden onset episodes were associated with significant changes in HRV just prior to onset. Thus, the low frequency component (adrenergic) and the low frequency/high frequency (adrenergic/vagal) ratio increased significantly as did the Poincare plot index. The researchers conclude that transient abnormal fluctuations in cardiac ANS control may predispose to the development of paroxysmal afib.

Abstract #1037

Elimination/Reduction Protocol

Case No. 701

Male afibber – **49 years** of age with **mixed AF** of **11 years standing;** no underlying heart disease
No. of episodes in 6 months prior to starting protocol: **75-80**
Afib burden in 6 months prior to starting protocol: **460 hrs**
No. of episodes in most recent 6 months after starting protocol: **0**
Afib burden in most recent 6 months after starting protocol: **0 hrs**
Time on protocol: **18 months**
Still need to avoid triggers?: **No**

Main components of effective protocol

Trigger avoidance: **None**
Diet changes: **None**
Supplementation: **Hawthorn extract**
Drug therapy: **None**
Stress management: **None**
Approaches to shorten episodes: **None**
Approaches to reduce ectopics: **None**

Background and details of protocol

I started taking a hawthorn extract supplement after a bit of web research. It was widely used as a heart "strengthener" since the Middle Ages, but tends to have gone out of use in parallel with the rise of pharmaceutical giants. However, it is widely used in China, Russia, and Brazil. My cardiologist is amazed at how this has helped and I will still undergo annual check ups. I have experienced no episodes for 18 months. I still take the hawthorn supplement but at a very reduced quantity, and occasionally a coenzyme Q10 supplement. I would urge any readers to try a good quality hawthorn extract, on its own, for at least a month. My exercise regimen has increased considerably with swimming, running and weight training, I but don't know whether this has helped.

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Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: editor@afibbers.org World Wide Web: http://www.afibbers.org