The importance of adequate serum and intracellular levels of magnesium and potassium are again emphasized in a Polish study which found that intravenous infusion of magnesium and potassium helps afibbers with low levels to convert to normal sinus rhythm. Another study, undertaken at St. David’s in Austin, Texas, reported in the “Indian Pacing and Electrophysiology Journal” found that afibbers who supplemented with fish oil prior to and following a pulmonary vein isolation procedure reduced their risk of experiencing afib recurrence by 39% during the first 8 weeks following the procedure. Perhaps even more important, they also reduced their risk of recurrence by 28% beyond the 8-week mark.

Australian researchers report that ablation success rates for vagal, adrenergic and random (mixed) afibbers are not significantly different, and Polish researchers confirm the importance of aldosterone in the genesis of atrial fibrillation. All this, and more, in this 97th 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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**Magnesium/potassium infusion helps convert AF to NSR**

WARSAW, POLAND. Although the mechanism underlying initiation of afib is still somewhat controversial, there is a growing consensus that slowed conduction velocity and dispersion of atrial refractoriness is involved. This, in turn, may result in multiple re-entry waves and AF. Potassium (K) and magnesium (Mg) play an important role in these mechanisms and guidelines for the management of AF usually recommend that serum levels of K and Mg be measured in AF patients and corrective action taken if electrolyte imbalances are found. (NOTE: Serum levels of K and Mg are not very predictive of the actual intracellular level in myocytes; however, it serum levels are abnormally low, intracellular levels will likely be very low).

Polish researchers report a study involving 115 patients (71 men and 44 women with an average age of 60 years) admitted to hospital with a first episode of afib that had lasted less than 20 hours. Electrolyte levels were checked in all patients upon admission and 16% were found to have a magnesium level below 0.7 mmol/L (1.7 mg/dL), while 3% had a potassium level below 3.5 mmol/L. The researchers observed that the patients with low electrolyte levels were significantly more likely to be on diuretics (hydrochlorothiazide) than were those with normal levels (40% vs. 18%).

The 22 patients with low K and/or Mg levels were given an intravenous infusion consisting of 1000 mL of 10% glucose to which 10 IU of rapid-action insulin, 80 mEq of potassium chloride (3100 mg
elemental K), and 8000 mg of magnesium sulfate (1600 mg elemental Mg) had been added. The infusion was maintained for up to 20 hours independent of whether the patient converted to normal sinus rhythm (NSR) or not. Twenty hours after initiation of therapy 86% of patients had regained NSR. A separate group of 31 patients with normal K and Mg levels were also given the infusion. In this case only 39% converted to NSR within the 20-hour trial period.

It is estimated that about 50% of patients with new onset afib convert spontaneously within 24 hours. Thus, the administration of the infusion to patients deficient in K and/or Mg is clearly effective in improving the rate of conversion to NSR. The researchers conclude, “An electrolyte imbalance seems to be an independent factor predisposing to atrial fibrillation. Serum K/Mg levels should always be measured in patients presenting with recent onset AF, because electrolyte supplementation (if needed) seems to be a very effective, safe and inexpensive method in the restoration of sinus rhythm.”


Editor’s comment: The findings of this study are clearly of major importance to afibbers contemplating a catheter ablation. It is odd indeed that the study was published in a relatively obscure journal such as the Indian Pacing and Electrophysiology Journal, especially in light of the fact that the participants were all treated at St. David’s Medical Center in Austin, Texas. Certainly,
if a completely safe drug had been found to reduce afib recurrence by almost 30%, it would have been trumpeted in major mainstream medical journals and achieved headline status in the general news media.

Cardioversion of AF following catheter ablation

Baltimore, Maryland. The recurrence of afib or flutter following a pulmonary vein ablation (PVI) procedure is not uncommon, especially during the 3 months post-procedure. If the recurring arrhythmia does not terminate spontaneously, then electrical cardioversion is used. Now a team of electrophysiologists from the Johns Hopkins Hospital report their experience with cardioversion of post-procedural persistent AF and atrial flutter.

Their study included 55 patients (85% male, average age of 58 years, 15% with coronary artery disease) who underwent catheter ablation for AF and subsequently required electrical cardioversion for persistent AF (45 patients or atrial flutter (10 patients). Thirty-five percent of patients had paroxysmal afib, 18% had persistent afib, and 47% were in permanent AF (long-standing persistent). All patients underwent a pulmonary vein isolation procedure using a wide area circumferential approach guided by electroanatomical (CARTO) mapping (Pappone protocol). Isolation of the pulmonary veins was the procedural end-point.

The study participants were followed for an average of 15 months. During the first 3 months (blanking period), 43 patients underwent cardioversion with 16% having complete success (no afib, no drugs), 21% having partial success (a 90% or better reduction in afib burden with or without the use of previously ineffective antiarrhythmic drugs), and the remaining 63% were classified as failures. Patients who underwent late cardioversion (beyond 90 days from procedure) had a complete success rate of 8%, a partial success rate of 17%, and a failure rate of 75%.

At the end of the 15-month follow-up, 15% were in normal sinus rhythm (complete success), while 20% had a partial success, and 65% had a failed outcome. The researchers conclude that more than 80% of patients who undergo cardioversion for persistent AF or atrial flutter following a PVI experience recurrence.


Editor’s comment: This study clearly shows that a failed ablation is a failed ablation and that trying to restore sinus rhythm with cardioversion does not alter this fact. What amazes me is that the Johns Hopkins team must have assumed that a simple circumferential PVI performed with electroanatomical guidance would be sufficient to cure persistent and permanent afib. The relevant medical literature abounds with examples that this is definitely not likely to work. Prof. Haissaguerre and colleagues in Bordeaux have demonstrated that permanent afib can indeed be successfully treated, but that it takes a very complicated and extensive approach to achieve this. In a study reported in 2005, the Bordeaux group found that only 5% of patients with persistent or permanent afib achieved full success with a PVI alone. Other steps necessary to achieve return to NSR involved isolation of the superior vena cava and the coronary sinus (thoracic veins), ablation of areas in the left atrium showing unusual electrical activity, and finally, linear ablation involving the cavotricuspid isthmus and the left atrial roof. Altogether 87% of patients were returned to normal sinus rhythm after undergoing one or more of these steps.[1,2,3]

Ablation success in lone AFibbers

MELBOURNE, AUSTRALIA. It looks like our persistent emphasis on distinguishing between vagal, adrenergic and mixed (random) AF has finally penetrated to mainstream medicine. Electrophysiologists at the Royal Melbourne Hospital included the following paragraph in the introduction of their study aimed at determining the relative prevalence of vagal LAF and ablation success among AFibbers:

Coumel and coworkers classified paroxysmal AF as either vagal or adrenergic depending on the type of triggers and the temporal distribution of the arrhythmic episodes. Patients with vagal AF were typically young males with episodic AF that characteristically began at night or following the intake of food. The arrhythmic episodes in this original description rarely or never progressed to persistent AF. In contrast, patients with adrenergic AF were older, often with evidence of organic heart disease. Episodes occurred during the day and were associated with exercise or emotional stress.

The Australian study included 209 consecutive patients with paroxysmal lone AF (of an average 10 years duration) referred for pulmonary vein antrum isolation (PVAI or Natale protocol). The average age of the study participants was 57 years and 77% were male. Patients were classified as having vagal AF if 90% or more of their episodes were triggered by a vagal stimulus such as resting or sleeping (96.4%), following a meal (96.4%), late post-exercise (51%), cold stimulus (20%), coughing (7%), and swallowing (2%) with most vagal afibbers having more than one trigger.

Patients in whom 90% or more of episodes were initiated by emotional or physical stress and exercise (AF during or immediately following exercise) were classified as adrenergic, while those who met neither of the above criteria were classified as random. All told, 27% had vagal AF, 7% adrenergic, and the remaining 66% had random AF.

All study participants had a PVAI after which they underwent clinical and electrographic follow-up at 3, 6, 9 and 12 months respectively, and at least every 6 months thereafter. Successful isolation of all pulmonary veins was achieved in 94.3% of the patients. However, 25 patients (12%) needed a second procedure due to recurrence of AFib caused by regained conduction between the pulmonary veins and the left atrium. At a mean follow-up of 21 months success rates were as follows:

<table>
<thead>
<tr>
<th>Vagal</th>
<th>Adrenergic</th>
<th>Mixed</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete success (no AFib, no drugs)</td>
<td>47%</td>
<td>69%</td>
<td>52%</td>
</tr>
<tr>
<td>Partial success (no AFib, but on drugs*)</td>
<td>28%</td>
<td>17%</td>
<td>30%</td>
</tr>
<tr>
<td>Failure</td>
<td>25%</td>
<td>14%</td>
<td>18%</td>
</tr>
</tbody>
</table>

* Previously ineffective antiarrhythmics

The differences in complete success rates were not statistically significant.

The Australian researchers conclude that PVAI appears to be similarly effective in patients with vagal, adrenergic, and random paroxysmal AF. They observed no ablatable vagal reflexes during their procedures, but suggest that this may be due to the fact that they were done under general anesthesia, which may have modified the autonomic response. They also noted that afibbers who experienced episodes following their PVAI did not change their trigger classification (from vagal to adrenergic or random, or vice versa).


Editor’s comment: This recent Australian study is clearly of great interest to our afib community. It confirms the existence of three different varieties of paroxysmal AF — vagal, adrenergic and random. The percentages found for these three forms are very close to the percentages found in our 2008 Ablation/Maze Survey — for vagal 27% vs. 33%, for adrenergic 7% vs. 7%, and for random 66% vs. 60%. The study also confirms that resting/sleeping,
heavy meals, and cold drinks are triggers for vagal afibbers, while emotional and physical stress are triggers for those with adrenergic afib. Of course, there are many more significant triggers than those reported here including caffeine, alcohol, food additive (MSG and aspartame), dehydration, and sleeping on the left side – to name a few. The overall success rate of 57% achieved by the Australian team is approaching the 65% average found for the 15 top-ranked institutions in our 2008 survey and is well above the 32% average for other than top-ranked institutions.

First long-term results of robot-assisted ablation

AUSTIN, TEXAS. Success rates for catheter ablations aimed at curing atrial fibrillation vary widely and depend almost entirely on the skill and experience of the electrophysiologist (EP) performing the procedure. The main limitations in achieving a successful result involve precision of catheter movement, stability and contact with atrial tissue, especially the pressure between the tip of the catheter and the atrial wall. An additional problem with catheter ablations is that they involve fluoroscopy imaging thus exposing both the EP and the patient to a significant amount of x-ray radiation.

Robotic guidance of the mapping and ablation catheters has evolved in an attempt to deal with some of the problems inherent in manual ablation. Two main systems are now available – the Hansen Robotic Medical system and the Stereotaxis system. Both share the feature of allowing the EP to perform an ablation procedure well away from the patient and thus reduces the radiation exposure to the EP by 90% or more. Both systems also feature a computer screen displaying a real-time image of the heart and a joystick used to maneuver the mapping and/or ablation catheters inside the atrium with great precision. However, while the Stereotaxis system employs large external magnets to orient the catheter tip in 3-dimensional space, the Hansen system uses a robot arm (similar to the da Vinci system used for radical prostatectomy) to guide the ablation catheter. Recently developed technology (Intellisense) measures the contact force between the catheter tip and the atrial wall, thus significantly reducing the risk of perforation.

Although both systems have been under development for at least 5 years, no large scale clinical trials have reported on their long-term efficacy in curing AF until now. In the December 2009 issue of the Journal of Cardiovascular Electrophysiology, Dr. Andrea Natale and colleagues report on their evaluation of the Hansen system. The study involved 390 afibbers (74% male with an average age of 62 years) of whom about 80% had lone afib (no underlying heart disease). Most of the patients (67%) had paroxysmal AF, 28% had persistent, and 5% had permanent (long-standing persistent) AF. Consecutive patients undergoing catheter ablation between September 2007 and February 2008 were assigned to undergo pulmonary vein antrum isolation (PVAI) + the creation of other lesions as necessary either using a manual procedure (197 patients) or a robot-assisted (RNS) procedure (193 patients) using the Hansen system. All procedures, both manual and RNS, were carried out by two EPs who performed about the same number of each type.

All patients underwent a standard PVAI which resulted in complete electrical isolation of the pulmonary veins in 100% of cases. Patients with persistent and permanent AF had additional lesions as deemed necessary. Average fluoroscopy time was significantly lower in the RNS group (49 minutes) than in the manual group (58 minutes). After the procedure patients were given an event recorder for 5 months and asked to transmit 4 times a week even if asymptomatic. A 7-day Holter monitor was obtained at 3, 6, 9 and 12 months post-ablation. After an average follow-up of 14 months (minimum 12 months), 72% of patients in the RNS group and 70% of those in the manual group were in normal sinus rhythm (NSR) without the use of antiarrhythmics. An additional 13% of RNS patients and 11% of manual patients were in NSR with the aid of previously ineffective antiarrhythmics (partial success).
<table>
<thead>
<tr>
<th>Success Rate*</th>
<th>Manual</th>
<th>RNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal AF</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>73%</td>
<td>71%</td>
</tr>
<tr>
<td>Permanent AF</td>
<td>68%</td>
<td>100%</td>
</tr>
<tr>
<td>All AF</td>
<td>81%</td>
<td>85%</td>
</tr>
</tbody>
</table>

* Aflib-free with or without the use of previously ineffective antiarrhythmics

Two patients in the manual group (1.0%) experienced complications (1 tamponade and 1 hematoma) as compared to 3 patients (2 tamponades and 1 hematoma) in the RNS group.

The research team concludes that, “Our results indicate that robotic navigation and ablation of atrial fibrillation is as safe and effective as manual ablation. In addition, with robotic navigation fluoroscopy time decrease with experience and complication rates are consistent with those reported for manual ablation”.


**Editor’s comment**: The results of this first study of the long-term efficacy and complication rates of robot-assisted ablation for afib are indeed encouraging.

### Cross-country skiing – A shortcut to AF?

OSLO, NORWAY. In 1998 Finnish researchers reported that middle-aged, elite orienteers had a 5 times higher incidence of lone atrial fibrillation (LAF) than did the general population. Now Norwegian sports medicine experts report that the prevalence of LAF in elite cross-country skiers is about 13% as compared to about 0.5% in the general population. The Norwegian study began in 1976 when 122 healthy, long-term trained cross-country skiers from 3 different age groups (26-33 years, 43-50 years, 58-64 years) were enrolled in the study. None of the participants had hypertension or heart disease at enrolment. Follow-ups were carried out in 1981 (117 participants) and in 2004-2006 (78 participants) and consisted of an ECG during rest and exercise and a maximal exercise test. Electrocardiography was added for the 2004-2006 examination.

The average age at which a first afib episode was observed was 53 years in the youngest age group at enrolment, 67 years in the middle age group, and 76 years in the oldest group with an average for all age groups of 62 years. At the most recent follow-up, 13 of the 78 skiers still participating in the study had experienced afib and the current prevalence was 12.8%. The Norwegian researchers observed that skiers with LAF had a lower resting heart rate (bradycardia) and a longer PQ interval (interval from beginning of p-wave [atrial contraction] to beginning of QRS interval [ventricular contraction]) than did skiers who did not develop LAF. The echocardiographic investigation in 2004-2006 also noted that “LAF skiers” had a larger left atrial diameter and area than did those skiers maintaining normal sinus rhythm.

The researchers did not find any correlation between years of practicing cross-country skiing and the risk of AF; however, they did notice that a long PQ interval is associated with an increased risk of developing AF later in life. They recommend that endurance athletes who develop LAF should stop or significantly reduce their training until they regain NSR.


**Editor’s comment**: These recent findings add to an impressive collection of evidence that endurance exercise and sports increase the risk of developing LAF. See [www.afibbers.org/conference/session64.pdf](http://www.afibbers.org/conference/session64.pdf) for further details. Although the Norwegian researchers stopped short of suggesting when to cut back on endurance exercise (lasting longer than...
45 minutes), their data would indicate that a resting heart rate below 50 bpm and a PQ interval above 0.20 seconds might serve as early warnings signs to start taking it easy.

**Association between AF and kidney disease**

NIIGATA, JAPAN. The main function of the kidneys is to remove excess water and waste products from the blood. The kidneys process about 200 liters of blood and produce about 2 liters of urine every day. An indication of the health of the kidneys can be obtained by evaluating their filtration capacity. An estimated glomerular filtration rate (GFR) above 60 mL/min is usually considered a sign of good kidney function, while a rate below 45 mL/min may indicate chronic kidney failure (CKF). The calculation of GFR is primarily based on the serum creatinine level, but also takes into account results of urine tests, age, gender, and other factors. An adequate kidney function is particularly important for afibbers supplementing with potassium and magnesium since any excess of these vital electrolytes are excreted by the kidneys.

In 2008 Japanese researchers reported a significant inverse correlation between AF and GFR. Now another group of Japanese researchers from Niigata University reports that AF is associated with an increased risk of developing chronic kidney disease, while chronic kidney disease is associated with an increased risk of developing AF. Their study included over 220,000 individuals participating in the annual health examinations in the Niigata Association for Comprehensive Health Promotion and Research.

During a mean follow-up of 6 years (over 1 million person-years) 1.3% of participants developed afib. The incidence of afib was significantly higher in participants with a baseline GFR less than 60 mL/min per 1.73 sq m than in those with a higher GFR (0.52%/year vs. 0.22%/year). Similarly, during the same 6-year period, 3.3% of participants experienced a decline in kidney function. Among patients with no AF at baseline, the annual incidence of kidney disease was 0.68%, while among those with AF at baseline, it was 1.8%.

The researchers also noted that the development of proteinuria (protein in the urine, a common forerunner of kidney disease) was higher among participants with AF at baseline than in those without. For afibbers without hypertension or diabetes at baseline, the incidence of proteinuria was 2.5%/year as compared to only 0.8%/year in those without AF at baseline. The researchers conclude that systemic inflammation, oxidative stress and an overactive renin-angiotensin-aldosterone system (RAAS) may be common factors in the development of both AF and chronic kidney disease. They also point out that treatment with ACE inhibitors and angiotensin receptor blockers (ARBs) slows progression of kidney disease and reduces the risk of developing AF.


**Editor's comment:** The Japanese study, unfortunately, did not report the incidence of cardiovascular disease at baseline, so it is not possible to deduce whether the risk of developing kidney disease also applies to lone afibbers. However, since the suggested common risk factors systemic inflammation, oxidative stress and inappropriate RAAS activation likely also apply to LAF; it is possible that declining kidney function could accompany long-term LAF. Thus, it would be prudent to include a creatinine test and urine analysis in one’s annual medical check-up. This would be particularly important for afibbers who rely on magnesium and potassium supplementation to keep their afib under control.

**Cardioversion and aldosterone levels**

KIELCE, POLAND. In the 2nd virtual LAF Conference in January 2003, the role of aldosterone in the initiation of AF episodes was discussed in considerable detail.[1,2] This was followed by an article in the March 2004 issue of *The AFIB Report* further elucidating the role of aldosterone in lone atrial fibrillation (LAF). Dr. Patrick Chambers also discussed the role of aldosterone in his article “P Cells and Potassium” published in the March 2005 issue of *The AFIB Report*. It is likely that aldosterone exerts its negative effects through one or more of the following mechanisms:
• Inflammation and fibrosis (tissue scarring and thickening);
• Increased tendency to blood clotting;
• Impaired fibrinolysis (impaired blood clot digestion and removal);
• Sodium retention;
• Potassium and magnesium loss;
• Disturbance of ANS balance;
• Increased activity of catecholamines (norepinephrine and epinephrine);
• Decreased heart rate variability;
• Increased production of reactive oxygen species (ROS), especially superoxide;
• Decreased production of nitric oxide (NO) and accompanying endothelial dysfunction.

Now a group of Polish researchers report that a decrease in aldosterone level is associated with the maintenance of normal sinus rhythm (NSR) following a successful cardioversion. Their clinical trial involved 45 patients with persistent non-valvular AF and normal left ventricular ejection fraction and 20 matched control subjects with no evidence of AF. The average age of the patients was 59 years and 81% were men. Twenty percent of the group had LAF. The 45 patients were scheduled for electrical cardioversion (CV) after having been in persistent afib for an average of 12 weeks. Plasma aldosterone levels were measured 24 hours prior to CV and again 24 hours after. The baseline aldosterone level was 152 pg/mL in the afib group and 130 pg/mL in the control group (p=0.11).

Forty-three of the initial 45 patients left the hospital in NSR and were examined again 30 days later. At this examination 24 patients (56%) were still enjoying sinus rhythm, while the remaining 19 (44%) had reverted to persistent AF. The Polish researchers noted that while there was no significant difference in aldosterone levels 24 hours prior to CV and 24 hours after in the group that reverted to AF (126 pg/mL vs. 118 pg/mL), there was a sharp decrease from 176 pg/mL to 101 pg/mL in the group that maintained NSR 30 days after CV (p=0.003).

They conclude that a rapid drop of more than 13 pg/mL following CV predicts sinus rhythm maintenance with 87% sensitivity and 64% specificity. They speculate that a largely unchanged aldosterone level after cardioversion may reflect more advanced disease of the atria with enhanced expression of angiotensin converting enzyme (ACE) and local activation of aldosterone excretion. They found no correlation between baseline aldosterone levels and sinus rhythm maintenance 30 days following cardioversion.


Editor’s comment: This study further emphasizes the crucial role of aldosterone in the genesis of atrial fibrillation and supports the evidence that ACE inhibitors, angiotensin receptor blockers (ARBs), or aldosterone antagonists may increase the chance of maintaining NSR following a cardioversion. See The AFIB Report, March 2004 for further information.