THE AFIB REPORT

Your Premier Information Resource for Lone Atrial Fibrillation!

NUMBER 35 **DECEMBER 2003/JANUARY 2004** **4th YEAR**

The amount of new information and research into atrial fibrillation has mushroomed recently. I review dozens of medical and cardiology journals every month and am very pleasantly surprised to note the increased emphasis on AF research. It would seem that mainstream medicine has finally realized that afib has reached epidemic proportions and takes an increasingly high toll in terms of lost work hours and diminished quality of life.

A fellow afibber has very generously provided me with a subscription to the two main arrhythmia journals, ***Journal of Cardiovascular Electrophysiology*** *and* ***Pacing and Clinical Electrophysiology****. These journals were not available here so I often had difficulties in locating the original articles of interest. The* ***Journal of Cardiovascular Electrophysiology****, like* ***The AFIB Report****, began publication just three years ago, but is already considered one of the very top journals as far as atrial fibrillation is concerned. Professor Michel Haissaguerre, Dr. Andrea Natale, Dr. Hakan Oral, Dr. David Van Wagoner, and other luminaries in the AF field are frequent contributors to the journal.*

There is no question that a great deal of valuable information to afibbers is now published in the medical literature. So, in order to make certain that we don't miss anything important, I have decided for the next few issues to focus on reporting the results of the research of others and suspend the LAF surveys for a while. The articles in the arrhythmia journals are not exactly what you would call light reading, but hopefully my summaries of the relevant information contained in them will be understandable.

Here is a sample of this month's findings:

- *Electrical cardioversion works better if you wait before going under the paddles.*
- *Aspirin is quite effective in preventing stroke and TIAs in low risk lone afibbers of all ages.*
- *Lone afibbers without hypertension, angina and diabetes who have not suffered a heart attack, stroke or TIA are no more likely to have a stroke than are matched members of the general population and would not benefit from warfarin therapy.*
- *ACE inhibitors may reduce afib frequency and silymarin (milk thistle extract) increases the efficacy of amiodarone in the treatment of atrial flutter.*

Highlights

Don't rush into cardioversion	p. 2
Atrial flutter after PV ablation	p. 3
LAF and atrial natriuretic peptide	p. 4
New model for stroke risk prediction	p. 5
Serotonin and atrial fibrillation	p. 6
PACs, PVCs and heart rate turbulence	p. 7
Silymarin increases effect of amiodarone	p. 8
NEWSBRIEFS	p. 9
AHA Conference, Nov. 9-12, 2003	p.10

Perhaps the most heartening news is the fact that at least some researchers have concluded that it is not AF as such that increases stroke risk, but rather the comorbidities (other health problems) that often accompany AF.

Just a reminder - if you haven't already done so, don't forget to get your copy of my book "Lone Atrial Fibrillation: Towards A Cure" at www.afibbers.org/lafbook.htm - it provides a wealth of information on dealing with LAF.

Wishing you and yours a Happy Holiday Season and lots of sinus rhythm in the coming year,
Hans Larsen

Don't rush into cardioversion

ANN ARBOR, MICHIGAN. Arrhythmia researchers at the University of Michigan have discovered that the timing of cardioversion (transthoracic) of afib episodes is all-important in determining the success of the procedure. Their study involved 315 afibbers who underwent cardioversion from 7 minutes to 8 years after the onset of their afib episode. Coronary artery disease was present in 24% of the patients, structural heart disease in 46%, valvular heart disease in 11%, and non-ischemic cardiomyopathy in 11%. Nine per cent were taking class I antiarrhythmics and 28% were being treated with class III drugs.

The researchers found that an immediate recurrence of AF (IRAF) within 1 minute was far more common if the cardioversion was attempted shortly after the episode began rather than after a wait of 24 hours or more. Overall, 20% of the patients experienced IRAF.

# of Patients	Episode Duration	Incidence of IRAF
48	less than 1 hour	56%
27	1-24 hours	37%
34	1-7 days	12%
45	1-4 weeks	12%
72	1-3 months	5%
36	3-6 months	10%
40	6-12 months	8%
13	1-8 years	12%

The researchers found that the risk of IRAF depended solely on the duration of the afib episode prior to the attempted cardioversion. Age, gender, structural heart disease, antiarrhythmic drug use, and energy level in cardioversion were not associated with IRAF incidence. They draw some very interesting conclusions from their observations:

- It is likely that the primary cause of IRAF is the continuing generation of ectopic beats in the pulmonary veins which would "reignite" AF as soon as the cardioversion "jolt" is over. The ectopic beat generation from active foci would be most active at the onset of the episode and would gradually decrease as the episode wears on. The following statement is of particular interest, "It is possible that arrhythmogenic pulmonary venous foci are activated by the rapid atrial activity that occurs during atrial fibrillation but that as the duration of atrial fibrillation lengthens, the cellular mechanisms responsible for this arrhythmogenic activity are progressively down-regulated or deactivated."

- It is very likely that the mechanism underlying IRAF (as above) is different from the mechanism involved in normal early recurrence of afib. Here progressive electrical and anatomic remodelling may play the greater role.

- The findings explain why IRAF is very common in connection with cardioversion performed during electrophysiology studies and ablation procedures.

- The findings also explain why internal cardioversion initiated by an ICD (implantable cardioverter-defibrillator) often results in IRAF if attempted shortly after the onset of the AF episode.

The researchers conclude that the ideal time for cardioversion may be approximately 24 hours after the onset when the risk of IRAF is low, electrical remodelling of the atrium is not pronounced, and when the need for anticoagulation prior to cardioversion has not yet arisen.

Oral, Hakan, et al. Effect of atrial fibrillation duration on probability of immediate recurrence after transthoracic cardioversion. **Journal of Cardiovascular Electrophysiology**, *Vol. 14, February 2003, pp. 182-85*

Editor's comment: It is quite clear from this article that one's chance of a successful cardioversion increases by waiting 24 to 36 hours before attempting it. This, of course, would also give one more time to see if the episode will terminate on its own. Blood clotting in the left atrial appendage and

the accompanying risk of stroke is not considered a problem unless the episode has lasted longer than 48 hours. The conclusion that the early stages, at least of an afib episode, are likely fuelled by repeated ectopic activity in the pulmonary veins is also interesting. It underscores the importance of trying to reduce PACs (premature atrial complexes) and, at this point, magnesium supplementation is probably the best way of achieving this. Another intriguing possibility is that ICD wearers may be better off if their ICD is set to attempt to convert an episode after an hour or so rather than as soon as it is detected. Obviously, individual experimentation would be needed to establish this.

Atrial flutter after PV ablation

MADRID, SPAIN. Spanish cardiologists report two cases (out of 30 ablations) in which atrial flutter developed in the left atrium after an otherwise successful pulmonary vein ablation. The ablations were performed on a 50-year-old woman and a 25-year-old man who both had highly symptomatic atrial fibrillation that was not controllable with drugs. Both procedures involved the use of a 4 mm catheter with a target temperature of 50 degrees C and maximum power of 50 watts. Activation mapping via an electroanatomic approach (CARTO system) was used to locate the veins from which the ectopics promoting the AF originated.

Atrial fibrillation was successfully eliminated in both cases, but 2 months after the procedure both patients developed atypical atrial flutter in the left atrium with a 2:1 ventricular response of 125 and 150 beats/minute respectively (the latter case was incessant). A new electrophysiologic study revealed that a flutter circuit had developed in the vicinity of the ablation scar tissue. An additional short ablation procedure eliminated the flutter and no more AF or atrial flutter episodes were experienced over a 6-month follow-up period.

The researchers point out that left atrial flutter occurring after a PV ablation should be investigated with a complete EP study and ablated as necessary before more drastic measures such as AV node ablation or ICD (pacemaker) implantation are considered.

Villacastin, Julian, et al. Left atrial flutter after radiofrequency catheter ablation of focal atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 14, April 2003, pp. 417-21*

Editor's comment: Our recent ablation survey revealed at least one case where an otherwise successful PV ablation resulted in the development of left atrial flutter. Thus it is possible that the overall incidence of this complication may be somewhere around 4%. Fortunately, it would seem that the condition is relatively easily corrected via an additional ablation procedure.

Hypertension and atrial fibrillation

HAMILTON, ONTARIO, CANADA. Hypertension (elevated blood pressure) modestly increases the risk of developing atrial fibrillation. However, because about 25% of the US population over the age of 18 years has hypertension it is nevertheless an important risk factor. Hypertension is associated with structural changes in the left atrium that again are associated with AF. These changes include left atrial enlargement, increased PACs (premature atrial complexes), and altered left atrial mechanical function and electrophysiology. Researchers at McMaster University believe that the appropriate pharmacological treatment of hypertension may also help to alleviate AF.

Antihypertensive treatment with beta-blockers or calcium channel blockers and ACE (angiotensin converting enzyme) inhibitors can reverse left ventricular hypertrophy and beta-blockers and hydrochlorothiazide (a diuretic) can reverse left atrial enlargement. Treatment with the ACE inhibitor trandolapril (Mavik) is associated with a 50% reduction in the incidence of a first afib episode among patients having experienced a first heart attack. A more recent study of amiodarone-treated AF patients, 40% of which had hypertension, concluded that treatment with another ACE inhibitor irebesartan (Avapro) resulted in a significant lengthening of the interval between afib episodes. The researchers conclude that blocking the renin-angiotensin system may reduce episode frequency independent of changes in blood pressure.

Healey, Jeff S. and Connolly, Stuart J. Atrial fibrillation: hypertension as a causative agent, risk factor for

complications, and potential therapeutic target. **American Journal of Cardiology**, *Vol. 91, No. 10A, May 22, 2003, pp. 9G-14G*

Editor's comment: Twenty per cent of 170 respondents in our recent survey reported that they had been diagnosed with hypertension and 65% used drugs to control the condition. None of them used ACE inhibitors. Unless there are specific contraindications afibbers with hypertension may wish to try an ACE inhibitor as this may significantly reduce their AF frequency. It is also possible that ACE inhibitor therapy may reduce frequency in afibbers with normal blood pressure.

LAF and atrial natriuretic peptide

MODENA, ITALY. Atrial fibrillation (AF) is known to cause the left atrium to expand and permanent afib is prone to make this expansion permanent (left atrial enlargement). It is also known that blood levels of atrial natriuretic peptide (N-terminal ANP) are elevated in patients with AF. A group of Italian researchers recently set out to investigate if there is any association between left atrial enlargement, ANP level, and method of cardioversion. Their study involved 196 patients with AF who had been referred for cardioversion. Half of them converted spontaneously to normal sinus rhythm within 48 hours of the onset of their episode (group A) while the other half (group B) were converted through the use of intravenous propafenone.

The average (mean) duration of AF was 27 hours in group A and 29 hours in group B. The left atrium was found to be dilated in all patients during the episode and atrial ejection force decreased in 57% of patients in group A immediately after conversion. Patients in group A (spontaneous converters) had significantly higher ANP levels during AF and somewhat higher levels when in sinus rhythm. There was a significant inverse correlation between ANP levels and atrial ejection force. There was no association between age, gender, and duration of AF and the propensity to convert spontaneously. However, patients with a high level of ANP during the episode were 3 times more likely to convert spontaneously than were those with low levels. A smaller left atrium also correlated with an increased chance of converting spontaneously.

Mattioli, Anna Vittoria, et al. Left atrial size and function after spontaneous cardioversion of atrial fibrillation and their relation to N-terminal atrial natriuretic peptide. **American Journal of Cardiology**, *Vol. 91, June 15, 2003, pp. 1478-81*

Editor's comment: This work confirms that ANP levels increase during afib and that higher levels are associated with a better chance of spontaneous conversion. The temporary decrease in atrial ejection force experienced after return to NSR could help to explain the feeling of tiredness and decreased physical performance often felt after an episode.

Aspirin effective in preventing stroke

OTTAWA, CANADA. A team of American, Canadian, Dutch and Danish medical researchers has concluded that a daily aspirin provides adequate stroke prevention in a large segment of afibbers irrespective of age. Individual patient data from 6 major clinical trials of the use of aspirin in stroke prevention was re-examined by the researchers. The trials involved 2501 patients with non-valvular AF who took 75 to 325 mg of aspirin daily. During 4689 person-years of follow-up 166 participants experienced a transient ischemic attack (TIA) or an ischemic (caused by a blood clot) or hemorrhagic (caused by a burst blood vessel) stroke. The overall event rate was 3.5/100 person-years (3.5% per year). This compares to the overall general population rate of 1.2/100 person-years observed in the large Framingham Heart Study. NOTE: Less than 2.8% of male participants and less than 2.2% of female Framingham Study participants had AF.

The researchers reasoned that afibbers without certain other risk factors for TIAs and stroke might have a significantly lower risk than would those with these risk factors. They determined the combined TIA and stroke incidence for a subgroup of 1661 afibbers who did not have hypertension (systolic blood pressure greater than 140 mm Hg), angina or diabetes and who had not suffered a previous heart attack, stroke or TIA. The overall TIA plus stroke

incidence in this low-risk group was 1.0 event per 100 person-years. This compares to an event rate for a gender and age matched cohort in the Framingham Study of 1.2 events per 100 person-years. In other words, this low-risk group of afibbers using aspirin daily for prevention had a TIA plus stroke rate slightly less than that observed in a comparable group of afib-free individuals. Afibbers who did not satisfy the requirements for low risk, on the other hand, had an event rate of 4.2 events per 100 person-years – significantly higher than the expected rate of 1.3 events per 100 person-years. Of the 2501 study participants, 588 (23.5%) were classified as low risk. Their mean age was 67 years and 23.6% were female. It is interesting to note that of the 900 patients older than 75 years 16% were classified as low risk. The prediction that low risk afibbers could safely use a daily aspirin for stroke prevention was validated in the remaining group of 840 study participants.

The researchers also looked at the effectiveness of oral anticoagulation (warfarin therapy) among participants in the 6 trials. The event rate in the low-risk group (as defined above) was 1.5 per 100 person-years (higher than in the aspirin group) and the rate in the remaining moderate- to high-risk group was 3.4 per 100 person-years (1 event per 100 person-years lower than in the high-risk aspirin group). The researchers conclude that irrespective of age, afibbers who satisfy the criteria for low risk can safely take aspirin for stroke prevention and would not benefit from oral anticoagulation. They estimate that about one quarter of all afibbers would fall in the low-risk group. NOTE: A summary of this article can be found at http://archinte.ama-assn.org/cgi/content/abstract/163/8/936

van Walraven, Carl, et al. A clinical prediction rule to identify patients with atrial fibrillation and a low risk for stroke while taking aspirin. **Archives of Internal Medicine**, *Vol. 163, April 28, 2003, pp. 936-43*

Editor's comment: The researchers specifically point out that their study did not address whether patients classified as low risk would have as favourable an outcome with no therapy as with aspirin. They also express uncertainty whether the benefits of aspirin offset the increased bleeding risk in low risk afibbers. The conclusion of this study is sterling news for lone afibbers. I would estimate that around 80% of the over 300 afibbers who have participated in our surveys fall in the low-risk group and thus would achieve adequate stroke protection by taking a daily aspirin.

Aspirin imparts its stroke prevention effect by preventing blood platelets from sticking together (aggregation). Vitamin E also works by inhibiting platelet aggregation and adhesion and two large studies carried out at the Harvard Medical School concluded that people who had taken 100 IU of vitamin E for 2 years or more had a 30% lower incidence of ischemic stroke – this is better than the protection offered by aspirin. Fish oils also inhibit platelet aggregation and adhesion as do garlic and ginkgo biloba. What all this adds up to is that a regimen of natural antiplatelet supplements may well be the best stroke prevention option for low risk lone afibbers and, of equal importance, this protection does not carry the risk of internal bleeding experienced with aspirin and warfarin use.

New model for stroke risk prediction

FRAMINGHAM, MASSACHUSETTS. Several studies have found that AF confers an increased risk of stroke. Fortunately, there is now a growing recognition that not all afibbers are at increased risk. As a matter of fact, it is becoming increasingly clear that it is not AF as such that increases stroke risk, but rather the comorbidities (other health problems) that often accompany AF.

A prestigious group of cardiologists and researchers from four US medical schools and universities now propose a new classification scheme which can reliably be used to estimate the stroke risk for an individual afibber. The researchers used data from 705 participants (mean age of 75 years, 48% women) in the Framingham Heart Study who had been diagnosed with AF and who were not being treated with warfarin. During a 4.3-year average follow-up period 111 of the participants experienced a stroke (ischemic or hemorrhagic) and 485 died from stroke or other causes.

The researchers found that advancing age, female sex, high systolic blood pressure, a prior stroke or TIA, and the presence of diabetes were the main factors in determining stroke risk. Thus a 74-year-old man with no hypertension, no diabetes and no prior stroke or TIA would have an annual stroke risk of 1.4% - quite similar to that experienced in the general population. A 74-year-old woman with none of the aforementioned risk factors would have a somewhat higher annual stroke risk at 2.6%.

Fourteen per cent of the study participants had a risk score of 4 or less corresponding to a predicted average annual stroke rate of 1.5% or less. In actual fact, this group had an annual stroke rate of 1.1% indicating that the risk prediction model is, if anything, conservative.

The researchers conclude that afibbers with a predicted annual stroke risk of 2% or less may not realize additional benefit from warfarin compared with aspirin and their risk of stroke may not exceed the risk of life-threatening bleeding with warfarin. Thus anticoagulation therapy may not be justified in individuals with low predicted rates of stroke.

They also evaluated the risk factors for stroke or death from any cause. In order to come up with an accurate prediction scheme they removed gender as a variable and added smoking, congestive heart failure, heart murmur (valvular heart disease), and left ventricular dysfunction to the risk factors. According to the risk table a 74-year-old male or female afibber with no other risk factors would have a risk of having a stroke or dying of 6% per year. NOTE: A summary of the published article can be found at
www.medscape.com/viewarticle/462627_print

and an Excel spreadsheet for calculating individual stroke and death risk can be found at
http://www.nhlbi.nih.gov/about/framingham/stroke.htm

Wang, Thomas J., et al. A risk score for predicting stroke or death in individuals with new-onset atrial fibrillation in the community. **Journal of the American Medical Association**, *Vol. 290, August 27, 2003, pp. 1049-56*
Waldo, Albert L. Stroke prevention in atrial fibrillation. **Journal of the American Medical Association**, *Vol. 290, August 27, 2003, pp. 1093-95 (editorial)*

Editor's comment: This extension of the Framingham Heart Study clearly supports the conclusion that lone afibbers with none of the specified risk factors for stroke are at low risk and will not benefit from anticoagulation with warfarin. I calculated my own stroke risk to be 1.2% per year (not taking into account the stroke prevention obtained from a healthy diet and lifestyle, supplementation with vitamin E, ginkgo biloba and fish oils as well as aspirin during and after an episode). This is well within the normal range and substantially lower than the suggested cut-off point for warfarin therapy of 2.0%. I believe this study and the van Walraven study also abstracted above should provide sufficient "ammunition" for low-risk afibbers who wish to question their physician's recommendation to initiate warfarin therapy.

Serotonin and atrial fibrillation

LONDON, UNITED KINGDOM. Serotonin (5-hydroxytryptamine) has recently been added to the list of triggers for AF. Serotonin is synthesized from the amino acid tryptophan through an intermediate step involving 5-hydroxytryptophan (5-HTP). Serotonin is a potent neurotransmitter and is stored in nerve terminals prior to release. It is also taken up by circulating blood platelets that can release it when activated. Serotonin is metabolized by monoamine oxidase (MAO) found in the intestine, liver and mitochondria.

Researchers at the St. Georges Hospital Medical School have just released a major review of the effects of serotonin on the cardiovascular system. Serotonin affects the heart both through its activation of the autonomic nervous system and also by direct action on receptors located in both the right and left atria. Depending on which type of receptors is stimulated serotonin may either activate the vagal (parasympathetic) or the adrenergic (sympathetic) system. The researchers believe that the existence of serotonin receptors (5-HT_4 type) in the atria may be part of a hormonal backup system to prevent bradycardia (excessively slow heart rhythm). Activation of 5-HT_4 receptors with its corresponding increase in adrenergic tone would thus be bad news for people with AF with underlying heart disease as well as for afibbers with the adrenergic variety of lone AF; however, increased activation of HT_4 receptors may actually be beneficial for vagally-mediated afibbers.

The researchers speculate that 5-HT_4 receptor stimulation in the atria may promote the generation of PACs (premature atrial complexes) by calcium overload leading to AF. There is also evidence that serotonin acts to prolong an afib episode. Serotonin uptake by platelets tends to increase with advancing age. There is also some evidence that platelet release of stored serotonin may be involved in the increased incidence of AF following bypass surgery.

Yusuf, Shamil, et al. 5-hydroxytrypptamine and atrial fibrillation: how significant is this piece in the puzzle? **Journal of Cardiovascular Electrophysiology**, *Vol. 14, February 2003, pp. 209-14*

Editor's comment: It is clear that the relationship between serotonin and AF is complicated and that serotonin may actually affect adrenergic and vagal afibbers differently. Thus tryptophan and 5-HTP may be OK for vagal afibbers to take, but not that great for adrenergic ones. This assumes, of course, that the benefits from an increase in adrenergic tone outweigh the disadvantage of possible calcium overload and increased PAC frequency. Similarly with the SSRI (selective serotonin reuptake inhibitor) antidepressants. Strong serotonin reuptake inhibitors (transport blockers) like paroxetine (Paxil), sertraline (Zoloft) and citalopram (Celexa) may work better for vagal afibbers than for adrenergic ones – although this is by no means certain as all SSRIs work on several other receptors than just the serotonin ones. Therefore the selection of a safe SSRI for lone afibbers is difficult and probably best achieved through trial and error. All SSRIs are definitely not the same when it comes to compatibility with LAF.

PACs, PVCs and heart rate turbulence

OULU, FINLAND. Heart rate turbulence caused by PVCs (premature ventricular complexes) is used to quantify mortality risk among patients having suffered a recent heart attack. An abnormal heart rate turbulence (HRT) is associated with an increased risk of subsequent death. HRT is obtained from 24-hour Holter recordings and have two components - turbulence onset (TO) and turbulence slope (TS). TO is defined as the relative difference between the mean (average) of the first two sinus (normal) R-R intervals (the time between two consecutive heart beats) following the compensatory pause after the ectopic beat and the average of the two sinus R-R intervals preceding the ectopic beat. TS is defined as the maximum slope of the regression line assessed over any sequence within 5 subsequent R-R intervals within the first 20 sinus beats following the ectopic beats.

A team of American and Finnish researchers now reports on their investigation into HRT after PVCs and PACs in healthy subjects without structural heart disease or atrial fibrillation. Their study included 16 men and 13 women with an average age of 51 years. The participants had an average of 33 PACs and 16 PVCs per subject over a 23-hour Holter monitoring period with significantly more subjects having PACs than PVCs. NOTE: The frequency of ectopic beats experienced by this group of non-afibbers is far lower than the estimated frequency experienced by a group of 95 afibbers participating in a recent LAF survey (100 PACs and 33 PVCs per day).

The researchers found that the mean value for TO after a PVC was significantly different from that after a PAC (-2.3% versus -0.9%) and that TS was significantly higher after a PVC than after a PAC (11 msec/R-R interval versus 5.1 msec/R-R interval). The TO and TS values were not associated with age, gender, blood pressure, body mass index, frequency of PVCs and PACs, and echocardiographic data. TO and TS values after PVCs were, however, related to baroreflex sensitivity (autonomic nervous system sensitivity to variations in blood pressure) and TS was correlated with ANS balance (sympathetic versus parasympathetic). TO and TS values after PACs were not correlated significantly with baroreflex sensitivity or ANS balance. It is thus clear that PVCs affect the ANS to a greater extent than do PACs.

Shortening of the R-R interval preceding a PAC was a relatively common finding indicating that the ANS may serve as a trigger of PACs. Shortening of R-R intervals typically is seen during normal inspiration, followed by prolongation of R-R intervals during expiration caused by respiratory vagal modulation. These phasic vagal effects may influence the electrophysiological properties of the atria, triggering the generation of PACs concurrently with specific respiratory cycles.

Lindgren, Kai S., et al. Heart rate turbulence after ventricular and atrial premature beats in subjects without structural heart disease. **Journal of Cardiovascular Electrophysiology**, *Vol. 14, May 2003, pp. 447-52*

Stein, Phyllis K. Heart rate turbulence: explorations of an emerging risk factor. **Journal of Cardiovascular Electrophysiology**, *Vol. 14, May 2003, pp. 453-54 (editorial)*

Editor's comments: This study contains several interesting findings that may throw further light on the factors involved in the initiation of an afib episode.

- PACs may be triggered by changes in ANS balance.
- PVCs significantly affect ANS balance. Is it possible that PVCs could initiate an episode through their effect on the ANS? I have

personally noted that my PVC frequency increases dramatically in the days leading up to an episode. My Holter recordings show a PVC frequency of about 2500/day.

- Is it possible that afibbers with a predominance of PVCs would be less likely to have a successful PV ablation or take longer to recover (Note: A PVA would not alter PVC frequency)? Is it conceivable that the higher degree of turbulence caused by a PVC could initiate PACs (from focal points outside of the pulmonary veins) through its effect on the ANS? I have not come across any research that has correlated PVC/PAC frequency with PVA success rate – perhaps this would be an interesting study.
- The study also suggests that breathing pattern can influence the frequency of PACs.

There is much to ponder!

Silymarin increases effect of amiodarone

INDIANAPOLIS, INDIANA. Researchers at the Indiana University School of Medicine have found that silymarin (milk thistle extract) significantly enhances the effect of amiodarone (Cordarone) in preventing sustained atrial flutter in dogs. Silymarin is a flavonoid-type antioxidant and is particularly effective in protecting liver cells against free radical damage. Amiodarone is known to produce large amounts of free radicals and it is believed that free radical damage is the mechanism by which amiodarone manifests its toxicity.

The effect of the added silymarin was quite spectacular. Sustained atrial flutter (flutter lasting longer than 30 minutes) occurred in 71% of control dogs, in 53% of amiodarone-treated dogs, in 67% of silymarin-treated dogs, but in only 13% of the dogs treated with amiodarone plus silymarin. The fact that non-sustained atrial flutter occurred in a similar number in the amiodarone-treated and in the amiodarone plus silymarin-treated dogs indicates that the addition of silymarin prevents the maintenance rather than the initiation of atrial flutter.

Other researchers have suggested that desethylamiodarone, the major metabolite of amiodarone, may be primarily responsible for shortening atrial flutter episodes.

Vereckei, Andras, et al. Combined amiodarone and silymarin treatment, but not amiodarone alone, prevents sustained atrial flutter in dogs. **Journal of Cardiovascular Electrophysiology**, *Vol. 14, August 2003, pp. 861-67*

Editor's comment: So what does this finding mean for afibbers? Bearing in mind that animal experiments are not always directly translatable to humans, I believe it is quite likely that silymarin acts by increasing the efficiency of liver cells to convert amiodarone to its more active (in preventing sustained atrial flutter) metabolite desethylamiodarone. So it would seem that those taking amiodarone for atrial flutter might benefit from supplementing with silymarin. This may decrease the duration of their episodes and/or lower their requirements for amiodarone. Any experimenting in this area should, of course, only be done under the supervision of a competent cardiologist.

A similar beneficial effect of silymarin supplementation may occur among afibbers taking amiodarone, but I want to strongly emphasize that I have no data whatsoever to support this speculation. Even more speculative is the possibility that afibbers taking propafenone (Rythmol) may benefit from silymarin. Propafenone is metabolized in the liver to 5-hydroxypropafenone (5-OHP), which is equally effective as propafenone itself in preventing and shortening afib episodes. If silymarin would allow quicker and more effective conversion to 5-OHP the effects of propafenone, whether used on a continuous or on-demand basis, might be enhanced. Obviously clinical trials are needed to prove or disprove this. It is not likely that silymarin supplementation would affect the effectiveness of flecainide (Tambocor), as this drug is not significantly metabolized in the liver to yield active metabolites.

NEWSBRIEFS

Primary aldosteronism: a common cause of hypertension. A low blood level of potassium can be a telltale sign of an excessive production of aldosterone by the adrenal glands. Patients diagnosed with essential hypertension (elevated blood pressure) are usually screened for primary aldosteronism (PAL) if they have low potassium levels. It is generally assumed that no more than 1% of hypertension patients have PAL. Australian researchers now throw serious doubt on this assumption. Within the first 2 years of the operation of a new hypertension unit at the Princess Alexandra Hospital they diagnosed PAL in 54 hypertension patients or in 10% of patients screened. Only 7% of the 54 had low potassium levels. Thirty-one of the PAL patients had bilateral PAL and responded well to aldosterone-blocking drugs. The researchers advocate screening for PAL of all patients with hypertension using the aldosterone/renin test. NOTE: Of particular interest to afibbers is the finding that aldosteronism does not always manifest itself through low blood levels of potassium.
Reuters Health Information, June 19, 2003

Amiodarone replacement on the horizon. Amiodarone is often effective in controlling atrial fibrillation, but primarily because of its high iodine content has serious side effects that can affect the thyroid gland, eyes and lungs. French researchers now report on their evaluation of a new drug, dronedarone, which is similar to amiodarone, but contains no iodine. The evaluation involved 199 afib patients who had just converted to NSR and were randomly allocated to receive 800 mg/day of dronedarone or a placebo. The patients were followed for 6 months. During this time the average (median) afib-free period was 60 days for the dronedarone group versus 5.3 days for the placebo group. Patients on dronedarone were also more likely to convert spontaneously and no proarrhythmic reactions were observed in the group. Less than 4% of patients on the dronedarone stopped treatment due to side effects (mostly gastrointestinal) and there were no cases of thyroid, ocular or pulmonary toxicity. The researchers conclude that dronedarone appears to be safe and effective for the maintenance of NSR in AF patients.
European Heart Journal, Vol. 24, August 2003, pp. 1481-87

Stress and stroke risk. Danish researchers have found a correlation between self-reported stress levels and the risk of a fatal stroke. Over 12,000 Danish men and women participated in the study. After 13 years of follow-up a total of 929 first strokes had occurred (0.6% per year) of which 207 (22%) were fatal within 28 days of onset of symptoms. Participants who reported a high stress intensity had an 89% higher incidence of fatal stroke than did participants who reported no stress. Participants who felt stressed on a weekly basis had a 49% higher fatal stroke rate than did non-stressed persons. The researchers point out that the trend towards increased stroke risk with increasing self-reported stress level was weak and that the observed correlation may be due to the fact that people who consider themselves stressed generally have an unhealthy lifestyle and an overall unfavourable risk profile for stroke.
Stroke, Vol. 34, April 2003, pp. 856-62

Air pollution and stroke. Researchers at the Taiwan Institute of Public Health report that the degree of air pollution directly affects the number of hospital admissions for stroke, both ischemic and hemorrhagic. The researchers correlated pollution levels in Kaohsiung with the number of strokes encountered on a particular day. The study period ran from 1997 through 2000 and included 23,179 stroke admissions. They found that high levels of carbon monoxide (CO), sulfur dioxide (SO_2), ozone (O_3), nitric oxide (NO_2), and inhalable particulate matter (PM10) were significantly associated with stroke admission on a warm day (temperature above 20 degrees C). On a cooler day only CO levels were associated with stroke admissions. By far the most significant associations were observed between stroke admission and air levels of NO_2 and PM10. Higher levels of these two pollutants corresponded to a 50% increase in stroke admissions as compared to normal levels.
Stroke, Vol. 34, November 2003, pp. 2612-16

American Heart Association Conference

Orlando, Florida, November 9-12, 2003
Published in *Circulation*, Vol. 108, No. 17, October 28, 2003

Vitamin C improves baroreflex sensitivity

Baroreflex sensitivity (BRS) is an indication of how quickly the heart rate reacts to a change in systolic blood pressure and is related to the health of the autonomic nervous system. It is measured in milliseconds per mm mercury and a low value has been associated with cardiovascular disease, diabetes and depression. BRS declines markedly with age. Researchers from the University of Colorado now report that an infusion of ascorbic acid (vitamin C) will completely eliminate BRS dysfunction in older men. They conclude that oxidative stress is an important cause of the age-related decline in BRS.
Abstract #262, p. IV-57

Blood clot formation during pulmonary vein ablation

Researchers at the Mayo Clinic report that blood clots (thrombi) form in the heart during a PVA despite adequate anticoagulation with warfarin and intravenous heparin. They analyzed ICE (intracardiac echocardiography) images taken during PVA in 270 patients and found that 21 (8%) of them had one or more thrombi despite the fact that TEE (transesophageal echocardiography) had shown no evidence of thrombi prior to the procedure. Most of the thrombi (76%) were located on the catheters and could be removed from the heart by withdrawing the catheters with aspiration (suction). The researchers conclude that ICE is effective in detecting thrombi formed during PVA and that this permits the expeditious withdrawal of affected catheters thus avoiding potential complications.
Abstract #1513, p. IV-321

Focal point ablation may be required for women

Electrophysiologists at the University of Pennsylvania determined the location of atrial fibrillation trigger points in 343 patients (85 women) who underwent pulmonary vein ablation (PVA). Women were found to be 3 times more likely than men to have trigger points outside the pulmonary veins. Thus, when performing PVAs on women, it may be necessary to check for other focal points and eliminate them as well. This would apply particularly to women who continue to have symptoms after a PVA.
Abstract #2805, p. IV-617

Recurrence of afib after ablation

Dr. Carlo Pappone and his group at the San Raffaele University Hospital in Milan report on the follow-up of 589 patients (55% male) who had undergone PVAs (ostial). Most of the patients (417) had paroxysmal AF with the remainder (172) having permanent AF. Fifty-one per cent of them had no structural heart disease. After a 3-year follow-up period 80% of successfully ablated patients were still in sinus rhythm while 20% had experienced renewed AF episodes. Recurrence tended to occur earlier among paroxysmal afibbers.
Abstract #2814, p. IV-619

Vagal afibbers may need special ablation techniques

Researchers at the University of Michigan have investigated the relative efficacy of PVA in vagal, mixed and adrenergic afibbers. They followed 224 patients with paroxysmal AF who had undergone successful PVA (ostial). Most (62%) had the mixed form of afib, 14% (30 patients) had the vagal variety while the remaining 14% were adrenergic. After an average follow-up of 13 months AF recurred in 55% of vagal afibbers, in 35% of mixed, and in 30% of adrenergic. The researchers also followed 30 patients (8 vagal, 20 mixed, and 2 adrenergic) who underwent a new procedure whereby the left atrium is ablated to encircle the left- and right-sided pulmonary veins. Among these patients vagal and adrenergic afibbers had no recurrence while the recurrence rate among mixed was 15%. The researchers conclude that left atrial substrate modification in addition to PVA may be necessary in order to ensure success among vagal afibbers.
Abstract #2934, p. IV-645

Warfarin of only modest benefit

A group of 7500 California Medicaid recipients with AF and one or more of the following conditions - hypertension (58%), congestive heart failure (48%), diabetes (34%) prior stroke (17%) or prior heart

attack (14%) participated in a recent study to evaluate the effectiveness of warfarin therapy. During follow-up stroke occurred in 514 patients with a rate of 3.4 per 100 person-years in patients treated with warfarin and a rate of 4.1 per 100 person-years for those not on warfarin. This corresponds to an overall absolute risk reduction of 0.7% per year. Bleeding occurred in 302 patients with a rate of 3.0 per 100 person-years in patients treated with warfarin and a rate of 2.2 per 100 person-years for those not on warfarin. This corresponds to an absolute increase in bleeding risk of 0.8% per year. The researchers conclude that, "Warfarin therapy, in clinical practice, has a relatively modest benefit in terms of reducing stroke rates, with the greatest benefit occurring among patients with moderate stroke risk. However, this benefit is somewhat offset by the increased risk of bleeding events."
Abstract #3419, p. IV-757

THE AFIB REPORT is published 10 times a year by:
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