

# THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

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*The inflammation saga continues. In a landmark study Greek researchers conclude that there is a definite association between recurrence of afib after cardioversion and the patient's blood level of biomarkers of inflammation and oxidative stress. However, it is still not clear whether inflammation and oxidative stress causes afib, or whether afib causes inflammation and oxidative stress. In any case, since both systemic inflammation and prolonged oxidative stress are "bad actors", it would seem prudent for afibbers to minimize these conditions by appropriate supplementation.*

*Polish researchers report a connection between weather conditions and hospital admissions for atrial fibrillation. They speculate that electromagnetic radiation generated by certain weather systems could explain the association. Could other sources of electromagnetic radiation (cell phones, etc) also be involved in precipitating afib episodes?*

*Also in this issue, German researchers report that the commonly used ablation end-point test, burst pacing, cannot be used to predict long-term success of the procedure, American and French researchers discuss the factors entering into the prediction of long-term success of pulmonary vein isolation, and researchers at Harvard Medical School report that daily walking at a brisk pace can reduce the risk of developing afib by about 50%. All this and more in this the 84<sup>th</sup> issue!!*

*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**

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propafenone, and flecainide in preventing recurrence over a one-year period is only about 50% or less. Amiodarone is somewhat more effective (prevents recurrence in about 65% of cases), but comes with serious potential side effects. Researchers at McMaster University now report on a study to determine the relative efficacy of radiofrequency (RF) ablation and treatment with antiarrhythmics.

Their study involved a meta-analysis of 6 randomized trials comparing RF ablation with antiarrhythmic medications in the treatment of AF. About two-thirds of the patients involved in the trials had structural heart disease and most had paroxysmal or persistent afib. Most of the trials were performed at high volume centers, with expert operators performing the ablations. A total of 348 patients were assigned to receive antiarrhythmics

## Antiarrhythmics vs. ablation

HAMILTON, CANADA. Current guidelines for the management of atrial fibrillation (AF) recommend first-line treatment with antiarrhythmics. However, the efficacy of antiarrhythmics such as sotalol,

(sotalol, class I agents or amiodarone), while 345 were assigned to undergo a PVI followed by linear ablation and ablation of fractionated electrograms as appropriate. Touch-up procedures were allowed within the blanking period of the trials (first 2 to 3 months after ablation).

At the end of the one-year follow-up period, only 27% of the drug-treated patients were still in sinus rhythm as compared to 76% in the ablation group – a relative risk reduction for recurrence of 65% for ablation vs. drug treatment. The researchers suggest that their findings raise a couple of interesting questions:

- *Should we wait for patients to fail antiarrhythmic medications before recommending catheter ablation?*
- *Is it possible that catheter ablation as a first-line treatment for AF will yield better results?*

*Nair, GM, et al. A systematic review of randomized trials comparing radiofrequency ablation with antiarrhythmic medications in patients with atrial fibrillation. Journal of*

**Cardiovascular Electrophysiology**, September 3, 2008  
*[Epub ahead of print]*

**Editor's comment:** It should be kept in mind that the above conclusions may not necessarily apply to lone afibbers. Class I drugs (flecainide, propafenone, disopyramide) can be quite effective in lone afibbers, but afib patients with underlying heart disease they may be dangerous. Thus, sotalol and amiodarone are the primary antiarrhythmics used among AF patients with underlying heart disease. The benefits of antiarrhythmics were evaluated in LAF Surveys 2 and 14. Class I drugs were found effective by about 55% of users in Survey 2 and by about 40% in Survey 14. Amiodarone was found effective by about 65% and sotalol by 32% in Survey 14. In considering the results of the meta-analysis, it should also be kept in mind that the ablations were performed by highly skilled operators. Personally, I would think that there would be little difference in efficacy between treatment with antiarrhythmics and ablations carried out by less experienced EPs.

## Ablation end-point testing not reliable

HAMBURG, GERMANY. It is common practice for electrophysiologists doing pulmonary vein isolations (PVI) to check the quality of their work by using burst pacing to try to induce atrial fibrillation, or other atrial tachycardias, after the completion of the ablation. If atrial tachycardias are not inducible, the procedure is often considered complete and successful. German researchers now report that post-procedural non-inducibility is in no way a reliable indication of long-term success (avoidance of future atrial tachyarrhythmias).

The study included 60 patients (45 men and 15 women) with paroxysmal AF. The majority (85%) had no underlying structural heart disease, but 33% had a history of hypertension. The patients all underwent a PVI using electroanatomical mapping (CARTO, Pappone method) to create two continuous lesion circles (CCLs) around the right and left pulmonary veins. The completeness of electrical isolation was checked with two Lasso catheters within the ipsilateral (same side) pulmonary veins at least 30 minutes after completion of the ablation.

Atrial arrhythmia inducibility was then evaluated using 10-second burst pacing from the coronary

sinus. Seventeen (28%) of the 60 patients (group II) developed sustained atrial tachyarrhythmias (AF in 8 patients, common-type atrial flutter in 6 patients, and left macro re-entrant atrial tachycardia in 3 patients). The remaining 43 patients (72%) did not develop tachyarrhythmias after burst pacing (group I). The researchers observed that the area encircled by the CCLs was significantly smaller in group II than in group I. There was also a trend for group II members to have a larger left atrial volume and area than found among group I members.

After an average follow-up of 16 months, 18 of the 43 patients (42%) in group I had experienced one or more episodes of atrial tachycardia (13 with recurrent AF and 5 with new atrial tachycardia with stable cycle length). In group II, 7 of 17 patients (41%) experienced atrial tachycardia (2 with recurrent AF and 5 with new atrial tachycardia with stable cycle length). All 25 patients with recurrent tachycardia underwent a repeat procedure and all showed signs of recovered electrical conduction between the pulmonary veins and the left atrium. Following the repeat procedure, 91% of group I and 94% of group II remained in stable sinus rhythm during the subsequent follow-up period of 21 months.

The researchers conclude that non-inducibility of post-procedural atrial tachyarrhythmia does not predict long-term success in paroxysmal afibbers having undergone a PVI. They also conclude that inducibility is associated with smaller isolated areas around the pulmonary veins.

Satomi, K, et al. *Inducibility of atrial tachyarrhythmias after circumferential pulmonary vein isolation in patients with paroxysmal atrial fibrillation: clinical predictor and outcome during follow-up.* **Europace**, Vol. 10, 2008, pp. 949-54

**Editor's comment:** It is interesting that the initial (first procedure) success rate was only about 58%, thus indicating that about half of all afibbers undergoing a PVI can count on needing a "touch-up" procedure before they are cured. It is also of interest that the immediate success rate as indicated by post-procedural non-inducibility is not a measure of long-term success. This should be kept in mind when evaluating trials of new catheters and robot-assisted ablation systems since such trials often equate success with lack of conduction or inducibility immediately following the procedure.

## Mesh catheter looks promising

FERRARA, ITALY. Currently radiofrequency (RF) pulmonary vein isolation (PVI) procedures employ 2 or 3 separate catheters for mapping, ablating and guidance. Manoeuvring 3 catheters in the small left atrium is very challenging indeed. Furthermore, the ablation rings burned around the pulmonary veins are produced one "dot" at a time, making the process time-consuming, while leaving the distinct possibility of gaps in the rings which can reinitiate afib. The use of the so-called cryo-balloon catheter makes it possible to produce an unbroken lesion ring, but still requires separate mapping.

Scientists and engineers at Bard Electrophysiology have now developed a new "mesh" catheter designed to perform both the mapping and ablation. The catheter looks somewhat like a metal-mesh balloon when expanded – it is, of course, deflated when it is advanced to the left atrium through a sheath (tube) inserted in the femoral vein. One part of the catheter is able to provide high definition voltage (potential) maps to guide the ablation and to check on its completeness, while a 6-mm band of electrodes (separated into 4 quadrants) delivers radiofrequency energy to create an unbroken ablation line around the edges of each pulmonary vein.

Italian EPs now report the first use of the *Mesh-Bard* catheter on a 45-year-old female afibbers who lapsed back into afib after an initially successful standard (CARTO) RF PVI. After remapping the left atrium, the EPs found evidence of lesion gaps in the

left inferior and right superior veins. A repeat ablation was performed using the *Mesh-Bard* catheter. One single 5-minute RF application in each vein eliminated the offending potentials. The overall procedure time was 2 hours with only 12 minutes of fluoroscopy time. The patient was discharged after 2 days with no antiarrhythmic therapy and has been in normal sinus rhythm for 3 months.

More recently, an EP in Liverpool (Broadgreen Heart and Chest Centre) used the *Mesh-Bard* catheter on 2 AF patients and found it to be efficient and safe with a significantly shorter procedure time than current standard PVI procedures.

Pratola, C, et al. *Paroxysmal atrial fibrillation ablation with the multipolar mapping and ablation catheter (Mesh-Bard).* **PACE**, Vol. 31, June 2008, pp. 753-56

**Editor's comment:** The new *Mesh-Bard* catheter looks to be a well thought out device that should materially reduce procedure time while providing more complete lesions, thus hopefully, reducing the need for repeat ablations. However, there is, as yet, no long-term data as to its ultimate success rate, nor is there sufficient data to pronounce on its safety, especially in regard to pulmonary vein stenosis and phrenic nerve injury. It is also clear that while the catheter may be successful in dealing with paroxysmal afib, which originates in the pulmonary veins, there is no evidence that it is also useful in ablations involving persistent and permanent afib.

## Late AF recurrence after pulmonary vein isolation

NEW YORK, NY. Most successfully ablated afibbers, myself included, do wonder sometimes if their cure is permanent or whether “the beast” will eventually rear its ugly head again. Researchers at the St. Luke’s-Roosevelt Hospital Center now report on the long-term “durability” of initially successful pulmonary vein isolation (PVI) procedures.

Their study involved 350 consecutive patients (65% male) with paroxysmal (86%) or persistent (14%) atrial fibrillation. The authors do not state the proportion of lone afibbers in the group; however, 41% had hypertension, 29% had hyperlipidemia, and 15% had coronary artery disease. All patients underwent a standard PVI with no additional lesions. At the end of the first year following the procedure, 264 patients (75%) were still in normal sinus rhythm without the use of antiarrhythmics. These patients were followed for an additional 34 months (on average) during which time 20 paroxysmal (8.7%) and 3 persistent (8.8%) afibbers experienced recurrent bouts of symptomatic afib. The risk of recurrence was substantially higher among those with hypertension (70% vs. 39%) and hyperlipidemia (61% vs. 30%). None of the 264 patients were taking antiarrhythmics; however, 57% were on beta-blockers, 48% on statins, 14% on ACE inhibitors, and 10% on angiotensin II receptor blockers.

An actuarial calculation concluded that the recurrence rate was 5.8% at 2 years, 8.8% at 3 years, 13% at 4 years, and 25% at 5 years. However, the authors point out that the number of observations made at the 4- and 5-year marks were not sufficient to achieve statistical significance.

Eighteen of the 23 patients with late recurrence underwent a repeat PVI with additional linear lesions as necessary. In each case, mapping showed that electrical conduction had been re-

established between the left atrium and at least one pulmonary vein. The researchers conclude that recurrence of afib after a seemingly successful PVI is related to one or more of the following factors:

- Presence of hypertension and/or hyperlipidemia (elevated levels of LDL cholesterol and/or triglycerides).
- Resumption of electrical connection at previously ablated sites.
- Failure to target all pulmonary veins during the initial ablation.
- Emergence of triggers outside the areas encircled by the PVI procedure.
- Progression of heart disease and modification of atrial substrate that would promote AF.

*Shah, AN, et al. Long-term outcome following successful pulmonary vein isolation: pattern and prediction of very late recurrence. Journal of Cardiovascular Electrophysiology, Vol. 19, July 2008, pp. 661-67*

**Editor’s comment:** When considering the above conclusion that about 9% of afibbers undergoing an initially successful PVI can expect to be back in afib within 3 years, it should be kept in mind that this conclusion is unlikely to apply to a healthy lone afibbers without hypertension or hyperlipidemia who had their ablation performed by a highly skilled EP, especially if this EP took the time to look for triggers outside the pulmonary veins and eliminate them. I am not aware of any published data on this, but from my own survey (and gut feel), I would be very surprised if the percentage of lone afibbers who go back into afib after 3-5 years would exceed 3% - assuming that their PVI was performed by a highly skilled EP. Incidentally, the 9% figure for long-term relapse is very similar to the published figure of 8% for the Cox maze procedure.

## Early recurrence and long-term failure

BORDEAUX, FRANCE. It is generally accepted that experiencing one or more afib episodes in the first month following a pulmonary vein isolation (PVI) procedure (early recurrence) is not a good sign and may indicate that the ablation was not successful. Thus, the question arises, “Should patients who experience episodes of AF (or atrial tachycardia) shortly after their first ablation be re-

ablated within the first month, or would it be better to wait at least 3 months before undergoing a repeat ablation?” A recent trial carried out at the Hopital Cardiologique du Haut-Leveque set out to answer this question.

The trial included 302 afib patients who had their first PVI between January 2004 and September

2007. The average age of the patients was 55 years and about 82% were male. Most of the patients (83%) would be classified as having lone atrial fibrillation and were about evenly split between paroxysmal and persistent afibbers. All trial participants underwent a PVI guided by electrophysiological mapping (Haissaguerre method) as well as a cavotricuspid isthmus ablation to prevent post-procedure right atrial flutter. Additional focal ablations and linear lesions were applied as necessary to achieve non-inducibility of AF by burst pacing at the end of the procedure.

Of the 302 patients ablated, 144 (48%) experienced no recurrence during the first month and received no further follow-up. NOTE: An early recurrence was defined as an episode of AF, atrial tachycardia, or ectopic activity lasting 3 minutes or more. Early recurrence was significantly associated with a lower left ventricular ejection fraction (60% vs. 65%) and longer duration of AF (87 months vs. 61 months). Of the remaining 158 patients with early recurrence, 7 could not be followed up for various reasons. Thus, 151 patients were available for the study to determine the merits, or otherwise, of repeat ablation within the first month following the initial procedure.

A total of 61 patients underwent an early re-ablation. After an 11-month follow-up, 49% experienced no further afib or tachycardia episodes. Among the 90 patients with early recurrence who did not undergo an early re-ablation, only 9% experienced no further arrhythmia incidence, with the remaining 91% requiring a repeat procedure. As far as a third procedure is concerned, this was needed by 36% of the group undergoing the early re-ablation and by 33% of the group undergoing late re-ablation.

Overall, the early re-ablation group underwent an average of 2.5 procedures, while the late re-ablation group underwent 2.2 procedures on average. The indication for a second ablation for AF was 50% of cases, atrial tachycardia was 46%, and incessant atrial ectopy was 4% of cases. The Bordeaux

researchers conclude that the vast majority (91%) of afibbers who experience a recurrence within the first month after their initial PVI will have late occurrences as well. They also state that,

*“Contrary to current thinking, early re-ablation within the first month is not deleterious, as there are fewer clinical recurrences compared with patients without early re-ablation. In all patients who have a second procedure, whether early or late, the rate of further ablation for clinical recurrences was the same; however, the total number of needed ablations was significantly higher in patients with early re-ablation”.*

The following statement from the report is also of interest:

*“Radiofrequency ablation has a proinflammatory effect leading to cellular dysfunction and is potentially pro-arrhythmogenic. Moreover, AF ablation modifies the autonomic nervous system by reducing vagal activity and increasing sympathetic activity that may explain these ER (early recurrences) after the procedure, due to changes on the atrial substrate”.*

*Lellouche, N, et al. Early recurrences after atrial fibrillation ablation: prognostic value and effect of early reablation. Journal of Cardiovascular Electrophysiology, Vol. 19, June 2008, pp. 599-605*

**Editor’s comment:** The initial procedure success rate reported here (48%) for the Bordeaux group is in line with the 46% reported in the 2007 ablation survey. The complete success rate after a second follow-up ablation would appear to be 83%, which is somewhat better than the 73% observed in our survey.

## Seasonal variation in AF episodes

LUBLIN, POLAND. It has been known since the time of Hippocrates that the weather (atmospheric conditions) influences people’s mood and health. As far back as the first half of the 19<sup>th</sup> century, Polish researchers reported an association between

short-term weather changes and a worsening of angina, increased incidence of heart attacks, and more pronounced fluctuations in blood pressure. More recent research has shown that levels of the stress hormone cortisol are lower at high barometric

pressures and that lower levels are associated with a lessening of depression. So, conceivably, a person with elevated cortisol levels would feel better on a sunny day.

Now Polish researchers report that weather conditions also affect the incidence of paroxysmal afib episodes. Their study involved 739 patients (52% females, average age of 65 years, range of 18-91 years) who were admitted to hospital because of an AF episode during the period 2005-2006. Patients with acute coronary syndrome, myocarditis, pericarditis, thyrotoxicosis, and respiratory problems were excluded from the study, as were those who had recently suffered a heart attack.

The researchers correlated the number of patients admitted each day with air temperature, atmospheric pressure, wind speed and cloudiness, and also investigated the effect of approaching cold fronts and warm fronts. On average, there was one admission per day related to afib episodes. However, there were 9 days on which 4 patients were admitted and 4 days on which 5 patients were admitted. There was a seasonal effect with more cases (2.4/day) reported in the winter (December to February) than in the spring and summer (1.7 cases/day during the period May to August).

The most interesting correlation though was between the approach of a cold front and the number of afib-related hospital admissions. All the high admission days (4-5 cases/day) occurred 24-36 hours prior to the arrival of a cold front. The researchers speculate that the effect may be due to the electromagnetic waves created in deep low-pressure systems and storm centers. These waves travel at the speed of light, whereas the front itself moves at 10-50 km/hr, thus explaining why the effect of an approaching cold front would be felt 24-36 hours in advance. The researchers found no

relationship between afib incidence and the approach of a warm front. However, they did notice that periods of constant high atmospheric pressure were associated with a significant decline in hospital admissions for AF.

*Gluszk, A, et al. Episodes of atrial fibrillation and meteorological conditions. Kardiologia Polska, Vol. 66, September 2008, pp. 958-63*

**Editor's comment:** The speculation that a temporary increase in exposure to electromagnetic radiation may precipitate afib episodes is indeed an interesting one and, if proven correct, could perhaps partly explain the current AF epidemic, which certainly coincides with a vast increase in our exposure to electromagnetic radiation. As way of explanation the Polish researchers make the following remarks:

*"Electromagnetic waves penetrate into the tissue to a depth depending on the electric resistance and wavelength. In the very low frequency generated by atmospheric conditions (up to 10 MHz) living tissue acts as a conductor in which an alternating electric field produces Foucault eddy currents practically induced in the entire body. These phenomena were also reported by Kozlowski, who claimed that electromagnetic field effects in the body tissues involve stimulation of particles and atomic movements which cause chemical reactions and bioelectric processes. Induction of these changes occurs in electromagnetic field of relatively low intensities. This was also underlined by Hessmann-Kosaris, who reported that even weak electromagnetic fields may affect metabolic processes of cells and cellular membranes".*

## Gender distribution in lone atrial fibrillation

ROCHESTER, MINNESOTA. Our LAF surveys have consistently found a greater proportion of men (75-80%) than women among respondents. An early survey (August 2002) also suggested the possibility that lone atrial fibrillation may be an inherited disorder in many cases. The survey found that 43 of 100 respondents (43%) had at least one close relative with cardiac arrhythmia. The most common carrier was the mother who accounted for

30% of the relatives, siblings 26%, and fathers 23%. Permanent afibbers reported the mother to be the carrier in 71% of cases. Researchers at the Mayo Clinic now confirm that LAF is indeed more common among men and that there is a definite familial connection.

Their study included 192 unrelated lone afibbers who were divided into 3 groups. Group 1 consisted

of 114 afibbers who had no relatives with atrial fibrillation (sporadic LAF), group 2 consisted of 44 afibbers who had 1 first- or second-degree relative with LAF (possibly familial LAF), and group 3 consisted of 34 afibbers who had 2 or more relatives with LAF (confirmed familial LAF). Thus, out of the total study population of 192 lone afibbers, 41% had a least one relative with LAF.

The proportion of men in groups 1, 2, and 3 were 82%, 84%, and 62% respectively. Sporadic LAF was more common among men (62%) than among women (51%). It was also clear that those with familial LAF (group 3) were more likely to have permanent afib (27%) than were those of groups 1 and 2 (8.2% and 6.8% respectively). As far as gender differences are concerned, the researchers observed that women afibbers were more likely to report palpitations and being awakened by palpitations at night than were men. Women were also more likely to have paroxysmal LAF (76% vs. 64% for men) and less likely to have persistent afib (11% vs. 25% for men).

The researchers conclude that the greater incidence of sporadic LAF among men would be partially due to x-linked recessive inheritance in which women, including the mother, may be asymptomatic carriers. They also conclude that sporadic and familial LAF are clinically indistinguishable.

*Chen, LY, et al. Lone atrial fibrillation: influence of familial disease on gender predilection. Journal of Cardiovascular Electrophysiology, Vol. 19, August 2008, pp. 802-06*

**Editor's comment:** The Mayo Clinic study found that 41% of the 192 study participants had at least one first- or second-degree relative with LAF. This percentage is almost identical to the 43% observed in our August 2002 LAF survey. The male to female ratio of 79:21 found in the Mayo Clinic study is also very close to the 78:22 ratio found in our 2007 ablation/maze survey. Comparing the above numbers gives a feeling of comfort that the findings reported in our surveys do indeed reflect the "real world".

## Walking helps prevent atrial fibrillation

BOSTON, MASSACHUSETTS. Although the average age at diagnosis of lone atrial fibrillation (LAF) is about 47 years, by far the majority of AF patients are diagnosed at age 65 years or older. Studies have shown that the 10-year risk of a 65-year-old developing AF is about 20%. Researchers at Harvard Medical School now report that older people can substantially reduce this risk by engaging in light to moderate exercise on a regular basis.

Their study included 5446 adults aged 65 years or older who enrolled in the Cardiovascular Health Study in 1989-1990. The participants were examined at baseline and every year for the 12-year follow-up period. About half the participants had hypertension, about 20% had coronary heart disease, 25% had chronic pulmonary disease, and about 18% had diabetes when entering the study. During the follow-up, 1061 new cases of AF were diagnosed either during the annual ECG recordings or from hospital discharge records. Thus, about 1 in 5 participants developed AF during the follow-up. At the start of the study and at the 3<sup>rd</sup> and 7<sup>th</sup> annual visits usual leisure-time activity (kcal per week), usual exercise intensity, and usual walking habits were assessed.

The researchers observed that study participants who walked 60 or more city blocks (3-4 miles) a week had half the risk of developing AF than did those who walked 4 blocks or less a week. Walking pace was also important with people walking at speeds greater than 3 mph (4.8 km/hr) having half the risk of those walking at speeds less than 2 mph (3.2 km/hr). Regular engagement in leisure-time activities was also protective with participants expending in excess of 1840 kcal/week having a 36% lower risk of developing AF than those expending less than 35 kcal/week.

The relationship between exercise intensity and AF risk was U-shaped, that is, a low level of exercise and high intensity exercise were significantly less protective than was a moderate level of exercise which reduced AF risk by about 28% (compared to no exercise at all). NOTE: All the above risk reduction estimates have been adjusted for age, gender, race, education level, smoking status, alcohol use, use of beta-blockers, and the presence of coronary heart disease, chronic pulmonary disease and diabetes.

The researchers noted that having suffered a heart attack or having congestive heart failure increased the risk of developing AF by almost 5 times. They

also point out that physical activity lowers blood pressure and resting heart rate, and improves glucose control, cholesterol levels, and mental well-being. They conclude that moderate physical exercise, especially walking, is associated with a significantly lower AF incidence in older adults.

*Mozaffarian, D, et al. Physical activity and incidence of atrial fibrillation in older adults. Circulation, Vol. 118, August 19, 2008, pp. 800-07*

**Editor's comment:** It is likely that the study underestimated the prevalence of paroxysmal AF, particularly the asymptomatic kind since ECGs were only obtained once a year or upon hospital admission. Nevertheless, walking half a mile a day at a brisk pace would seem to be a small price to pay to reduce the risk of non-lone atrial fibrillation by about 50%.

## New insights into the mechanism of lone AF

ATHENS, GREECE. Researchers at the University of Athens have just published an article regarding the association between lone atrial fibrillation (LAF) and inflammation and oxidative stress. The paper is highly technical, but could contain some important clues in relation to the development and recurrence of persistent LAF. In order to summarize the article it is necessary to become familiar with some technical terms.

### Description of Terms

#### Markers of Inflammation

- **Cytokine** – A chemical messenger protein released by white blood cells to facilitate communication by immune system cells.
- **CRP (C-reactive protein)** – A general indicator of systemic inflammation and infection.
- **TNF (tumour necrosis factor alpha)** – A cytokine that promotes the inflammatory response which in turn causes many of the problems associated with autoimmune disorders such as rheumatoid arthritis, Crohn's disease, asthma, psoriasis, etc.
- **IL-6 (interleukin-6)** – A cytokine secreted by macrophages (large white blood cells that destroy or ingest foreign substances) to stimulate immune response to trauma.
- **IL-10 (interleukin-10)** – An anti-inflammatory cytokine that can inhibit the production of inflammatory cytokines such as TNF.
- **sICAM-1 (soluble intercellular adhesion molecule-1)** – An important biomarker of inflammatory processes, especially in atherosclerosis and cancer.
- **sVCAM-1 (soluble vascular cell adhesion molecule-1)** – An important biomarker of inflammatory processes, particularly those involving endothelial cells (cells lining the heart and blood vessels). There is evidence that fish oil can decrease SVCAM levels in men over the age of 55 years.

#### Markers of Oxidative Stress

- **Malondialdehyde (MDA)** – A prominent marker of oxidative stress formed by the oxidation of polyunsaturated fatty acids.
- **Nitrotyrosine (NT)** – A marker for cell damage and inflammation caused by reactive nitrogen species (nitrogen oxide and peroxyntirite).

The Greek study involved 41 afibbers with persistent LAF (average age of 47 years, 27 males, 14 females). All participants were carefully screened to rule out hypertension, heart failure, coronary artery disease, valvular heart disease, myocarditis, and any other cardiomyopathy. Patients with diabetes, thyroid dysfunction, active inflammation, cancer, infection, renal failure, obstructive pulmonary disease, or alcohol or drug abuse were also excluded from the study. Thus, the study group truly consisted of otherwise healthy lone afibbers. A group of 41 equally healthy volunteers (matched for age, gender, and body mass) served as control (group C).

All study participants had blood samples drawn at baseline (24 hours before pharmaceutical conversion, or 1 hour before electrocardioversion) and at 1 hour, 24 hours, 1, 2, 4 and 6 weeks after cardioversion. All samples were analyzed for the above-mentioned biomarkers for inflammation and oxidative stress. Pharmaceutical conversion was attempted with amiodarone and all participants (except the control group) remained on amiodarone during the study period. During the 12-month follow-up after cardioversion, 25 of the participants



remained in sinus rhythm except for 7 who experienced short episodes of afib (group A). Among the remaining participants, 8 had recurrence of persistent afib, 4 experienced episodes lasting longer than 30% of total ECG recording time, and 4 had paroxysmal episodes lasting longer than 6 hours (group B). In other words, cardioversion was largely successful in group A, but unsuccessful in group B. The results of the blood analyses were as follows:

### Baseline Values

- CRP levels were higher in group B than in groups A and C (no difference between A and C).
- TNF levels were higher in group B than in group A and both were elevated compared to group C.
- IL-6 was undetectable in controls, but 3 times higher in group B than in group A.
- IL-10 was lower in group B than in group A, but both were significantly higher than in the control group.
- sICAM-1 was highest in group B, followed by group A and controls.
- sVCAM-1 was about the same in groups A and C, but substantially lower in group B.
- MDA levels were significantly higher than controls in groups A and B with group B levels being twice as high as those in group A.
- NT levels were significantly higher than controls in groups A and B with group B levels being about 50% higher than in group A.

From the above data it is clear that recurrence of afib was associated with a higher level of inflammation and oxidative stress.

Comparing the changes in the biomarkers evaluated post-cardioversion, the researchers conclude that the following markers could reliably (80% certainty) distinguish between afibbers who would largely remain in sinus rhythm (group A) and those who would not (group B). Thus, maintenance of sinus rhythm was associated with a low baseline level of MDA, a low level of IL-6 one week after cardioversion, and low levels of sICAM-1 and NT two weeks after cardioversion. The most reliable and potent markers of success were a greater than 36.1% decrease in IL-6 one week after cardioversion, a decrease in sICAM-1 of more than 5.2% two weeks following cardioversion, and a decrease in NT of more than 22.2% two weeks after cardioversion.

The researchers conclude that there is an association between persistent lone atrial fibrillation and the presence of oxidative stress and inflammation. They also point out that CRP is not a useful marker when it comes to LAF. Unfortunately, they also state, "*It is still unclear whether the elevated levels of inflammatory and oxidative markers have a causative relation to AF or they are epiphenomena of the arrhythmia*". In other words, it is not clear which is the "chicken" and which is the "egg".

*Leftheriotis, DI, et al. The predictive value of inflammatory and oxidative markers following the successful cardioversion of persistent lone atrial fibrillation. International Journal of Cardiology, July 18, 2008 [Epub ahead of print]*

**Editor's comment:** Inflammation and oxidative stress have long been associated with atrial fibrillation. However, this is the first study to prove that the association is present in true lone afib and thus is not due to comorbid heart disease. The uncertainty as to whether the inflammation and oxidative stress causes afib or whether the continued presence of afib causes oxidative stress and inflammation, of course, makes it difficult to translate the findings of the study to practical advice for afibbers. It seems intuitively possible that inflammation could be either the cause or effect of afib, but it is a little harder to visualize how the presence of afib could result in oxidative stress. Perhaps the most likely explanation is that we are dealing with a vicious cycle in which inflammation and oxidative stress begets afib and afib begets inflammation and perhaps, oxidative stress. In this case, it should be possible to break the cycle either by cardioversion, or by dampening inflammation and oxidative stress. Since both systemic inflammation and oxidative stress have been implicated in a wide range of diseases and disorders, it would seem prudent for all afibbers to supplement with antioxidants (vitamin C, vitamin E, selenium, coenzyme Q-10, alpha-lipoic acid, etc) and anti-inflammatories (fish oils, Zyflamend, beta-sitosterol, bromelain, curcumin, boswellia, quercetin, Moducare).

## Evaluation of new cryo-balloon technique

BAD NAUHEIM, GERMANY. In 1998 Professor Michel Haissaguerre at the Hopital Cardiologique du Haut Leveque in Bordeaux reported that paroxysmal atrial fibrillation was mainly triggered by “rogue” cell clusters in the pulmonary veins. Early ablation techniques aimed at isolating the pulmonary veins from the left atrium by using radiofrequency (RF) energy to “burn” a ring of lesions just inside the vein. Unfortunately, this led to several cases of pulmonary veins stenosis (narrowing of the diameter of a vein by 50% or more). Thus, newer RF ablation techniques place the lesion ring in the left atrium itself rather than inside the veins, thus avoiding the danger of stenosis.

Nevertheless, placing a complete lesion ring just inside the vein is still theoretically at least, the best way of ensuring a complete electrical barrier between the potentials originating in the veins and the left atrium itself. The search for a technique that could achieve this without the danger of stenosis eventually led to the development of cryoablation in which a catheter or inflated balloon (cryo-balloon) cooled with liquid nitrogen is used to create the lesion ring. Early experiments showed that lesions created with cryoablation did not cause pulmonary vein stenosis.

German electrophysiologists now report on the evaluation of a new cryo-balloon device (*Artic Front*, Cryocath, Quebec, Canada) and an 8-mm cryo-catheter (*Freezor Max*) also developed by Cryocath. Their clinical trial involved 293 patients with paroxysmal afib and 53 with persistent afib. The average age of the patients was 59 years (62% male). They had suffered from symptomatic afib for an average of 7 years and had tried at least two antiarrhythmic drugs with no success. Forty-five percent of the study participants had hypertension and another 17% had mild heart disease, but none had advanced structural heart disease.

The patients all underwent pulmonary vein isolation using either a 23-mm or a 28-mm diameter balloon (when inflated) and the 8-mm catheter as required to reach spots missed by the balloons. The procedure was performed under conscious sedation using electrophysiological mapping with Lasso catheters and fluoroscopy as needed. Total average procedure time was about 3 hours (170 minutes), fluoroscopy time averaged 40 minutes, and total cryo application averaged 46 minutes. Each vein, on average, received 2.8 cryo-balloon applications lasting about 5 minutes each. All patients remained on warfarin and antiarrhythmic medication for the first 3 months following the procedure (blinking period).

After the blinking period patients were scheduled for quarterly follow-up visits, which included 7-day Holter ECG recordings. After an average 12-month follow-up, 74% of paroxysmal afibbers had experienced no recurrence of AF without the use of antiarrhythmics. NOTE: A total of 79 paroxysmal afibbers were lost to follow-up for one reason or another; thus, the success rate based on the total number of patients undergoing the initial ablation is probably somewhere between 54% and 74%. The success rate among persistent afibbers was only 42%. The main adverse event during the trial was phrenic nerve palsy (PNP), which was observed in 26 patients (11%) during ablation of the right superior vein. Most (90%) of PNPs occurred during the use of the 23-mm balloon. All cases of PNP were fully resolved in less than a year. No cases of stenosis, atriopharyngeal fistula, stroke or death occurred, but 2 patients (0.8%) did develop left atrial flutter during the blinking period. No other atrial tachycardia or flutter developed during follow-up.

The German researchers conclude that cryoablation is safe and effective for paroxysmal afibbers, but not recommended for those with persistent AF. NOTE: Five of the 16 authors of this paper had received financial support from Cryocath.

*Neumann, T, et al. Circumferential pulmonary vein isolation with the cryoballoon technique. Journal of the American College of Cardiology, Vol. 52, July 22, 2008, pp. 273-78*

**Editor’s comment:** This large-scale trial of ablation using the cryo-balloon technique confirms that the procedure is safe and reasonably effective for paroxysmal afibbers, but much less so for persistent afibbers. This is not really too surprising since the cryo-balloon technique only addresses isolation of the pulmonary veins, but does not involve linear ablations and other substrate modifications necessary to adequately deal with persistent AF. It is, unfortunately, not clear from the article why only 214 of the original 293 paroxysmal afibbers were followed up in arriving at the 74% success rate. Thus, the quoted success rate would seem to be a bit uncertain and could, presumably, be as low as 55%.

## Lifestyle and stroke risk

BOSTON, MASSACHUSETTS. There is overwhelming evidence that maintaining a healthy lifestyle (not smoking, eating a healthy diet, engaging in regular, moderate exercise, and maintaining optimal body weight) can reduce the risk of cancer, diabetes, and cardiovascular disease more than any other intervention.

Researchers at the Harvard Medical School now report that a healthy lifestyle also materially reduces the risk of suffering a stroke, particularly one caused by a blood clot or the rupture of atherosclerotic plaque (ischemic stroke). The Harvard researchers describe a low-risk lifestyle as:

- Not smoking
- A body mass index < 25 kg/m<sup>2</sup>
- At least 30 minutes/day of moderate physical activity
- Modest alcohol consumption (5-30 g/day for men, 5-15 g/day for women)
- Scoring within the top 40% of a healthy diet score

A healthy diet was defined as follows:

- High intake of vegetables, fruits, nuts, soy and cereal fiber
- High ratio of chicken plus fish to red meat
- High ratio of polyunsaturated to saturated fat
- Low intake of *trans*-fatty acids
- Daily supplementation with multivitamins for 5 years or more

The Harvard lifestyle/stroke risk study is a very large one involving 43,685 men enrolled in the Health Professionals Follow-up Study (begun in 1986) and 71,243 women from the Nurses' Health Study (begun in 1976). All participants were free of cancer and cardiovascular disease at baseline. The mean age at baseline (study entry) was 50 years for women and 54 years for men.

During follow-up, a total of 994 strokes (600 ischemic, 161 hemorrhagic [caused by a burst blood vessel], and 233 of unknown type) were documented among male participants. A total of 1559 strokes (853 ischemic, 278 hemorrhagic, and 428 of unknown type) were documented among female participants. Women with all 5 low-risk factors as defined above were found to have an 81% lower risk of suffering a stroke (79% lower risk of suffering an ischemic stroke) compared with women who had none of these low-risk factors, i.e. a highly unhealthy lifestyle. Corresponding risk reductions for men were 69% for total stroke and 80% for ischemic stroke. Unfortunately, only 2% of women and 4% of men had all 5 low-risk factors. Heavy smoking was, by far, the most significant risk factor for stroke followed by obesity (BMI over 30 kg/m<sup>2</sup>), lack of exercise, and excessive alcohol consumption.

Adherence to a healthy diet was clearly more important for women than for men with the very worst diet increasing total stroke risk by 47%, ischemic stroke risk by 33%, and hemorrhagic stroke risk by 70% among women. Corresponding figures for men were 16%, 16%, and 10%. The researchers conclude that 47% of all strokes (54% of ischemic strokes) among women can be attributed to lack of adherence to a low-risk lifestyle. Corresponding figures for men are 35% and 52%.

*Chiuve, SE, et al. Primary prevention of stroke by healthy lifestyle. Circulation, Vol. 118, August 26, 2008, pp. 947-54*

*Gorelick, PB. Primary prevention of stroke – Impact of health lifestyle. Circulation, Vol. 118, August 26, 2008, pp. 904-06 (editorial)*

**Editor's comment:** It is not clear how many person-years were involved in these follow-up studies. However, assuming that follow-up was completed in 2006 (last dietary evaluation was in 2002) would result in a maximum follow-up for women (nurses) of 2.14 million (30 x 71243) person-years and 0.87 million (20 x 43685) person-years for men (health professionals). Thus, total stroke rates would be 0.11%/year for men and 0.07% for women. These are indeed very low rates when compared to the oft-quoted rate of 1%/year among the general US population. I noticed this discrepancy in a 14-year follow-up study of the health professionals published in

2003. Following is an explanation provided by Dr. Ka He, the lead author (personal communication to me, November 30, 2003):

The annual incidence of new and recurrent stroke in the US is about 700,000 according to the American Stroke Association. Based on a population of 270,000,000 the annual rate is 0.26 per 100 person-years, or 0.26% per year. Stroke risk, of course, increases with age so it would clearly be higher if, for example, only people over 50 years of age were considered. Says Dr. He, "In our study, we only count the first event not recurrent stroke. Also, the participants are all healthcare professionals. They are health-conscious and relatively healthy (they were free from any CVD and diabetes). I would not be surprised if there is relatively low rate of stroke in our cohort."

## **Elimination/Reduction Protocol**

**Sharon Glass (southernkitty@bellsouth.net)**

**Female** afibber – **67 years** of age with **vagal AF of 3 years standing**; no underlying heart disease

No. of episodes in 6 months prior to starting protocol: **4**

Afib burden in 6 months prior to starting protocol: **20 hrs**

No. of episodes in most recent 6 months after starting protocol: **3**

Afib burden in most recent 6 months after starting protocol: **37 hrs**

Time on protocol: **26 months**

Still need to avoid triggers?: **Yes**

### **Main components of effective protocol**

Trigger avoidance: **MSG, aspartame, alcohol, caffeine, high glycemic index foods, heavy evening meals, dehydration, stress, sleeping on left side**

Diet changes: **Elimination of wheat and gluten, modified paleo diet**

Supplementation: **Magnesium, potassium, taurine, coenzyme Q10, B vitamins, low sodium V-8 juice, L-Theanine as needed.**

Drug therapy: **None**

Stress management: **Relaxation**

Underlying disease conditions: **Digestive problems and hypoglycemia**

Approaches to shorten episodes: **Resting, magnesium, potassium, taurine**

Approaches to reduce ectopics: **Magnesium, potassium, taurine, low sodium V-8 juice, L-Theanine**

### **Background and details of protocol**

In retrospect I believe that I had episodes of afib before being diagnosed in September 2005. After being diagnosed I had such severe reactions to medications for afib that I determined to learn all I could about afib and its possible causes and possible natural means of eliminating or reducing episodes.

My first goal was to determine my nutrient and mineral intake on a daily basis. I did an extensive project to find the areas where my body was not in balance. In June 2006 after an afib episode I recorded everything I ate and drank for 20 days on a program called [www.fitday.com](http://www.fitday.com). The information was invaluable to me. The program showed me the nutrients derived from my intake of food and clearly showed me what I was lacking. In those 20 days I discovered that I was getting some nutrients in excess through food and decided not to supplement them. I made the decision to take individual supplements for those I was lacking instead of a multi. I also added the recommended supplements for afib. Cont'd .....

I changed my lifestyle and eating habits and did my best to eat good, nutritious food with extra protein, veggies of all types especially green, limited or stopped my intake of grains, low sodium V-8 juice for potassium. I did lose over 30 pounds when I changed to whole foods and was concerned about my low weight. However, I have maintained my weight at about 120-123 lbs and feel great. I have been able to find gluten free bread and other gluten free foods which add more calories and fiber (which is very important to the digestive system.) After I completed the project I was able to make an educated decision about adding particular supplements that I lacked in my daily foods. I believe the lack of proper food nutrients is a big part of what causes afib and will continue to watch the foods that I eat and the things I drink.

**Conclusion:** I believe this was a positive experience, although not a cure as evident in outbreaks of afib since October 2007. I strongly believe the reasons for the outbreak were directly connected with my straying from my protocol whether consciously or unconsciously. I also remind myself that many things factor into what causes afib and it might not be my protocol failure at all. Recently I went back on FITDAY to check my nutrients again and discovered that I was not getting the RDA of 4700 mg of potassium a day through my foods and the supplements. So, I have now made it an important point to get that on a daily basis. I feel it is very important for the body to be in balance and for a person to be as healthy as possible so episodes of afib will be easier to endure for the overall person.

Listed below are the supplements I am currently taking. Some I have increased since the last protocol posting and I have so indicated. I choose not to take a multi vitamin but to continue targeting those I'm missing in my food. I'm careful to take recommended afib supplements religiously. I have explained the other supplements I'm taking and why.

Magnesium – Chelated – 200 mg x 3 per day.

Q-Absorb Co-Q10 – 100 mg @ 1 per day

D - "Source Natural" Vitamin. D, 1,000 IU 4 x a day = 4,000 IU per day

E - "NOW" Gamma E Complex @ 400 IU 1x day

C - "Country Life" Vitamin C with Rose Hips, 1000 mg x 3 per day = 3,000 Mg

NOTE: If I feel a cold coming on I increase my Vitamin C another 1,000-2,000 mg per day

B's - Super B Complex by "Wellness Resources" includes all of the "B's" RDA requirements.

One per day.

B-12 Sublingual one per day under tongue.

Zinc – "Natural Factors", Chelate 25 mg @ 1 per day

Potassium Gluconate – "NOW Brand" 540 mg, powder (1 tsp), 4-5 tsp per day in water or juice.

Taurine - "NOW Brand" 500 mg X 6 a day- If I have a stressful day or afib episode I increase another 1,000 mg. *I believe Taurine is the main supplement that slows my heart rate during afib.*

RXOmega-3 Factors EPA 400 mg, DHA 200 Mg x 2 a day "Michael Murray's Brand"

Glucosamine Sulfate 2 @ 750 mg – (for knees)

"Cran Clearance" Cranberry concentrate pill form - 680 mg @ 1 per day - for a healthy urinary tract.

L-Theanine – When needed for stress or during an afib episode.

With this regime of minerals and supplements, diet changes and avoiding stress as much as possible I went for 1 1/2 years with no sign of afib. Then on Oct. 13th 2007 I had a six-hour episode which self converted. Since October of 2007 I have had four afib episodes, March - 2008 – 17 hours; May 2008 - 9 hours, July 2008 – 21 hours and October 22 – 7 hours. I believe all were related to food, stress and digestive issues.

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