Lone Atrial Fibrillation

Toward a Cure – Volume V

By

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Introduction

Since the publication of *Lone Atrial Fibrillation: Towards a Cure* in December 2002 research into atrial fibrillation has grown exponentially. This emphasis on AF research is not coincidental. Recent studies conclude that more than 5.5 million Americans and Europeans now suffer from atrial fibrillation and that the incidence of the disorder increased by 300% between 1986 and 1996. Another study reached the sobering conclusion that one out of every four men and women over the age of 55 years will develop atrial fibrillation during their lifetime. It is estimated that about 20% of all AF patients have lone atrial fibrillation, that is, atrial fibrillation without any underlying heart disease. Truly an epidemic of enormous proportions.

Over the past year **The AFIB Report** has kept subscribers informed of new developments in atrial fibrillation research as reported in the leading journals such as *Journal of Cardiovascular Electrophysiology, Pacing and Clinical Electrophysiology, Circulation*, etc. The subjects covered in our journal summaries range from details of the latest ablation procedures, their outcome and potential complications, to the safety and efficacy of antiarrhythmic drugs. The latest insights into the mechanism of atrial fibrillation as well as important information about stroke risk and prevention are also covered. In addition, *The AFIB Report* has, in detail, covered the results of our most recent LAF survey dealing with the effectiveness of ablation and surgical procedures for eliminating LAF. Numerous afibbers who have found ways of controlling their afib through means other than ablation and surgery have shared their experience for the benefit of others and specific approaches to AF management and stroke prevention have been thoroughly researched and the results disseminated in *The AFIB Report*.

Truly, the 2007 issues of *The AFIB Report* are a treasure trove of immensely valuable information. Unfortunately the vast volume of data contained in the newsletter makes it very difficult to quickly and conveniently locate a particular piece of information. My new book ***Lone Atrial Fibrillation: Toward a Cure – Volume V***, hopefully, solves this problem. Its 220 pages contain all the information published in the 2007 issues arranged in logical sections. The comprehensive subject index

makes it easy to find the elusive, but important information you know is there – somewhere! In addition, the wealth of important new LAF information contained in *Lone Atrial Fibrillation: Toward a Cure – Volume V* makes it an ideal and essential companion to *Lone Atrial Fibrillation: Towards a Cure* and *Lone Atrial Fibrillation: Toward A Cure – Volumes II, III, and IV*.

This book would not have been possible without the whole-hearted support of my wife Judi who was instrumental in seeing it come to fruition. Without her word processing skills, editing advice, and encouragement I couldn't have accomplished it. Wanda Craig, Kerry Acker, John Hagan and Ian McLaren deserve my special thanks for taking the time to put their own personal afib experience into words for others to share.

My gratitude also to the many afibbers who participated in LAF Surveys 12 and 14 – thereby helped other afibbers find a way to manage their condition. Finally, a huge thank you to the many enthusiastic and caring contributors to the Bulletin Board, and to the subscribers to *The AFIB Report* without whose support my research would not have been possible.

Hans R. Larsen
Victoria, BC, Canada
February 2008

AFIB Journeys

Fascinating Rhythm: Atrial Fibrillation – The Beat Goes On

John C. Hagan III, MD

Teaser: ***As runners pound out mile after mile, year after year wondering what part of our musculo-skeletal system will self-destruct next, we believe our exercise creates a heart and lungs that are indestructible. Wrong!***

We runners worry a lot about injuries. Run long enough, far enough, fast enough and something is sure to ache, break, swell, tear, twist, bleed, blister or grow arthritic. The usual suspects: feet, ankles, knees, hips, back. On the other hand, there are parts of our bodies we never expect to fail. We pride ourselves in our heart and our lungs. As runners pound out mile after mile, year after year wondering what part of our musculo-skeletal system will self-destruct next, we believe our exercise creates a heart and lungs that are indestructible.

My heart, it seems, had not got the indestructible message. Thus my consternation one evening a year and a half ago to feel my heart racing about 190 beats per minute. I haven't been able to generate that kind of tachycardia with maximal exercise effort for 40 years. Not a good thing. I hadn't exercised in two days. In fact, I had just showered and was preparing to go to bed. I retrieved my stethoscope from our home first aid kit. I'm no longer facile with medical instruments unless they have lenses and lights in them. After a brief re-familiarization, I listened to my heart sounds. Hmmm. Irregularly irregular and astonishingly fast. Hey, runners don't get atrial fibrillation (AF) do they? After 30 minutes, I decided to go to the hospital to find out.

With my by now concerned wife, I drove to North Kansas City Hospital. I noted how much different it looked approaching the emergency room as a patient rather than as attending physician. It was, well, scary and intimidating. My complaint of a cardiac arrhythmia moved me to the front of a very long line of waiting, less emergent emergencies. Once hooked up to an EKG monitor, my AF diagnosis was confirmed. "What's with you runners and atrial fibrillation?" an ER doctor I know came over to ask. "The last four physicians treated here in the ER with AF are all big time runners." I had no answer but I vowed to find out.

I was converted with medications to sinus rhythm and hospitalized for an extensive work-up. These tests confirmed my heart was in good shape

and there were no other contributing factors to the AF. This, my cardiologist explained, was "lone" AF—the best kind to have. I was discharged on medication and aspirin; the AF returned. I was placed on beta blockers and the AF vanished. But so did all my energy, my exercise capacity and much of my ability to remain conscious when standing up.

Since I treat glaucoma patients with beta blocker eye drops, I thought I had a good understanding of side effects in this ubiquitous class of medications. To put up with these side effects for weeks on end gives one an entirely new perspective. I was breathless after climbing a flight of stairs, running was reduced to laborious walking. Support hose were necessary to deal with significant orthostatic hypotension. I developed a progressive constant cough and post nasal drainage. I was depressed. I was sick and tired of being sick and tired.

Ultimately I decided I could no longer put up with beta blockers. Off medications, the AF returned and I was hospitalized to try yet another medication. When I inquired why I had to be in the monitored coronary care unit, I was told, albeit gently, that some patients developed potentially fatal "pro-arrhythmias." For three days I watched my pulse blip regularly on the monitor. Thankfully, I was not pro-arrhythmic.

This story, thus far, has a happy ending. I measured serial home blood pressures and my cardiologists agreed that I had mild hypertension that should be treated. I'm on medications for AF and hypertension that are well tolerated. I run and exercise as easily as I did 5 years ago. I've given up caffeine and decongestants with pseudoephedrine. I don't drink alcohol beverages. I get some extra heartbeats now and again especially if I get upset or angry. I try to not get upset or angry.

Learning Good Things From a Bad Experience

This whole "heartening" experience has been a great teacher to me personally and professionally. It has made me a better husband, father, grandfather and friend. It has made me a more skillful and empathetic physician. In my ophthalmology practice, I have reduced my utilization of beta blockers to the absolute minimum. I inquire about side effects frequently on all patients and beta blocker patients in extreme detail.

As a patient, I experienced the value of a readily and constantly available high quality emergency and trauma center. In the hospital, I was reminded of the tremendous importance of good nurses, our partners in healthcare. We must work with the nursing and hospital systems to insure that patient-to-nurse ratios do not rise to the level that quality of care diminishes. I was reminded of how valuable—whether rendered by a physician, nurse, technician or any hospital or medical practice employee – a smile, a kind word, a gentle touch and a caring and empathetic

demeanor are in dispelling fear and anxiety. I saw how the malpractice insurance crisis is affecting patient care. My cardiologists were losing associates and unable to find replacements. They were working unbelievable hours to staff their clinics and hospitals. My office appointments were often at 6:30 AM.

I've learned that nothing "guarantees" perfect health. This was re-emphasized by the recent death of our young, athletic, non-smoking contributing editor Alan Clark MD from lung cancer. I'm at peace with my own mortality. I exercise and run to improve the quality of my life not necessarily to extend it.

I have learned the value of living each day as if it were my last. I revel in the high honor of belonging to the distinguished profession of medicine. I am re-dedicated to championing medicine in its frequent socio-economic-legal-legislative battles.

I have discussed "lone" AF with my three running colleagues at North Kansas City Hospital. Each tells a story similar to mine. I wrote an acquaintance cardiologist that I met at Emory who, like me, was a member of the Atlanta track club. He's now team physician to the Atlanta Braves and the Falcons. He responded that AF was one of the more common problems he deals with in these highly trained athletes. He also informed me that he himself has AF that is often triggered by very cold drinks.

That's it. My conclusions, anecdote piled on anecdote, is that endurance athletes with physiological bradycardia are at increased risk of "lone" AF. Overall exercise reduces the risk of coronary artery disease, aids in the treatment of hypertension, hyperlipidemia, depression and weight control. In moderation, exercise is one of the most important life habits one can have. As I wrote in 1974, in the long run it's survival of the fittest[1].

Reference

Hagan III JC. "The Doctor as a Coronary Candidate: Survival of the Fittest", *Resident and Staff Physician*, August 1974

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My Experience with Traditional Chinese Medicine and LAF

Wanda Craig

It was a beautiful spring day in Charlotte, North Carolina about 4 years ago. My husband and I were eating chicken Caesar salads at a sidewalk café and enjoying the warm sunshine. All was well in my world. Suddenly, my heart began racing. I was concerned but not alarmed, so I did not go to the doctor until the next day. My doctor ordered a series of tests and heart monitoring. I was diagnosed with arrhythmia—lone atrial fibrillation (LAF). My heart was strong, my thyroid was functioning well, my blood chemistry was normal—they found nothing to blame. "It's just one of those things," she said. I was immediately put on Coumadin, a blood thinner, and also Diltiazem. Later, because I was only 52 at the time, my cardiologist took me off Coumadin but prescribed low-dosage aspirin therapy. I told him I had been on the Atkins Diet for about a month and asked if that could have triggered it. He did not think it did, but to this day I am convinced that the change in diet upset my body's balance.

For about six months, I felt much better and had episodes about once a month that lasted a couple of hours. Then my ankles began swelling to twice their size, so my cardiologist put me on flecainide, which I took for over three years. Even on medication, I continued to have intermittent episodes several times a week that lasted for several hours. Common triggers were cold drinks, alcohol, caffeine, and stress. My cardiologist said "break-throughs" while on medication were normal. But I felt tired all the time and could sense that my body was getting weaker. One morning I woke up and decided I was going to heal myself.

After reading some research by Dr. Lam I increased my dosage of CoQ10 to 200 mg/day and added magnesium, fish oil, L-Carnitine, and Lipoic Acid. I also decided to try acupuncture to return my body to balance. Li Jie Chu, a wonderful acupuncturist in Charlotte, felt confident she could help me. She prescribed two acupuncture treatments a week and Chinese herbs to take twice daily. After two months, I could tell I was getting stronger, so I decreased my flecainide by taking one pill each night instead of the usual twice a day. My heart went crazy, so I had to go back to taking the prescribed dosage twice a day. After a few weeks, I then tried taking half of a pill twice a day to keep the dosage more even, but I began having frequent AF episodes, so I returned again to taking two 50 mg pills a day. I was getting discouraged. After three months of acupuncture, I was no closer to being drug free, so I decided to stop the treatments. Then my inner "wise woman" voice said, "Keep going." So I

kept going and tried again to wean myself off the flecainide. This time when I took just one pill each night, I had no problems. I continued this dosage for about a month, and then began taking one pill every other night. At first, I had short, mild AF episodes as my body was learning its rhythm again. As Li Jie reminded me, my heart had "forgotten" how to function without drugs. After another month, I stopped the flecainide altogether. I took my last pill on October 31, 2006—Halloween night. My heartbeat has continued to grow steady, and after eight months of acupuncture, I feel great. I am finally drug free.

A couple of words of caution are in order. It is never wise to stop your medication without medical supervision. I asked my doctor and cardiologist to help me find a natural treatment. Neither signed on to help me, so I did it on my own out of desperation. I understood the risk, but I felt the risk of staying on medication the rest of my life was worse. While I am happy to share my happy ending, I also do not want to be responsible for anyone taking risks without understanding the potential consequences. I chose not to live in fear and dependence, but you have to make those decisions for yourself.

Another thing to keep in mind is that I also made significant lifestyle changes. I began yoga and learned to breathe properly, which helps regulates the nervous system. I continue to take all the supplements listed above plus the Chinese herbs and eat a balanced diet of fish, chicken, fruit and vegetables. I gave up alcohol completely, limit caffeine, and drink lots of water. The benefits are definitely worth the small sacrifices I have made.

I encourage anyone suffering from LAF to do the research, try acupuncture with a certified practitioner, take heart-healthy supplements, pay attention to your body's reaction to what you eat and drink, and above all—do not give up. I believe LAF is a symptom of the body's imbalance and can be managed without drugs. My story has a happy ending, and I believe yours can too.

My Amazing Maze

Kerry Acker

I was diagnosed with afib in early January of 2003. A full battery of medical tests showed no heart disease, a normal sized left atrium and no other medical conditions that would cause my afib. It took me six months of consultations, research and trial and error to determine the most effective medical and lifestyle regimen. With the help of this board, I learned that I was a lone vagal persistent afibber and settled upon the following regimen:

1. Cardizem, which kept my heart at a safe and relatively comfortable rate during my episodes, which usually lasted 15-20 hours. Although my rate was comfortably low, the arrhythmia was usually very uncomfortable and resulted in considerable anxiety, discomfort and feelings of dread.
2. Flecainide, taken only at the onset of an episode and then twelve hours later. I usually converted within a few hours of my second dose. (Thanks to Hans for informing me about this option.) My EP did not believe this occasional use of flec would be effective, although she did not otherwise object to my plan to use it in this manner. She was wrong and a year or so later, the "pill in the pocket" became an accepted medical practice.
3. High doses of fish oil, together with a good multivitamin.
4. One full aspirin (325mg) per day.

In addition to the above, I found that the use of benzodiazepines on an intermittent basis helped to control my episodes. After I read a note in Hans' book, I tried using Ativan immediately upon inception of PACs, and found that it would terminate the PACs, and would thereby prevent the onset of an episode. I later switched to Valium, a longer acting benzo, which had the same effect. While I could not prevent all episodes, since many of my episodes were not preceded by PACs, I did obtain some measure of relief with this use of benzos. However, once an afib episode had started, I found that the Valium did not help in converting me to NSR, although in some cases it made me more comfortable. In any event, I recognized that long-term use of benzodiazepines was not a result I wanted or that would be medically desirable.

During 2003, my episodes occurred about once every two weeks. Then, miraculously, without any changes in my meds or lifestyle, I had two years of relative calm. I experienced about nine episodes each year in 2004 and 2005, a major improvement over 2003. Then, literally on the first day of January 2006, my episodes returned with abandon, and I suffered

more afib in the first three months of that year than I did in all of 2004 and 2005 combined. I decided that it was time to do heavy research into all available interventional options.

Over the next six months, I met with the EP group at the University of Pennsylvania, a top tier catheter ablation center. I also had a consultation with the Wolf group in Cincinnati about their "mini-maze" procedure. Finally, I met with a surgeon who performs the full Maze procedure. In between these visits around the country, I did daily reading and research into the available procedures, and I read posts from others who had had them done, queried doctors (and their assistants) through online websites, etc.

Even though I am a relatively young (50) lone afibber, I eventually decided not to undergo a catheter ablation or the less comprehensive "mini-maze". Rather I opted for a full Maze. Even though both of the former procedures are less invasive than the full Maze, I decided, based on the extensive research I had done and discussions I had had, that a comparison of the risk factors and success rates for all three procedures, led to the inescapable conclusion that a full Maze was my best option.

I concluded that both the catheter ablation and the full Maze presented specific and sometimes different risk factors, but in the case of a healthy, fifty year old lone afibber the relative overall risks were not necessarily greater with the Maze. According to my surgeon, the risks of stroke, bleeding or infection are no higher for the full Maze procedure than for an ablation or mini-maze, and some of the other risks of an ablation – esophageal perforation, pulmonary vein stenosis and extensive radiation exposure -- are non-existent in the full Maze procedure.

I was further influenced by the length of time that the Maze procedure has been around. It was developed in 1987 and twenty years of research and practice has resulted in a uniform set of lesions used by all of the top tier Maze surgeons, with the major difference in technique being the energy source used to create the lesions.

I was struck by the fact that while the procedures performed at the top ablation centers have a number of similarities, there are substantial differences in the nature of the ablation procedure, depending on who is performing it. This made me uncomfortable, because it seemed clear that there was not yet uniformity among the EPs as to the best way of doing the procedure. I concluded that more time was needed for the best protocols to be established and adopted by most top EPs, and frankly, I did not want to be one of the case studies that helped them to develop that protocol. (With respect to the modified, or "mini" Maze procedures, although they hold great promise, I believe they are too new to consider

right now and, in any event, the success rates are even lower or at best the same as catheter ablations.)

Moreover, I was not particularly impressed with the overall success rate of first catheter ablations (around 70%), with a slightly higher success rate for touch-ups after a first one. On the other hand, when I first met in March of 2006 with the surgeon who later did my Maze, he stated that he personally had had an overall 90% success rate, defined as afib- free, without meds, for at least one year following the surgery. Although he did not have formal data, he expressed the opinion that my age, health and nature of my afib would probably give me an even greater likelihood of success. While this seemed to be an extraordinarily high success rate, I felt confident that he had given me honest statistics after I queried him at length and followed up with my own research. Since my worst nightmare would be to have a procedure done (whether ablation or surgery) and then find that I still had afib, the success rate was a key factor for me.

After careful consideration, I concluded that the full Maze offered me the most time- tested procedure along with the best overall chance of success with a relatively low risk profile.

I chose one of the best Maze surgeons in the world, Dr. Niv Ad who had trained with the founder of the original Maze, Dr. James Cox. Dr. Ad (pronounced "Ahd") has performed more than 500 full Cryosurgical Maze procedures to date. Approximately 200 of those have been performed with his surgical team at Inova Fairfax Hospital in Falls Church, Virginia. Contrary to popular belief, the procedure does not have to be performed using a sternal incision and is far less complex than the original "cut and sew" procedure since the scalpel has been replaced by traditional energy sources, i.e., cryoenergy and bi-polar radiofrequency. Ultrasound and microwave energy are also used. Dr. Ad uses only cryoenergy as he feels it is the safest technology in which transmurality of the lesions can be seen and verified.

Initially I assumed that I would have the minimally invasive Maze procedure, as I had been told by Dr. Ad that I was an ideal candidate for it (no underlying health or cardiac issues, optimal weight, etc.) However, in my initial visit with him, we had an extensive discussion about the pros and cons of doing the Maze using the minimally invasive incision versus a median sternotomy. During that discussion, Dr. Ad told me that a major advantage of a sternal incision is that the time on heart-lung bypass is far less than with the minimally invasive procedure. In addition, he acknowledged the common sense conclusion that the surgeon would have better visualization of the heart with a sternal incision. Finally, he also advised that the sternal incision is generally less painful during recovery than the incision used in the minimally invasive procedure (which

is very similar to the one used in the Wolf procedure). However, he also assured me that the full Maze can be performed safely and effectively using the minimally invasive right side incision. Over the next few months, as my afib continued to plague me and I did more research and reading, I started to seriously consider the median sternotomy. When I scheduled my procedure with Dr. Ad, it was with the assumption that I would be having the minimally invasive procedure done, but he let me know that I could change my mind right up until the moment before I went to the OR. Finally, the day before the surgery, I made up my mind that I would opt for the median sternotomy, because I liked the idea that the surgeon would have better visualization, and I particularly was more comfortable with the idea of significantly less time on bypass. When I saw Dr. Ad on the morning of surgery, I told him that I wanted a median sternotomy, and therefore the procedure went ahead in that manner. However, I stress that this was a personal decision, and that the procedure, in all likelihood, would have been just as effective had I elected to have the right side incision instead.

The actual surgery takes about an hour, and I was hospitalized for about four days. I had a few minor, expected and totally controllable complications of the surgery which were dealt with while I was still in the hospital. Because I had traveled from out of town to see Dr. Ad in Virginia, I remained in the area for about a week after I was discharged, just in case of any complications.

Post-operatively, I was fortunate to have the luxury of taking plenty of time to limit my activities, primarily due to the sternal incision. I was restricted from lifting more than 5 pounds, and many other normal daily activities (such as driving, or even sitting in the front seat of a car) had to be put on hold for about 6-8 weeks, although I could have returned to work in two. (With the lesser invasive incision, full activities can be resumed much more quickly.) I experienced some discomfort in the area of my incision for a few weeks, but it was controllable with medications, and, as indicated above, the pain with a minimally invasive incision is often worse because of the cutting of certain nerves. The only pain I experienced was when I coughed or laughed but this went away in about two weeks.

I recently marked the six-month anniversary of my surgery, and I have been afib-free since day one. Up to 50% of patients experience some post-op afib for up to three months after surgery. This is expected and if the procedure has been successful, the afib generally disappears after about three months. I was very fortunate to be free from afib immediately after the surgery, as well as from PACs and other uncomfortable symptoms that had previously been associated with my afib.

Other than fatigue and weakness for about four weeks after the surgery, the recovery has gone very well and I now feel back to normal. I have resumed my cardiovascular and weight training and I am no longer concerned about eating or drinking anything that might trigger an episode.

One of the other advantages of the Maze surgery is the ability of the surgeon to deal with potential causes of afib if discovered during the procedure. In my case, Dr. Ad tested my Ligament of Marshall and, not surprisingly, got a very strong vagal response. This small ligament is vestigial so snipping it does not affect heart function but eliminates any possible role that it may have in atrial fibrillation. However, deactivation of the Ligament of Marshall can cause a temporary increase in resting heart rate, which I did experience. That has slowly subsided and will probably improve over the next few months, although the current rate is perfectly acceptable and given the vagal nature of my afib, may even be preferable.

The final step in the procedure is closure of the left atrial appendage, which is known to be a primary source of clotting, and hence stroke. Many surgeons opt to remove it entirely, but because there may be some hormonal functions performed by this appendage, Dr. Ad chooses instead to oversew it. I am well aware of the studies showing that lone afibbers are not at any greater risk of stroke than the general population. Nevertheless, if my afib does ever return, I will sleep just a little better at night knowing that a primary source of clotting has been shut down.

I have no doubt that I made an unusual decision to opt for a full Maze, in that most relatively young lone afibbers would probably go for an ablation before considering surgery. However, given the relative risks, options, and likelihood of success, I certainly would encourage any chronic afibber who is considering some form of interventional therapy to at least consider and research the full Maze.

Only a handful of surgeons in this country qualify as top-notch Maze surgeons, and they are primarily located in major metropolitan areas. However, most of these surgeons do not have the extended waiting time that is the usual for top ablation EPs. Shorter waiting time might also be a factor for those whose afib may have taken a sudden turn for the worse and might be looking at a year-long waiting list, with the possibility of a second procedure, in the case of an ablation.

I lived with afib for several years, some worse than others. In the end, I could no longer tolerate the uncertainty and discomfort of this condition as I entered my sixth decade of life. Some of the people closest to me could not understand how I would elect to have what they thought of as “open heart surgery,” when my afib was only intermittent, and probably not life-threatening. However, I was always aware that another episode

was just around the corner, and even when it wasn't, I always felt that it was. I found myself restricting enjoyable activities, modifying my diet in ways that were not acceptable to me (and often didn't make any difference anyway), and in general, I always felt as though my afib was controlling me, instead of the other way around. Once I met a surgeon whom I felt completely comfortable with and confident in, who was willing to answer my many questions, I felt that a full Maze was the way to go. I went into the procedure knowing that I was taking a risk – a low, but not insignificant one– which I had weighed against the toll that afib was taking on my life. I went ahead, and today, six months later, I am glad I did. It was well worth it.

Hydrotherapy Benefits and Afib

Ian McLaren

As a relative newcomer to the afib scene, I would like to pass on a positive experience which seems to have resulted in a cure for the disorder – at least in my case. I first experienced afib in April 2006 shortly after my 75th birthday. I had been to a local beach for a swim, and was dismayed to find that I was huffing and puffing after swimming only 50 meters or so. It may have been something to do with a couple of bouts of anemia I had experienced a year or two earlier caused, I believe, by long-term use of aspirin following an angioplasty. The afib episodes didn't occur in a series, but simply arrived and stayed, more or less constant after diagnosis. After being referred by our GP to a cardiologist I was placed on a regime of strictly monitored doses of warfarin (Coumadin), digoxin (Sigmaxin) followed by Isoptin (verapamil). When these didn't work, Aratac 200 (amiodarone) was added to the cocktail. Simultaneously I was taking Losec (omeprazole) for a suspected leaking blood vessel, and Lipitor for something else. It was all rather confusing. There were periods of modest improvement, but overall the pulse remained erratic and sometimes fast – up to 110 beats per minute. I despaired of regaining the active life I had enjoyed up until then. Further medications were prescribed, and within a few months I was taking five or six daily. Two electrical cardioversions were carried out, neither of which restored correct rhythm for more than 24 hours. The medications were not only failing to correct matters, but seemed to be producing bad side effects. Something else needed to be done.

Whilst by no means a health freak, I have had a lifelong interest in Yoga, martial arts, and other philosophies which advocate self-help. I lacked the energy to do Yoga, however, I came upon a book by American Dr Frederick M Rossiter, entitled *Water for Health & Healing*. It described various ways in which water may be used to promote health, including the use of hot and cold showers for improving the heart and blood circulation. Whilst I observed no direct reference to afib, it occurred to me that if electrical cardioversions were supposed to shock the heart into correct rhythm (with a success rate of only 50%) it seems maybe the shock of switching from hot to cold water during a shower would have a similar effect. My first experimental attempt convinced me of the possibility, as it is certainly a heart-stopping experience, especially in the middle of a Tasmanian winter with temperatures not far above freezing. The trick is to run the hot water as high as can be tolerated, then turn it completely off and run fully cold for maybe 20 seconds or so, then back to hot, then cold again. Two or three bursts of this are usually enough, finishing with cold water. It feels great when you finish.

After going through this ceremony twice a day for a week or two I began to feel an improvement, and cut back to once a day, while continuing to take the medications. Within a month I found my pulse running at a steady 72 beats per minute and felt confident enough to begin dispensing with the medications, one at a time in the order they had been prescribed until I was using only warfarin. I gave that up last September when it became obvious that it was responsible for the internal bleeding. In place of the warfarin I now take 1000 IU vitamin E daily, vitamins C and B complex, use lots of garlic, and eat a largely vegetarian diet. The pulse has stayed regular except for a period when I had a bad cold. The stress of this apparently put it back into afib, however, when I resumed the hot and cold showers (no they were NOT responsible for the cold!) it regained normal rhythm.

It is now more than six months since I used any medications, and the afib, if not entirely cured, at least is not a bother any more. Any undue stress seems to upset the rhythm, but nowhere nearly as badly as at the beginning, and it soon settles down. The bad side effects, including internal bleeding, went away with the medications. I have no idea whether hot and cold showers will work for everyone – they may even be risky for some, but I would be happy if others managed to escape this dreadful condition without using drugs.

November 2007

P.S. The "beast" returned a few weeks ago and has so far refused to respond to the hot/cold showers. It appears to have been triggered by a virus. A little disappointing after 14 months virtually symptom-free and no medications! Anyway, I am persevering.

Journal Summaries

Incidence & Management

Status of AF in Scotland

GLASGOW, UNITED KINGDOM. A group of researchers has just completed a study aimed at determining the prevalence (total number of cases of a disease in a given population at a specific point in time) and incidence (total number of new cases of a disease diagnosed during a specific time period – usually a year) of atrial fibrillation (AF) in Scotland. The study involved 55 primary care practices serving a total of 362,155 patients. The researchers determined the overall prevalence of AF (NOTE: no distinction was made between heart disease-related AF and lone AF) to be 0.94% in men and 0.79% in women. The **prevalence** increased markedly with age from 0.03% in individuals less than 45 years of age to 7.1% in persons over the age of 85 years. An 18% lower prevalence was found among socio-economically deprived individuals compared to affluent individuals (as measured by postal code of residence). It is possible that this difference is related to the shorter life expectancy of deprived individuals, or to the fact that affluent patients are more likely to receive electrocardiograms.

Other studies have concluded that the prevalence of AF among men and women between the ages of 75 and 84 years has risen from 7.3% to 9.5% in men and from 6.2% to 7.2% in women over the period 1994-1998. Most of the AF patients involved in the study had heart disease (32%) and/or hypertension (25%), while less than 5% had suffered a stroke.

The **incidence** (new cases per year) of AF rose from 0.01% in men below the age of 45 years to 0.04% in those between the ages of 65 and 74 years, and peaked at 0.09% for those aged 85 years and older. The corresponding numbers for women were 0%, 0.03%, and 0.07% respectively.

Most AF patients (71%) received rate control medication such as beta-blockers (28%), calcium channel blockers (42%), or digoxin (43%). Only 20% received an antiarrhythmic drug (amiodarone – 12%, sotalol – 6%). The researchers point out that the use of digoxin has decreased from 70% in 1996 to 43% in 2001. In this study, women were 25% more likely than men to be prescribed digoxin. Antithrombotic therapy was prescribed for 78% (aspirin – 44% and warfarin – 42%).

In an accompanying editorial Gregory Lip and colleagues at Birmingham University conclude that *AF is certainly the new "epidemic"* with 15.9 million people in the US alone expected to have the disease by 2050. Other studies have concluded that the lifetime risk of developing AF is now 24% in men and 22% in women at age 55 years.

Murphy, NF, et al. A national survey of the prevalence, incidence, primary care burden and treatment of atrial fibrillation in Scotland. **Heart**, *Vol. 93, 2007, pp. 606-12*

Lip, GYH, et al. Atrial fibrillation – the growing epidemic. **Heart**, *Vol. 93, 2007, pp. 542-43*

Editor's comment: It is particularly gratifying to note that the use of digoxin has declined by 39% from 1996 to 2001. Digoxin is not as effective for rate control, as are beta- and calcium channel blockers and should never be taken by lone afibbers. Also, it is good to see the growing awareness of the fact that AF has now reached epidemic proportions. It is unfortunate that this study, like many others, did not distinguish between lone and heart disease-related AF. Of interest is the finding that the overall prevalence of AF was almost equal among men and women (ratio 54:46) whereas lone afib is significantly more prevalent among men (80:20).

New scale for measuring AF severity

TORONTO, CANADA. "*Because of its high incidence and the considerable disability that it may generate, atrial fibrillation (AF) is increasingly recognized as an important clinical problem in medical practice"* and *"the primary purpose of any therapy in AF is to improve patient well-being"*. These two statements do, in my opinion, signal a quantum shift in medical thinking about afib. Not only do they recognize that afib can generate considerable disability – ie. cannot be dismissed as a mere "nuisance", but also that patient well-being, not stroke prevention, should be the attending physician's primary concern, especially in regard to lone afibbers.

The above statements are contained in a report prepared by a group of Canadian EPs and cardiologists describing the development of a new scale for gauging the severity of afib. The scale is called the "Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale" or CCS-SAF Scale for short.

Afib is classified as first documented episode, recurrent paroxysmal, recurrent persistent, or permanent where paroxysmal episodes are defined as being self-terminating, persistent episodes as requiring medical intervention for termination, and permanent afib as not being convertible to normal sinus rhythm.

Rating an afibber on the Scale begins by determining the symptoms – palpitations, dyspnea (shortness of breath), dizziness, syncope (light-headedness or fainting), chest pain, weakness, or fatigue, accompanying documented AF. The severity of these symptoms is then assigned to one of five classes. Class 0 indicates that the afib is asymptomatic. Class 3 indicates a moderate effect on the patient's quality-of-life such as moderate awareness of symptoms on most days in patients with persistent/permanent AF, or more common episodes (eg. more than every few months), or more severe symptoms, or both, in patients with paroxysmal afib. Class 5 indicates a severe effect on quality-of-life and would include frequent and highly symptomatic episodes in patients with paroxysmal afib or episodes accompanied by syncope.

The Scale is now in the process of being tested. Preliminary results indicate that it is valid and reliable in providing an estimate of the effect of AF on a patient's quality-of-life.

Dorian, P, et al. A novel, simple scale for assessing the symptoms severity of atrial fibrillation at the bedside. Canadian Journal of Cardiology, *Vol. 22, No. 5, April 2006, pp. 383-86*

Editor's comment: The development of the CCS-SAF Scale is a welcome development and a good start in giving AF, especially lone AF, the attention it deserves. It should also be a useful tool in deciding on priorities in regard to ablation and maze procedures. I am a bit surprised that the Scale does not address the question of afib burden (number of episodes times duration), but perhaps this very valid measure of afib severity will be added later.

Mechanistic Insights

Aldosterone and atrial fibrillation

MINEAPOLIS, MINNESOTA. Medical doctors at the Veterans Affairs Medical Center report the case of a 58-year-old African American man whose afib episodes were found to be clearly related to low serum levels of potassium resulting from Conn's syndrome (primary hyperaldosteronism). The man presented with palpitations, dizziness, chest pain, and muscle cramps. He reported having AF episodes occurring every 1 to 2 weeks. Upon admission his serum potassium level was found to be 2.7 mEq/L (reference range: 3.5 – 4.5 mEq/L). He was treated with intravenous potassium chloride (40 mEq [1560 mg]) every 4 hours for an 8-hour period as well as an esmolol (beta-blocker) infusion (100 mcg/kg/min).

The atrial fibrillation ceased once the potassium serum level normalized. After a diagnosis of Conn's syndrome (serum aldosterone of 82.7 ng/dL [normal range: 4 – 31 ng/dL] and renin of 0.07 ng/mL/hr [normal range: 0.7 – 5 ng/mL/hr]) he was discharged with a prescription for 25 mg/day of spironolactone and 10 mEq/day (390 mg/day) of potassium chloride. On this regimen his palpitations disappeared and he has now been afib-free for a year. The doctors conclude that hypokalemia (low potassium levels) may increase the risk of developing paroxysmal AF in patients with hyperaldosteronism (Conn's syndrome).

Aloul, BA, et al. Atrial fibrillation associated with hypokalemia due to primary hyperaldosteronism (Conn's syndrome). **PACE**, *Vol. 29, November 2006, pp. 1303-05*

Editor's comment: this paper is of particular interest to me as I had a similar experience myself prior to my successful ablation. My aldosterone was elevated and my renin was substantially suppressed, particularly immediately prior to an episode; my potassium level was also at the lower end of the normal range (3.5 mEq/L). Unfortunately, supplementation with spironolactone and potassium did not solve my problem. You can read more about the connection between hypokalemia, hyperaldosteronism and AF in Session 26 of the Conference Room Proceedings http://www.afibbers.org/conference/session26.pdf

Differences between AF and atrial flutter

VANCOUVER, CANADA. Canadian researchers have compared stroke incidence and mortality between a group of 781 patients with newly-

diagnosed AF and 96 patients with newly-diagnosed atrial flutter. Most of the patients had underlying heart disease or hypertension, but 19% were classified as having lone AF, while 17% were classified as having lone atrial flutter. The patients were followed for an average (median) of 6.9 years during which time 65 ischemic strokes (10 fatal) and 7 hemorrhagic strokes (5 fatal) occurred. This corresponds to an annual stroke rate of 1.33% a year among afibbers and 1.24% a year in patients with atrial flutter. Not a significant difference, but certainly well below the 5-fold increase in stroke risk often quoted for patients with AF.

It is of interest that 57% of afibbers and 43% of atrial flutter patients were on warfarin at the time of their stroke. The estimated overall mortality rate in the group was about 3% a year with no significant difference between afibbers and atrial flutter patients. There were no strokes in the lone atrial flutter group (no mention is made in the report of strokes in the lone AF group) and patients with lone atrial fibrillation or flutter were found to have significantly smaller left atria than those with hypertension or underlying heart disease.

The researchers also observed that 28% of patients originally presenting with atrial flutter later converted to AF. They question the hypothesis that the main cause of ischemic stroke in atrial fibrillation and flutter is the formation of clots in the left atrial appendage and point out that high-risk patients with AF have been found to have a 63% incidence of aortic plaque. Thus, ischemic strokes in atrial fibrillation and atrial flutter patients are more likely related to comorbid conditions than to the fibrillation or flutter as such.
Lelorier, P, et al. Prognostic differences between atrial fibrillation and atrial flutter. American Journal of Cardiology, *Vol. 93, March 1, 2004, pp. 647-49*

Editor's comment: The observation that atrial fibrillation and atrial flutter involve comparable risks of stroke and overall mortality is indeed interesting as is the observation that stroke risk may be more related to comorbid conditions than to fibrillation or flutter as such. This supports my own long-held conviction. It is also of interest that over half of the study participants were on warfarin when they suffered their stroke – not exactly a ringing testimony to the effectiveness of warfarin!

Long-term progression of lone AF

ROCHESTER, MINNESOTA. More than 50 years ago cardiologists at the Mayo Clinic began following a group of lone afibbers in order to determine their long-term prognosis and survival. The group consisted of 34 participants with the paroxysmal variety, 37 with persistent afib, and 5 with permanent afib at entry to the study. Lone AF was defined as atrial fibrillation without underlying structural heart disease or hypertension (no

age limitation). Atrial fibrillation was defined as paroxysmal if it terminated on its own, as persistent if cardioversion (electrical or drug-assisted) was required to terminate episodes, and as permanent if sinus rhythm could not be restored or maintained despite intervention. The average age at diagnosis was 44 years and 78% of the group was male. Thirty-four percent of study participants were prescribed digoxin within 30 days of their first episode. The number of "digoxin users" had increased to 75% at the latest follow-up.

After an average follow-up of 30 years, 29% of paroxysmal and persistent afibbers had progressed to permanent AF. It is interesting to note that 68% of persistent afibbers became paroxysmal and 22% became permanent during follow-up. Only 6% of paroxysmal afibbers became persistent, while 41% became permanent. In most cases the progression to permanent AF occurred within the first 15 years after diagnosis.

Survival in the study group at 92% at 15 years and 68% at 30 years was similar to or even slightly better than expected for an age- and sex-matched group of Minnesotans (86% and 57% at 15 and 30 years respectively). Twelve of the reported deaths were due to cardiovascular causes, while the remaining 15 deaths were due to other causes. The development of congestive heart failure (19% of group at 30 years follow-up) was not significantly higher than expected (15%).

During the follow-up, 5 strokes (0.2%/person-year) and 12 transient ischemic attacks (0.5%/person-year) occurred in the group – mostly among permanent afibbers. All strokes and TIAs occurred in participants who had developed one or more risk factors for stroke during follow-up (hypertension in 12 patients, heart failure in 4, and diabetes in 3). Not a single stroke or TIA occurred among lone afibbers with no risk factors for stroke. This prompted the following remark from the researchers:

Our long-term data suggest that the increased risk of stroke in atrial fibrillation is due to "the company it keeps".

In other words, lone atrial fibrillation as such is not a risk factor for ischemic stroke. The overall conclusion of the study is highly reassuring to lone afibbers,

After >30 years of follow-up of our rigorously defined cohort, findings confirm that overall survival is not affected adversely by lone atrial fibrillation.

In an accompanying editorial, Dr. Lars Frost of the Aarhus University Hospital in Denmark makes the following interesting comment, *Cardiologists with strong political influence have suggested that a*

diagnosis of lone atrial fibrillation should be restricted to patients <60 years of age, although there is not evidence of any threshold values by age regarding the risk of stroke in patients with atrial fibrillation – or in any other medical condition for that matter.
Jahangir, A, et al. Long-term progression and outcomes with aging in patients with lone atrial fibrillation. Circulation, *Vol. 115, June 19, 2007, pp. 3050-56*
Frost, L. Lone atrial fibrillation: Good, bad, or ugly? Circulation, *Vol. 115, June 19, 2007, pp. 3040-41*

Editor's comment: It is indeed encouraging to receive further confirmation that lone AF does not shorten lifespan nor increase stroke risk. It is also a cause for celebration that the conversion from paroxysmal and persistent AF to permanent is less than 1% per person-year. It is likely that it would have been closer to 0% if the majority of study participants had not been prescribed digoxin. This "medicine from hell", for lone afibbers at least, may not only prolong episode duration, but may actually convert paroxysmal AF to permanent.[1,2]
[1] Sticherling, C, et al. Effects of digoxin on acute, atrial fibrillation: Induced changes in atrial refractoriness. Circulation, Vol. 102, November 14, 2000, pp. 2503-08
[2] Falk, RH. Proarrhythmic responses to atrial antiarrhythmic therapy. In ***Atrial Fibrillation: Mechanisms and Management,*** *edited by Rodney H. Falk and Philip J, Podrid, Lippincott-Raven Publishers, Philadelphia, 2nd edition, 1997, p. 386*

Gene abnormalities in AF patients

As an outgrowth of the Human Genome Project, Cleveland Clinic researchers have discovered 35 gene variations (single-nucleotide polymorphisms [SNPs]) that either increase AF risk or protect against it. The study involved 112 afib patients (100 with underlying heart disease) and 600 controls in which the researchers compared 250,000 SNPs. Nineteen of these were found to be protective, while 16 were associated with an increased risk.
http://www.theheart.org/printArticle.do?primaryKey=792617

Electrocardiogram may predict development of AF

GHENT, BELGIUM. As the heart muscle contracts it generates a current that spreads into the fluids surrounding the heart and can be measured on the surface of the body. An electrocardiogram (ECG) measures the electrical activity of the heart. It involves the placing of small electrodes on the chest around the heart area and on the arms and legs, usually using a total of 12 leads. A normal ECG shows a characteristic form consisting of a P wave, a QRS complex, and a T wave. The start of the P wave is the start of an individual contraction (heart beat) and the beginning of the depolarization of individual myocytes (heart cells). In

healthy young men the mean duration of the P wave is about 77 milliseconds (52-115 ms).[1]

Researchers at Ghent University now report that it may be possible to predict the development of atrial fibrillation (AF) as much as 10 years before the first episode actually occurs. Their study included 40 patients aged 55 to 74 years who were participants in the Belgian Interuniversity Research on Nutrition and Health Survey. After a 10-year observation period, these patients had all developed AF. Their baseline ECGs were compared to those of 120 study participants (matched for age and gender) who had not developed AF.

The researchers noted that the participants who developed AF were more likely to suffer from hypertension and to be overweight, although not obese (BMI < 30). However, the most interesting observation was that participants who developed AF had substantially longer P waves at baseline than did those who did not (mean P wave duration 120 ms vs. 110 ms). It was also apparent that the presence of a deflected P wave (a wave with a slight indent in the down slope) was significantly more common among those destined to develop AF (55% vs. 13%). Overall, the researchers estimate that a patient with a long-duration, deflected P wave has a 13-fold greater risk of developing AF within a 10-year period than do gender and age matched controls with normal P waves.

De Bacquer, D, et al. Long-term prognostic value of P-wave characteristics for the development of atrial fibrillation in subjects aged 55 to 74 years at baseline. American Journal of Cardiology, *Vol. 100, 2007, pp. 850-54*

Editor's comment: The prevalence of heart disease (heart attack, angina, and left ventricular hypertrophy) was less than 10% in the groups studied, so if it is likely that the results of the above study would be applicable to lone AF as well. Thus, the careful study of P wave shape and duration on a routine ECG could perhaps be used to give advance warning of an increased risk for the development of AF and thus motivate people to take preventive measures such as reducing emotional and work-related stress, moderating vigorous physical activities, and go easy on caffeine and alcohol. It is also of interest that P wave duration can be used to predict whether or not paroxysmal AF will turn into permanent (chronic) AF.[2]

[1] Gialafos, EJ, et al. P wave analysis indices in young healthy men. PACE, Vol. 26. January 2003, Pt. II, pp. 367-72

[2] Yasushi, A, et al. Prediction of transition to chronic atrial fibrillation in patients with paroxysmal atrial fibrillation by signal-averaged electrocardiography. Circulation, Vol. 96, 1997, pp. 2612-16

Risk Factors & Triggers

AF in athletes

KANSAS CITY, MISSOURI. Sustained, vigorous exercise is associated with a permanent increase in vagal tone and a lower than normal resting heart rate. The first indication that athletes might be more prone to developing atrial fibrillation came in 1998 when Finnish researchers reported that middle-aged orienteers (distance runners) experienced 5 times the prevalence of lone afib than did age-matched controls. The excess prevalence of lone afib was particularly high in the 46-54 year age group where the prevalence among orienteers was 4.2% as compared to 0.5% in controls. On the plus side, the researchers also noted that the orienteers had a lower incident of coronary artery disease and much lower mortality than did controls.

An Italian study, also reported in 1998, involved 1772 athletes with an average (mean) age of 21 years. Over a 5-year follow-up period, 6% of these athletes experienced one or more episodes of atrial fibrillation. A more recent Spanish study reported that the proportion of athletes in a group of lone afibbers was much higher than the proportion in the general population (63% vs. 15%). The Spanish researchers conclude that long-term, vigorous exercise may predispose to AF. They also make the interesting observation that the athletes tended to have their episodes during sleep or after meals when vagal tone is elevated.

In contrast, a recent study by the Italian National Olympic Committee found no significant difference in afib prevalence between athletes and the general population, but did notice that athletes tended to have enlarged left atria. The authors of this article (all MDs with AF engaged in long-distance running) conclude that lone atrial fibrillation is a common arrhythmia in conditioned athletes and may be more common than in the general population, especially among males. They point out that the use of beta-blockers, antiarrhythmics, and warfarin in athletes is problematical and suggest that early radiofrequency ablation may be the best option for athletes with lone atrial fibrillation.
Farrar, MW, et al. Atrial fibrillation in athletes. Missouri Medicine*, Vol. 103, May/June 2006, pp. 297-301*

Inflammation and atrial fibrillation

TRABZON, TURKEY. There is considerable evidence that inflammation is an underlying cause of atrial fibrillation. Turkish researchers now report

that patients with AF have considerably higher levels of the inflammation markers C-reactive protein (hs-CRP) and interleukin-6 (IL-6) than do normal controls. Their study involved 85 patients with afib (30 paroxysmal or new-onset, 24 persistent, and 31 permanent). Eighteen were classified as lone afibbers since they did not have hypertension or structural heart disease.

The average CRP and IL-6 levels for controls were 0.23 mg/dL and 11.6 pg/mL respectively as compared to 0.63 mg/dL and 29 pg/mL for the entire afib group. Persistent afibbers had the highest CRP levels at 0.83 mg/dL followed by permanent afibbers at 0.60 and paroxysmal at 0.51 mg/dL; the CRP level among lone afibbers was 0.44 mg/dL. IL-6 levels were highest among permanent afibbers (37.3 pg/mL) followed by paroxysmal at 28.4 and persistent at 21.8 pg/mL. IL-6 level for lone afibbers was 26 pg/mL. The researchers conclude that inflammation may play a significant role in AF although its role in lone afib is still controversial.

Gedikli, O, et al. Inflammatory markers according to types of atrial fibrillation. ***International Journal of Cardiology****, 2007 [Epub ahead of print]*

High pulse pressure – A new risk factor for atrial fibrillation?

WALTHAM, MASSACHUSETTS. Atrial fibrillation (AF) is associated with advancing age, increased systolic (the high value) blood pressure, diabetes, hypertension, heart failure, valvular disease, heart attack, obesity, left atrial enlargement, ventricular hypertrophy, and impaired ejection fraction. Now researchers at Boston University School of Medicine report that increased pulse pressure (difference between systolic and diastolic pressure) is also a strong risk factor for the development of AF.

Their study involved 5331 participants in the Framingham Heart Study who were free of AF at time of enrolment. The median age of the participants was 57 years and 55% were women. They were followed for 16 years during which time 363 men and 335 women developed AF. Prior to developing afib 182 participants (54% of afibbers) had either experienced a heart attack or developed heart failure.

The researchers found a highly significant correlation between pulse pressure and the risk of developing AF. Thus, while participants with a pulse pressure of 40 mm Hg or less had a risk of 5.6%, those with a pressure above 61 mm Hg had a risk of 23.3%. After adjusting for mean arterial pressure and known clinical risk factors for AF, the researchers conclude that each 20 mm Hg increase in pulse pressure is associated with a 24% increase in the risk of developing afib. They speculate that increased arterial stiffness (hardening of the arteries) and abnormalities

in left ventricular function lies behind the increase in pulse pressure and the development of abnormal left atrial structure and function. They also point out that blockage of the renin-angiotensin system has been shown not only to reduce pulse pressure, but also to reduce the incidence of new and recurrent AF.

Mitchell, GF, et al. Pulse pressure and risk of new-onset atrial fibrillation. Journal of the American Medical Association, *Vol. 297, February 21, 2007, pp. 709-15*

Editor's comment: Blood pressure readings prior to ablation were available for 41 afibbers who participated in LAFS-8. All were lone afibbers (no heart disease) with no hypertension and no use of anti-hypertensive medications. The mean systolic blood pressure of the group was 116 mm Hg (median of 120 mm Hg, range of 90-150 mm Hg). The mean diastolic pressure was 74 mm Hg (median of 70 mm Hg, range of 60-90 mm Hg). Overall, 54% of the group had a pulse pressure of 40 mm Hg or less. This compares to only 25% of participants in the Framingham group having a pulse pressure of 40 mm Hg or less. Also, while 24% of the Framingham group had a pulse pressure higher than 61 mm Hg, no one in the LAFS-8 survey had a pulse pressure above 60 mm Hg. These differences may add another piece of evidence to the idea that lone afib really is different from the more common form of afib, which involves structural heart abnormalities (my speculation). There were no differences in pulse pressure between vagal, mixed, adrenergic, and permanent afibbers, nor was pulse pressure associated with age or age at diagnosis.

Alcohol consumption and atrial fibrillation

BOSTON, MASSACHUSETTS. There is evidence that binge drinking, particularly among younger people, can trigger atrial fibrillation. However, it is not clear if there is a relationship between moderate alcohol consumption and the risk of developing AF when it comes to older people. Researchers at the Beth Israel Deaconess Medical Center now provide answers to this question.

Their study included 5609 adults 65 years and older who reported their use of wine, beer, and spirits on an annual basis. The study participants were grouped according to their drinking habits – abstainers, less than 1 drink a week, 1-6 drinks a week, 7-13 drinks a week, and more than 14 drinks a week. During the 9-year follow-up, 1232 participants (22%) developed afib. Advanced age, male gender, hypertension, coronary heart disease, heart failure, large left atrial size, high total cholesterol level, and a high creatinine level were the main risk factors for AF. There was no indication that alcohol consumption over the range evaluated had any statistically significant effect on the risk of developing AF in this group of older afibbers. Nor was there any significant association between alcohol

consumption and mortality. However, the researchers did note that former drinkers had a higher mortality and risk of AF than did the remainder of the group. They speculate that this is because former drinkers may have given up drinking when they became aware of some serious deterioration in their health.

The researchers conclude that moderate alcohol consumption is not associated with an increased risk of developing AF, or with an increased mortality among patients with diagnosed AF.

Mukamal. KJ, et al. Alcohol consumption and risk and prognosis of atrial fibrillation among older adults: The Cardiovascular Health Study. **American Heart Journal,** *Vol. 153, February 2007, pp. 260-66*

Sleep apnea and obesity linked to AF

ROCHESTER, MINNESOTA. Both obesity and obstructive sleep apnea (OSA) have been linked to an increased risk of atrial fibrillation. It is not known, however, whether these two conditions act in concert or whether they are independent risk factors. Researchers at the Mayo Clinic recently released a study aimed at determining risk factors for AF with particular emphasis on obesity (BMI>30) and OSA. Their study included 3542 Olmsted County adults without past or current AF who were referred for polysomnography to determine the quality of sleep. The study participants were followed for an average of 4.7 years in order to determine the incident of new onset AF. During the follow-up period 133 participants experienced a first incidence of atrial fibrillation. The researchers observed the following risk factors for participants under the age of 65 years: age, male gender, hypertension, smoking, coronary artery disease, elevated BMI (body mass index) and a decrease in nocturnal oxygen saturation (a cardinal feature of OSA). In contrast, in men over the age of 65 years only heart failure predicted the development of AF. After adjusting for other risk factors the researchers concluded that among subjects under the age of 65 years the cumulative probability of developing afib was about twice as high in subjects with OSA as compared to those without OSA. Furthermore, the use of continuous positive airway pressure (CPAP) did not affect the incidence of a first afib episode. For participants over 65 years of age only heart failure predicted the development of AF. In this group participants with heart failure had an 8 times higher risk of developing AF than did those without heart failure. Obesity (BMI>30) was independently associated with the development of AF with about a 7% added risk for each BMI unit above 25.

Gami, AS, et al. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. **Journal of the American College of Cardiology**, *Vol. 49, February 6, 2007, pp. 565-71*

Pros and cons of vigorous exercise

DALLAS, TEXAS. The American Heart Association, in collaboration with the American College of Sports Medicine, has issued a consensus statement regarding the benefits and dangers of vigorous exercise. The groups agree that habitual exercise delays the development of atherosclerosis and reduces the incidence of coronary heart disease. On the other hand, vigorous physical activity can also transiently increase the risk of heart attack (acute myocardial infarction) and sudden cardiac death (SCD), particularly in individuals who are normally sedentary. Snow shoveling is highlighted as a particularly dangerous activity for normally sedentary individuals.

Highlights of the statement are:

- Among college athletes and other young people who die during exercise, the most common pathological findings are hereditary or congenital cardiovascular abnormalities such as Marfan syndrome, mitral valve prolapse, and arrhythmias.

- Among older people, the most common cause of exercise-related death is coronary artery disease with evidence of acute, coronary plaque disruption. Increased platelet activation has been reported in sedentary individuals who engage in unaccustomed high-intensity exercise but not in physically conditioned athletes.

- The incidence of exercise-related death is low among high school and college athletes with an estimated absolute risk of about 1 per 133,000 men and 1 per 769,000 women athletes. A recent Italian study found a sudden death rate of 1 per 33,000 young athletes a year.

- The incidence of exercise-related deaths in healthy older adults is also quite low with estimates ranging from 1 death per year for every 7,620 joggers to 1 death per 82,000 members of a fitness club. Nearly half of these deaths were among members who exercised infrequently or less than once a week. The estimated risk of an exercise-related heart attack ranges from 1 per 593 to 1 per 3,852 in apparently healthy, middle-aged men.

- The death rate related to exercise among patients with diagnosed heart disease is estimated at 1 per 116,402 exercise-hours. Although low, this number is 8 times higher than the corresponding number for healthy individuals.

- Vigorous exercise, while being beneficial in the long term for healthy adults, increases the risk of SCD by a factor of about 8 when compared to the SCD incidence during sedentary activities. The risk increase is particularly pronounced in normally sedentary individuals who engage in strenuous activity.

- Between 4 and 10% of heart attacks experienced by healthy individuals occurred within an hour of stopping vigorous exercise. For patients with coronary heart disease, the relative risk of cardiac arrest during vigorous exercise is estimated at 6 to 164 times greater than expected without exertion. The post-exercise risk of a heart attack is 50 times higher for sedentary individuals than for those who habitually exercise vigorously.

- Habitual vigorous exercise appears to reduce the overall risk of coronary artery disease in healthy adults; however, it may increase both exercise- and non-exercise-related sudden death in young people with cardiovascular disease.

- SCD and heart attacks occur more frequently in the morning than in the afternoon; however, there is no compelling evidence that this is related to time of exercise.

- Young athletes should be screened for cardiac abnormalities before participating in athletics. Doing so resulted in a decrease of 89% in SCD among young Italian athletes. Older adults at risk for coronary artery disease should also be screened prior to undertaking a vigorous training program. This is particularly important for diabetics.

- Patients with known heart disease should include at least 5 minutes each of warm-up and cool-down in their training session in order to avoid inducing cardiac ischemia.

The statement concludes that habitual physical exercise is substantially more likely to be beneficial than harmful in healthy individuals with no underlying heart disease. It is also likely that exercise is more beneficial than harmful for older adults with heart disease, but beginning an exercise program requires close supervision and prior screening. "*Consequently, physical activity should be encouraged for most individuals in accordance with the Centers for Disease Control and Prevention/ACSM recommendations for at least 30 minutes of moderate-intensity physical activity such as brisk walking on most, preferably all, days of the week.*"

Thompson, PD, et al. Exercise and acute cardiovascular events: Placing the risk into perspective. Circulation, *Vol. 115, May 1, 2007, pp. 2358-68*

Editor's comment: It is clear that moderate to vigorous daily exercise has long-term beneficial effects on cardiovascular and pulmonary health. The danger of death or heart attack during or after exercise is low in healthy adolescents and adults who regularly exercise. However, young athletes need to be screened for heart disease prior to engaging in strenuous athletics. Regular exercise is still recommended for adults with heart disease, but these individuals should be checked by their doctor before beginning a training program and should start out slowly, as should normally sedentary individuals who wish to become physically fit. Habitually exercising adults, particularly men, should also bear in mind that too prolonged and vigorous physical activity may increase the risk of developing atrial fibrillation by a factor of 5. For those individuals with atherosclerosis, it is of interest that fish oil has been found to improve plaque stability[1].

[1] Thies, F, et al. Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomized controlled trial. The Lancet, Vol. 361, February 8, 2003, pp. 477-85

AF-related stroke risk independent of age

JERUSALEM, ISRAEL. The above average stroke risk observed among AF patients is believed to be primarily due to blood clot formation in the left atrium and, more specifically, the left atrial appendage (LAA). Several studies have shown that clots (thrombi) in the LAA are common in patients with AF and underlying heart disease, but none have been observed in lone afibbers. There is also evidence that the risk of ischemic stroke increases with age, but it is not clear whether this increased risk is due to LAA thrombi. Nevertheless, current guidelines call for anticoagulation of all AF patients above the age of 75 years. This despite the fact that elderly patients face a high risk of internal bleeding and hemorrhagic stroke when treated with warfarin.

Israeli researchers now question the merits of blanket anticoagulation in afib patients above the age of 75 years. Their study included 381 AF patients between the ages of 30 and 98 years. The participants were divided into two groups – one (A) of patients less than 75 years old (257 aged 75 years or less with an average age of 63 years) and another (B) of patients 75 years or older (124 with an average age of 81 years). All participants underwent transesophageal echocardiography (TEE) to check for LAA thrombi. Thrombi were detected in 8.1% of group A and 7.2% of group B. No LAA thrombi were detected in lone AF patients irrespective of age and anticoagulation status. The prevalence of LAA thrombi in patients with underlying heart disease did not differ between those on

warfarin and those not on warfarin, and all thrombi were found in the LAA (none in the left atrium cavity as such).

The researchers conclude that age as such is not correlated with the prevalence of LAA thrombi, which would appear to be entirely related to underlying heart disease. They suggest that the use of anticoagulant therapy (warfarin) should perhaps be limited to those with heart disease or other risk factors for stroke.

Mazouz, B, et al. Age alone is not a risk factor for left atrial thrombus in atrial fibrillation. **Heart** *[published online June 25, 2007]*

Editor's comment: The above findings are good news indeed for lone afibbers, especially for those above the age of 75 years. There is no evidence of an increased prevalence of LAA thrombi in lone afibbers irrespective of age. Thus, the conventional recommendation of warfarin therapy after age 75 years would appear to have no basis in fact for lone afibbers.

Sleep apnea and cardiac arrhythmias

TOLEDO, SPAIN. Obstructive sleep apnea (intermittent loss of breathing during sleep) is a common disorder affecting about 4% of middle-aged American men and about 2% of middle-aged American women. It is strongly linked to increasing age and obesity. Obstructive sleep apnea (OSA) is characterized by a collapse of soft muscle tissue in the throat leading to blockage, restricted airflow and ultimately deoxygenation of red blood cells. OSA can be diagnosed during a sleep study (polysomnography) and its severity is described via the apnea-hypopnea index (AHI), which represents the number of obstructive respiratory events per hour of sleep. An AHI of less than 10 is considered normal, an AHI of 10-20 is mild, 20-30 is moderate, and more than 30 events per hour characterizes severe OSA. OSA can usually be successfully treated by the use of a continuous positive airway pressure (CPAP) machine which supplies a constant, uninterrupted flow of air pressurized just enough to keep the airway open.

OSA is an insidious disorder that, if left untreated, can cause a number of serious problems including increased heart rate, blunted heart rate variability, systemic inflammation, atherosclerosis, arterial hypertension, insulin resistance, type II diabetes, and increased risk of inappropriate blood coagulation.

Cardiac arrhythmias are common in patients with OSA. They occur mainly at night, in contrast with arrhythmias in patients with structural heart disease, which occur mainly during daytime. A nighttime AF episode in an OSA patient starts out with a bradycardia (abnormally low heart rate) due

to parasympathetic (vagal) hyperactivity followed by tachycardia (an abnormally high heart rate) as a consequence of awakening from sleep. Nighttime bradycardia and subsequent AF episodes in OSA patients can, in most cases, be avoided by the use of a CPAP machine. A recent study observed OSA in 49% of 151 patients with atrial fibrillation, so it clearly is not an uncommon cause of AF. It is also of interest to note that patients with OSA tend to have a greatly increased frequency of premature ventricular beats (PVCs) during sleep as compared to the frequency during wakefulness. They also, in general, tend to have more ventricular ectopy (non-sustained ventricular tachycardia and ventricular bigeminy, trigeminy, and quadrigeminy). Again, treatment with a CPAP machine has been found to reduce ventricular ectopy quite substantially.

Arias, MA and Sanchez, AM. Obstructive sleep apnea and its relationship to cardiac arrhythmias. **Journal of Cardiovascular Electrophysiology**, *Vol. 18, September 2007, pp. 1006-14*

Editor's comment: It is clear that OSA is a common condition that can lead to many serious disorders. A connection with afib is also clear and there is growing evidence that the use of a properly calibrated CPAP machine cannot only prevent OSA, but may prevent OSA-related afib as well. Thus afibbers who have interrupted sleep, daytime sleepiness, or a greater incidence of PVCs (measured on a Holter monitor) during the night might do well to consider a properly conducted sleep study and the use of a CPAP machine if indicated.

Cardioversion

Prediction of effectiveness of cardioversion

LUND, SWEDEN. Electrical cardioversion is generally not very effective in converting persistent afib (episodes lasting longer than 7 days and not converting on their own) to normal sinus rhythm (NSR). Although the immediate success rate may be 90% or better, as few as 25% of patients remain in NSR one year after the cardioversion. Even when using antiarrhythmic drugs only about 50% of cardioverted patients remain in NSR after a year. It is clearly of interest to be able to predict whether cardioversion is likely to be worthwhile in specific individuals.

Researchers at Lund University Hospital now report that a simple measurement of atrial fibrillatory rate (AFR) derived from a standard electrocardiogram (ECG) can predict the long-term success of cardioversion. AFR is essentially a measurement of atrial refractory period and can be determined by identification, templating and removal of the ventricular components of the ECG. The Swedish study involved 175 patients with persistent afib (37% had lone AF) who had an ECG prior to undergoing standard electrical cardioversion. The mean AFR of the entire group was 383 fpm (fibrillations per minute) and the average arrhythmia duration prior to cardioversion was 94 days.

The majority (71%) of the study participants were on a beta-blocker, while 29% were on digoxin (digitalis, Lanoxin). Congestive heart failure and a low left ventricular ejection fraction were both associated with a lower chance of remaining in NSR after cardioversion. After adjusting for possible confounding variables the researchers concluded that an AFR greater than 384 fpm was associated with a 3.2-fold increase in the risk of relapse, while being on digoxin was associated with a 2.3-fold increase. The researchers also observed that patients who had been in persistent afib for 30 days or less were more likely to be symptomatic when arriving at the hospital (97% vs. 62% for patients with longer-standing afib). The short duration (less than 30 days) afibbers were also significantly less likely to be on digoxin (7% vs. 33%) or beta-blockers (45% vs. 77%) and were also more likely to have lone AF. The difference in AFR between short duration afibbers who remained in NSR (348 fpm) and those who relapsed (424 fpm) was statistically highly significant ($p=0.003$). The difference in cardioversion outcome was also highly significant in the 16 patients who were on antiarrhythmic drugs (mainly sotalol) with those maintaining NSR having an AFR of 292 fpm vs. 382 fpm for the relapsers.

The Swedish researchers conclude that AFR prior to cardioversion is higher in patients relapsing into afib than in those remaining in NSR. They speculate that a higher AFR is associated with more extensive electrical remodeling.

Holmqvist, F, et al. Atrial fibrillatory rate and sinus rhythm maintenance in patients undergoing cardioversion of persistent atrial fibrillation. European Heart Journal, *Vol. 27, 2006, pp. 2201-07*

Editor's comment: This study, once again, demonstrates that digoxin (digitalis, Lanoxin) is a very bad drug for afibbers. Not only is it associated with a poorer cardioversion outcome, but it is also clear that there is a very strong (p=0.003) association between its use and the increased duration of persistent afib episodes. The same applies to beta-blockers where use is associated with a longer duration of episodes (p=0.001). The Swedish researchers point out that digitalis is known to increase intracellular calcium overload which, in turn, is believed to be the key process of atrial remodeling. The morale of this story is my oft-repeated assertion that digitalis has no place in the treatment of lone afib and that the use of beta-blockers on a continuous basis should be postponed as long as possible.

Cardioversion success and inflammation

OSLO, NORWAY. Electrical cardioversion is the standard treatment for persistent afib episodes that do not terminate on their own. Unfortunately, it is not very effective with more than half of patients having another afib episode within a few months of conversion. There is some evidence that treatment with angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs) help prevent episodes in atrial fibrillation patients with hypertension or left ventricular dysfunction.

Based on this observation Norwegian researchers decided to test whether pre- and post-cardioversion treatment with the ARB candesartan (Atacand) would increase the length of time spent in sinus rhythm after electrical cardioversion. The researchers speculated that inflammation might play a role in determining the efficacy of cardioversion and that candesartan therapy might therefore be beneficial since there is some indication that it may help to reduce inflammation in the cardiac wall.

The clinical trial involved 171 patients with persistent AF who were randomized to receive a placebo or candesartan (8 mg/day pre-procedure and 16 mg/day post-procedure) for 3-6 weeks prior to cardioversion and for 6 months following cardioversion. Serum levels of inflammatory markers – high-sensitivity C-reactive protein (hs-CRP), tumor-necrosis factor alpha, interleukin-6, P-selectin, E-selectin, CD-40 ligand, and

vascular cell adhesion molelcule-1 – were measured at baseline and end of study.

After 6 months 40 patients (26%) were still in sinus rhythm, while the remaining 74% had not been successfully cardioverted or had experienced one or more afib episodes since their initially successful conversion (usually within 2 weeks after cardioversion). The researchers observed that the patients still in sinus rhythm after 6 months had significantly lower levels of hs-CRP and E-selectin than did those who relapsed into AF. As a matter of fact, patients with an hs-CRP level above 5.22 mg/L (0.52 mg/dL) had a 60% increased risk of relapse compared to patients with lower levels. There was no indication that candesartan therapy had any effect on inflammation markers, effectiveness of cardioversion, or afib recurrence. It is also of interest that successful restoration of sinus rhythm did not change the level of inflammatory markers.

Tveit, A, et al. Effect of candesartan and various inflammatory markers on maintenance of sinus rhythm after electrical cardioversion for atrial fibrillation. American Journal of Cardiology, *Vol. 99, 2007, pp. 1544-48*

Watson, T, et al. Cardioversion for atrial fibrillation: Does inflammation matter? American Journal of Cardiology, *Vol. 99, June 1, 2007, pp. 11617-18*

Editor's comment: This study confirms that a moderate to high level of systemic inflammation (elevated hs-CRP level) is detrimental to the maintenance of sinus rhythm after an initially successful electrical cardioversion. Thus, it may be beneficial for persistent afibbers awaiting cardioversion to take steps to bring their hs-CRP level down during the obligatory wait time prior to cardioversion. Inflammation and hs-CRP levels can be safely and effectively reduced by supplementation with such natural anti-inflammatories as fish oils, beta-sitosterol, *Moducare*, curcumin, boswellia, or *Zyflamend*.

Natural Treatments

Diet and venous thromboembolism

MINNEAPOLIS, MINNESOTA. Venous thromboembolism (VTE) in which blood clots form in the veins of the lower part of the legs is becoming increasingly common among air travellers. VTE is also a common feature after certain surgical procedures and can progress to pulmonary embolism, which can be fatal. VTE is believed to involve an increase in blood coagulability, blood stasis (lack of circulation), and damage to the wall of the vein. This makes the condition somewhat similar to embolic stroke in afibbers resulting from blood stasis in the left atrial appendage. The main risk factors for VTE are high levels of homocysteine, factor VIII, and von Willebrand factor.

A team of American and Norwegian researchers now reports that a diet high in fruit and vegetables, and fish, and low in red meat is an excellent defense against VTE. Their study involved almost 15,000 middle-aged adults who participated in the Atherosclerosis Risk in Communities study. The participants (average age of 54 years, 68% overweight or obese) were followed-up for an average of 12 years during which 196 were diagnosed with VTE. The analyses of food frequency questionnaires completed at baseline and year six showed that even a moderate daily intake (more than 2.5 servings) of fruit and vegetables reduced the risk of VTE by 27% to 53% (compared to less than 2.5 servings a day). One or more weekly servings of fish were associated with a 30% to 45% lower risk as compared to consuming fish rarely.

Individuals eating red or processed meat more than 1.5 times a day had a 2 times higher risk of developing VTE than did those consuming less than ½ serving a day. The researchers also observed that participants with a moderate folate intake (more than 160 micrograms a day) had a 34% to 51% lower risk of VTE than did those with intakes below 160 micrograms a day. Those with the highest intake (> 2.26 mg/day) of vitamin B6 had a 63% lower risk of VTE as compared to those with an intake below 1.25 mg a day. Finally, those with an omega-3 fatty acid intake (mainly from fish) above 390 mg a day had a 30% to 46% reduced risk when compared to participants whose intake was less than 100 mg a day.

The researchers conclude that a diet including more plant food and fish, and less red and processed meat is associated with a lower incidence of VTE.

Steffen, LM, et al. Greater fish, fruit and vegetable intakes are related to lower incidence of venous thromboembolism. Circulation, *Vol. 115, January 16, 2007, pp. 188-95*

Editor's comment: Folic acid, vitamin B12, and vitamin B6 are all essential for maintaining low homocysteine levels. Vitamins C and E are highly effective in lowering the level of von Willebrand factor – a key factor in the coagulation sequence leading to VTE. There is also growing evidence that vitamin B6 is highly effective in preventing ischemic stroke. Researchers at Harvard Medical School and Massachusetts General Hospital have discovered a strong association between stroke risk and low blood levels of pyridoxal-5'-phosphate (PLP), the main metabolite of vitamin B6. This increased risk of stroke with low PLP levels was entirely independent of homocysteine levels confirming that vitamin B6, on its own, has significant stroke prevention properties. The researchers found that study participants with a plasma level of PLP of more than 80 nanomol/L had a 90% lower risk of stroke and transient ischemic attacks (TIAs) than did participants with a level below 20 nanomol/L. The risk decrease was independent of the presence of other risk factors such as hypertension, diabetes, and atrial fibrillation[1]. The researchers also noted a strong inverse correlation between C-reactive protein level and PLP level indicating that vitamin B6 may also have strong anti-inflammatory properties – an added plus for afibbers.

The 90% relative reduction in stroke risk among people with high PLP levels is very significant and compares extremely favourably with the oft-quoted relative risk reduction afforded by warfarin (64%) and aspirin (25%). Clearly, ensuring adequate blood levels of PLP is a must for all afibbers. Vitamin B6 is converted to its active metabolite PLP in the liver and there is some evidence that the liver can only handle about 50 mg of vitamin B6 at a time. Experiments have shown that the plasma concentration of PLP does not increase further if 100 mg rather than 50 mg of pyridoxine (vitamin B6) is ingested at any one time. So it is assumed that the conversion to PLP is limited by the liver's conversion capacity[2]. Other experiments have shown that supplementing (orally) with 40 mg of vitamin B6 will increase average plasma concentration from about 23 nmol/L (range: 18-37 nmol/L) to about 230 nmol/L within 3 days of beginning supplementation. No further increases were observed with 40 mg/day supplementation for a 12-week period[3].

The 230 nmol/L concentration achieved is well above the 80 nmol/L concentration associated with the 90% reduction in stroke risk observed by the Harvard researchers[1]. So 40-50 mg/day would seem to be sufficient for stroke protection and is considered entirely safe[3]. Vitamin B6 itself is, however, water-soluble and any excess is totally eliminated in the urine within about 9 hours. To keep the vitamin B concentration up, it

would be necessary to take two or three 50 mg doses per day. However, in the case of stroke protection, one 50 mg dose per day is likely to be quite adequate, as PLP concentration does not vary much during the day once steady state conditions are achieved. Adequate amounts of vitamin B2 and magnesium are required in order to convert vitamin B6 to PLP.

[1] Kelly, PJ, et al. Low vitamin B6 but not homocysteine is associated with increased risk of stroke and transient ischemic attack in the era of folic acid grain fortification. Stroke, Vol. 34, June 2003, pp. e51-e54

[2] Khaw, KT and Woodhouse, P. Interrelation of vitamin C, infection, haemostatic factors, and cardiovascular disease. British Medical Journal, Vol. 310, June 17, 1995, pp. 1559-63

[3] Zempleni, J. Pharmacokinetics of vitamin B6 supplements in humans. Journal of the American College of Nutrition, Vol. 14, 1995, pp. 579-86

All fish are not equally healthy

MONTREAL, CANADA. The American Heart Association and similar organizations have long extolled the virtue of consuming fish once or preferably twice a week as a powerful preventive measure against cardiovascular disease. Although there is increasing evidence that most fish now contain mercury (especially methylmercury), it is still felt that regular fish consumption is beneficial overall.

University of Quebec researchers now question the assumption that fish consumption is universally beneficial. They do not question whether an increased intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is beneficial – this has pretty well been proven beyond a doubt. However, they do question whether all fish actually ends up contributing to the body's stores of EPA and DHA when consumed.

Their study involved 243 moderate consumers of fish living in the areas surrounding four lakes in the province of Quebec. The participants were interviewed to determine their consumption of 12 freshwater and 30 marine (saltwater) fish over the preceding three months and then had blood samples drawn for the determination of fatty acid (especially EPA and DHA), mercury, and selenium content. The age of the participants ranged between 18 and 74 years, 53% were men and 26% were considered obese (BMI >30). No relation was observed between fish intake and BMI, or between fish intake and alcohol intake. The 243 participants were divided into 4 groups according to daily consumption (occasional – < 24 grams/day, low – 24-41 grams/day, moderate – 41-66 grams/day, and high – > 66 grams/day). The average (mean) estimated intake of DHA + EPA from fish was 223 mg/day and that of omega-6 fatty acid (from fish) was 95 mg/day giving a very healthy ratio of omega-6 to omega-3 of 0.32. Much to their surprise, the researchers found no correlation between the total intake of fish or the intake of locally caught fish and serum levels of EPA and DHA. They did, however,

find a strong correlation between the intake of salmon and trout and serum levels of EPA and DHA.

They conclude that, even though food tables may show that some lean fish do contain EPA and DHA, for some reason consuming these fish does not increase serum levels of EPA and DHA. Thus, the advice to eat fish on a regular basis needs to be revised to apply to only saltwater fish (especially salmon, mackerel, trout, sardines, and herring). The researchers also noted an increased blood methylmercury concentration in frequent fish eaters. They conclude that no matter how many locally caught freshwater fish are eaten, serum EPA + DHA levels are not affected.

Philibert, A, et al. Fish intake and serum fatty acid profiles from freshwater fish. American Journal of Clinical Nutrition, *Vol. 84, December 2006, pp. 1299-1307*

Editor's comment: This study clearly shows that one needs to be very selective in what kind of fish or shellfish one eats in an attempt to obtain the benefits of the fish oils EPA and DHA. For example, lobster, flounder, sole, plaice, haddock, scallops, cod, halibut, and oysters are unlikely to supply any meaningful amounts of EPA and DHA. Thus, while fish consumption should probably still be encouraged, although mercury contamination is an ever-growing concern, it would seem prudent to ensure an adequate daily intake of EPA + DHA by supplementing with a high quality (molecular distilled) fish oil.

Fish oils are safe!

LOUISVILLE, KENTUCKY. Harold Bays, MD at the Louisville Metabolic and Atherosclerosis Research Center has addressed the question, "Does therapy with fish oils rich in omega-3 fatty acids increase the risk of bleeding, and are they contraindicated in patients treated with antiplatelet and anticoagulant therapies?" Dr. Bays concludes that clinical trial evidence does not support the idea that fish oils (EPA [eicosapentaenoic acid] and DHA [docosahexaenoic acid]) increase bleeding, even when given in combination with aspirin or warfarin. He also makes two other interesting observations:

- Fish oils inhibit thrombosis and may thus decrease the risk of ischemic stroke. However, one needs to take at least 1000 mg of EPA + DHA (not just 1000 mg of fish oil) a day to achieve significant cardiovascular benefits.

- It may be wise to stop fish oil supplementation 4-7 days prior to major surgery, except in the case of coronary artery bypass surgery where continued supplementation may help prevent post-procedure atrial fibrillation.

Dr. Bays also addressed the question, "Do prescription and/or supplement omega-3 fatty acid products contain excessive vitamin or toxins, such as mercury, polychlorinated biphenyls, dioxin, or other contaminants, in sufficient concentrations to pose a potential health risk?" Again, his answer is negative. This conclusion is largely based on a 2006 ConsumerLab evaluation of 42 commercially available fish oil supplements. All but two were found to contain the amount of EPA and DHA stated on the label, were free of mercury, PCBs and dioxins, and were not oxidized (rancid). Among the brands that passed the ConsumerLab evaluation were Carlson, Coromega, Metagenics, Nordic Naturals, Kirkland and Puritan Pride.

Dr. Bays cautions that a high fish oil intake through the consumption of large amounts of fish may present a risk for environmental toxin exposure, especially methylmercury, PCBs, organochlorine pesticides and dioxins. He points out that oxidized mercury is insoluble in oil, so would not be expected to represent a significant toxicity risk in fish oil supplements.

In an accompanying editorial Dr. William Harris of the University of South Dakota emphatically endorses Dr. Bays' conclusion that fish oils do not increase bleeding risk even if taken in combination with aspirin or warfarin.

Bays, HE. Safety considerations with omega-3 fatty acid therapy. American Journal of Cardiology, *Vol. 99, No. 6A, March 19, 2007, pp. 35C-43C*
Harris, WS. Omega-3 fatty acids and bleeding – Cause for concern? American Journal of Cardiology, *Vol. 99, No. 6A, March 19, 2007, pp. 44C-46C*

Editor's comment: The finding that fish oils do not increase bleeding and can safely be taken in combination with aspirin and warfarin is very reassuring as is the conclusion that 95% of fish oils supplements sold in health food stores are pure and safe.

Fish oil incorporation in myocardial tissue

ADELAIDE, AUSTRALIA. There is ample evidence that increased fish or fish oil consumption is associated with a reduced risk of cardiac mortality, especially sudden death. It is believed that this benefit arises from the incorporation of the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) into the phospholipid membrane of cardiomyocytes (heart cells).

Australian researchers recently reported some very exciting findings regarding the actual mechanism and effectiveness of increasing the EPA + DHA content of myocytes and erythrocytes (red blood cells) by daily supplementation with fish oil. Their study involved 60 patients scheduled

for on-pump bypass surgery and/or valve repair. The patients were divided into six groups of 10 patients and received supplements as follows:

Group 1	6 grams/day EPA + DHA (50:50) for 7 days prior to surgery
Group 2	6 grams/day EPA + DHA (50:50) for 14 days prior to surgery
Group 3	6 grams/day EPA + DHA (50:50) for 21 days prior to surgery
Group 4	6 grams/day of alpha-linolenic acid (ALA) in the form of flax oil for 21 days prior to surgery
Group 5	6 grams/day of olive oil for 21 days prior to surgery
Group 6	no supplements

Blood samples and biopsy specimens from the right atrium were taken during surgery. The samples were analyzed for fatty acid content and the following results obtained:

	Baseline Control Group	Fish oil 21 days	Flax oil 21 days	Olive oil 21 days
Myocytes				
Fatty acid content				
% of total fatty acids				
EPA	0.49	2.97	0.75	0.55
DHA	4.83	8.52	5.18	5.39
EPA + DHA	5.31	11.50	5.93	5.94
ALA	0.13	0.15	0.34	0.13
Arachidonic acid	20.84	15.99	20.01	20.02
Erythrocytes				
EPA	0.71	3.14	1.20	0.84
DHA	4.44	7.56	4.53	5.25
EPA + DHA	5.15	10.70	5.73	6.09
ALA	0.11	0.09	0.30	0.11
Arachidonic acid	14.21	11.67	14.36	14.51

The above results lead to the following observations:

- Fish oil supplementation for 21 days resulted in a substantial increase in both EPA (500%) and DHA concentration (76%) in cardiomyocytes. This was mirrored by a proportional increase in red blood cells (340% for EPA and 70% for DHA).

- The increase in EPA + DHA was at the expense of a decrease in pro-inflammatory omega-6 arachidonic acid of 23% in the fish oil group (21 days). Supplementation with flax or olive oil had no effect on arachidonic acid levels.

- Supplementation (for 21 days) with flax oil (alpha linolenic acid) increased myocyte EPA concentration by a statistically insignificant 53% and DHA concentration by only 7%

indicating that the efficiency of ALA conversion to EPA, and especially DHA, is low.

- No significant differences were found between the olive oil group and the control group.

- Analysis of data obtained after an average 10 days of fish oil supplementation showed that DHA is initially incorporated into heart cells at a rate twice that of EPA.

No excessive bleeding during surgery was observed for any of the groups involved in the study.

The researchers conclude that daily supplementation with 6 grams of EPA + DHA rapidly increases the EPA + DHA content of cardiomyocyte phospholipid membranes at the expense of a decrease in arachidonic acid level. They point out that these optimal rates of EPA + DHA incorporation are not likely to be matched at lower doses of fish oil. They also make the interesting suggestion that high-dose fish oil supplementation could be beneficial for patients recovering from a heart attack.

Metcalf, RG, et al. Effects of fish-oil supplementation on myocardial fatty acids in humans. American Journal of Clinical Nutrition, *Vol. 85, 2007, pp. 1222-28*

Editor's comment: The finding that high-dose fish oil supplementation rapidly increases myocyte membrane concentrations of EPA and DHA is indeed fascinating and could be of extreme interest to afibbers. Long-chain omega-3 fatty acids like EPA and DHA are known to increase membrane fluidity which may, in turn, be beneficial for afibbers. The relationship between omega-3 and omega-6 fatty acids and AF was first discussed in 2002 in an essay by Erling Waller about the path he took in order to vanquish his afib which had plagued him for 10 years. I would like to share Erling's thoughts with you.

"After much study about cardiac cells, and the significance of cell membrane integrity and cellular energy in maintaining NSR, I finally focused in on the nutritional requirements of cells and the all important issues of omega-6 to omega-3 ratio, EPA and DHA fish oils, coenzyme Q10, l-carnitine, and magnesium.

Omega-3 (w3) and omega-6 (w6) are families of the essential polyunsaturated fats. They are essential in the diet because they are required and the body can't produce them. Probably everyone consumes too much w6 fats relative to the w3s since they are abundant in our food supply. The task for me was to know the sources and reduce their intake. The principal sources of w6s and w3s in our foods are the vegetable oils

such as soybean, safflower, sunflower, canola, etc. If the food label lists polyunsaturated fats it's w6 and w3. The ratio of w6 to w3 in these food oils is too high to be conducive to health, and the methods used in extracting the oils make them unsuitable for consumption. "Virgin" applied to olive oil implies that gentle, low heat, non-destructive methods were used in extracting the oil, I've never seen that word used for other oils in our food. By reducing food oils and other common sources of polyunsaturates, and by adding supplemental w3s in the form of EPA/DHA fish oils I was able to improve my ratio. I have never aimed for a certain daily amount of w6, and would have a hard time doing so – I just watch my step. I figure that if I just stay low on most foods with oils I will still be getting plenty of w6, a required nutrient. But by doing so my intake of w3 is reduced. The most important w3s, EPA/DHA, are not in these oils anyway. They are either made in the body from other w3s in food (which for many is problematic), or they need to be supplemented. I usually take daily 4 capsules of fish oil providing 720 mg EPA and 500 mg DHA, but some days only 2 or 3 capsules. For a long time I was taking more than I am now. I absolutely stay away from hydrogenated oils which seem to be everywhere in processed foods. Hydrogenation produces "trans" fats with a molecular shape that screws up cell membranes. The book "Fats that Heal, Fats that Kill" by Udo Erasmus is powerful knowledge. Some days I only take 2 capsules, some days none, but I'm out of the woods now (in a maintenance mode) and am enjoying being less fussy about these things."

Fish oils and arrhythmias

PITTSBURGH, PENNSYLVANIA. Researchers at the National Institutes of Health and 10 major US hospitals and universities provide an excellent summary of the current knowledge regarding the benefits of omega-3 fatty acids in the prevention of cardiac arrhythmias. There is overwhelming evidence that an adequate intake of the long-chain omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) is highly protective against sudden cardiac death (SCD), which is caused by ventricular arrhythmias in 80-90% of cases. A high blood level of EPA and DHA was associated with an 81-90% reduction in SCD in a group of healthy people without known coronary heart disease. As little as 1 gram a day of EPA and DHA (found in oily fish and fish oils) has also been found to be highly protective against SCD in patients having suffered a pervious heart attack. The American Heart Association now recommends that all adults consume fish, preferably fatty, at least twice a week, and that patients with coronary heart disease consume 1 gram a day of EPA and DHA combined.

The effect of oily fish consumption or fish oil supplementation on atrial fibrillation is less clear. One study involving 4815 men and women 65

years or older (mean age of 73 years) found that consumption of baked or broiled fish was associated with a significantly reduced risk (31%) of developing AF over a 12-year follow-up period. In contrast, a study involving 48,000 much younger people (mean age of 56 years) found an increased risk (34%) of AF with increased fish consumption over a 5.7-year follow-up period. A randomized trial of fish oil supplementation (850 mg EPA+DHA) prior to bypass surgery found that 15% of patients randomized to fish oil developed post-procedure AF as compared to 33.3% in the control group.

The researchers suggest that the reason for the discrepancy between the results of the trial involving older people and the one involving younger people could well be that fish oils tend to increase parasympathetic (vagal) tone and this could be detrimental in younger people, while it may be beneficial in older people where sympathetic (adrenergic) tone tends to dominate. Older people would also be more likely to have systemic inflammation and atrial fibrosis which may be reduced by a high intake of long-chain omega-3 fatty acids.

Dietary supplementation with long-chain omega-3 fatty acids (fish oils) is known to change the composition of lipid membranes toward greater fluidity. There is also evidence that fish oil supplementation inhibits a number of sodium, potassium and calcium channels in a beneficial way and reduces the production of pro-inflammatory thromboxanes – all actions that could reduce the incidence of cardiac arrhythmias.
London, B, et al. Omega-3 fatty acids and cardiac arrhythmias: Prior studies and recommendations for future research. Circulation, *Vol. 116, September 2, 2007, pp. 320-35*

Editor's comment: The authors of this very detailed and highly technical report are clearly convinced that long-chain omega-3 fatty acids (EPA and DHA) play a crucial role in reducing the risk of sudden cardiac death and possibly atrial fibrillation. They propose several research projects to investigate this further – hopefully the harbinger of a trend to consider diet and dietary components as important factors in the development and maintenance of AF.

Prevention & Treatment with Antiarrhythmics

New antiarrhythmic drugs for AF

INDIANAPOLIS, INDIANA. It is becoming increasingly clear that atrial fibrillation is now epidemic and that there simply are not enough skilled EPs/cardiac surgeons available to cure a significant number of patients with an ablation or maze procedure. Thus, the search for new, effective antiarrhythmics is gaining renewed impetus. Currently available antiarrhythmics are, with the possible exception of amiodarone, frequently ineffective and all can result in serious adverse effects.

The use of class I antiarrhythmics, especially if underlying heart disease is present, is highly problematical and little, if any, research is being done to develop new versions of these drugs (disopyramide, flecainide, propafenone) which work by blocking sodium channels. Instead attention is being focused on developing new class III antiarrhythmics that block potassium channels.

Dronedarone has a molecular structure very similar to that of amiodarone, but lacks the iodine component which is believed to be responsible for amiodarone's adverse effects on the liver, lungs, and thyroid gland. Preliminary clinical trials have shown that dronedarone may reduce the risk of afib recurrence by about 25% and does not exhibit liver/lung/thyroid toxicity.

The problem with most antiarrhythmics is that they not only affect the myocytes (heart cells) in the atria, but also those in the ventricles. Unfortunately, what is good for the atria may not be good for the ventricles. Some very recent research has shown that the ultra-rapid delayed outward potassium current I_{kur} plays a much more prominent role in regulating the myocyte potential in the atria than in the ventricles. Thus, research to specifically block I_{kur} looks promising with such experimental drugs as RSD-1235, AVE-0118 and AZD7009 undergoing preliminary trials.

Agents that affect the fluidity of cell membranes are also being scrutinized with the most promising candidate so far being fish oil. A recent study involving patients undergoing coronary artery bypass surgery found that

patients who took 2 grams/day of EPA + DHA (the main components of fish oil) reduced their risk of post-operative afib by 50%.

There is now also increasing evidence that the renin-angiotensin aldosterone system (RAS) is important in the initiation and possibly maintenance of afib. For example, it now appears that atrial stretch upregulates angiotensin II. Thus, several existing angiotensin-converting enzyme (ACE) inhibitors (enalapril), angiotensin receptor blockers (valsartan), and aldosterone receptor blockers (eplerenone) have all shown some promise in preventing afib.

Finally, statin drugs (atorvastatin) have also been found useful in preventing post-operative AF. The authors of the report conclude that new antiarrhythmic agents hold great promise, but further studies are needed to define their role in the treatment of patients with AF.
Padanilam, BJ and Prystowsky, EN. New antiarrhythmic agents for the prevention and treatment of atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 17, Suppl. December 2006, pp. S62-S66*

Editor's comment: It is interesting that the idea of cell membrane integrity (fluidity) being a crucial factor in afib was first advanced by Erling Waller (the inventor of Waller Water), an early contributor to *The AFIB Report* and bulletin board. Erling has described how he permanently cured his afib through diet changes and supplementation with fish oil and other natural supplements in the November 2002 issue. His story can also be found on pages 177-180 of *Lone Atrial Fibrillation: Towards A Cure* (volume I). Of equal interest is the fact that the role of the RAS in AF was first discussed in the conference room (session 2) in January 2003 and has subsequently been the topic of several follow-up sessions.

Pill-in-the-pocket approach endorsed in the UK

LONDON, UNITED KINGDOM. It is estimated that 1.5% of the population of the UK now suffer from atrial fibrillation. About 200,000 of these patients have recurrent episodes and frequently visit emergency departments in order to have their episodes terminated by chemical or electrical cardioversion. Cardiologists at the University of London now suggest that many patients with paroxysmal afib can safely cardiovert themselves by taking a 300-mg dose of flecainide or a 600-mg dose of propafenone preferably within 5 minutes of experiencing the first signs of an afib episode. They base their recommendation on a study involving 210 patients with paroxysmal atrial fibrillation, less than 12 episodes a year, and no serious underlying heart disease. The researchers noticed a very significant drop in emergency department visits by the 210 patients once they began using the pill-in-the-pocket approach (form an average of 45 visits a month for all 210 patients to 5 visits a month). They point out

that the on-demand approach should also be applicable to patients with mild hypertension or well controlled ischemic heart disease.

However, it is important that the first dose of the antiarrhythmic (propafenone or flecainide) be administered in a hospital setting. After taking the pill, the patient should rest seated or supine until the palpitations cease or for up to 4 hours. If the heart rate noticeably quickens or if dizziness or blackouts occur, the patient should be hospitalized immediately.

Camm, AJ and Savelieva, I. Some patients with paroxysmal atrial fibrillation should carry flecainide or propafenone to self treat. **British Medical Journal**, *Vol. 334, March 24, 2007, p. 637*

Editor's comment: Many afibbers have been using the pill-in-the-pocket (on demand) approach to good effect ever since our first two courageous experimenters (Patrick Chambers and Gert Mueller) tried it for the first time 5 years ago.

Efficacy and safety of amiodarone questioned

PITTSBURGH, PENNSYLVANIA. Amiodarone (Cordarone, Pacerone) is usually considered the most effective drug for the suppression of atrial fibrillation and maintenance of sinus rhythm. On the other hand, its serious adverse effects make its long-term use problematical. Researchers at the University of Pittsburgh have just released the results of a study aimed at determining the sustainability and safety of long-term amiodarone therapy.

The study involved 168 afib patients who were treated with amiodarone and followed for 3 years. Seventy-seven percent of the group had paroxysmal AF, while the remaining 23% had the persistent variety. Most of the participants had hypertension (53%), coronary artery disease (27%) or congestive heart failure (19%), and 47% had a pacemaker or ICD (implanted cardioverter-defibrillator) – in other words, a fairly sick group and not necessarily representative, in their response to amiodarone, of a group of lone afibbers. The follow-up included routine visits to the clinic every 6 months during which the patients' symptoms and satisfaction with the therapy were discussed and extensive testing carried out including physical examination, ECG, liver and thyroid function tests, and a chest x-ray. Eye examinations were performed at a maximum interval of 12 months. The starting dose of amiodarone was 400 – 1200 mg/day tapering to 50 – 350 mg/day for long-term therapy with the median dose being 200 mg/day.

The efficacy of the amiodarone treatment was not impressive with 51% of the group reporting one or more AF episodes following the first 3 months

of therapy. Patient satisfaction with the treatment was also less than sterling with 55% discontinuing it because of ineffectiveness (25%), intolerance (12%), or toxicity (18%). Intolerance to the drug showed up as fatigue, insomnia, nausea, vomiting, constipation, tremor, weakness, blurred vision, nocturnal halo vision, and photosensitivity. The most serious adverse effect was pneumonitis (inflammation of the lungs), which occurred in at least 7% of the patients and most often signaled its presence with the development of an unexplained cough. Four percent of study participants developed hyper- or hypothyroidism, 3% developed liver toxicity (ALT and/or AST more than 3 times upper limit of normal), 2% developed vision problems, and 1% developed cardiac problems (bradycardia or ventricular tachycardia). The researchers conclude that for most patients a less than 50% chance for short-term success of an elective, potentially toxic therapy is not acceptable.

In an accompanying editorial, Dr. John Hill of the Princess Alexandra Hospital in Brisbane, Australia points out that amiodarone also increases the bleeding risk associated with warfarin therapy and that afibbers with a low body mass index (BMI) are more likely to develop pulmonary fibrosis from amiodarone therapy than are their more corpulent confreres.

Chandhok, S and Schwartzman, D. Amiodarone therapy for atrial rhythm control. Journal of Cardiovascular Electrophysiology, *Vol. 18, July 2007, pp. 714-18*
Hill, JN. Amiodarone for atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 18, July 2007, pp. 719-21*

Editor's comment: This study confirms the result of the survey reported in my first book *Lone Atrial Fibrillation: Towards A Cure.* Here 41% had found amiodarone therapy beneficial, while 59% reported serious side effects with the most common being thyrotoxicosis. Amiodarone is truly a drug of last resort for lone afibbers and is doubly dangerous without adequate and frequent follow-up examinations and tests.

Gender differences in AF treatment

GRONINGEN, THE NETHERLANDS. Neither the Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) trial nor the Rate Control Versus Electrical Cardioversion (RACE) study found any significant difference in mortality relating to the treatment of persistent afibbers with rate control versus rhythm control + cardioversions. Now Dutch researchers have taken a closer look at the RACE study results to see if the above finding applies to both men and women.

The RACE study involved 192 female patients and 330 males with persistent AF, ie. episodes that could only be terminated with cardioversion. The average age of the males was 67 years versus 71 years for females. Female patients were more likely to experience palpitation (33% vs 24%) and fatigue (47% vs 35%) during an episode

than were men. Females in the study were also more likely to have hypertension (63% vs 41%) and diabetes (17% vs 6%) than were male participants. Men, however, had a higher incidence of coronary artery disease (31% vs 21%) and were more likely to have experienced a heart attack (19% vs 8%).

Lone afibbers accounted for 26% of male participants and 12% of female. Most participants (73%) were on anticoagulation medications. They were followed for an average of 2.3 years during which 21% of female patients and 19% of males reached the primary endpoint of death from cardiovascular causes (7%), heart failure, stroke (6.7%), bleeding, severe adverse effects from antiarrhythmic drugs, or pacemaker implantation.

Detailed analysis of the data, however, clearly showed that women randomized to rhythm control + cardioversion fared significantly worse than women assigned to rate control. The primary endpoint occurred in 33% of women treated with rhythm control versus 11% among those treated with rate control. Women on rhythm control were 3 times more likely to die from cardiovascular causes, 6 times more likely to develop heart failure, and 5 times more likely to experience thromboembolic complications (stroke) than were women assigned to rate control with beta-blockers, calcium channel blockers, or digoxin. Women generally scored lower than men on Quality of Life evaluations, but there were no differences in QoL scores between women on rate control and those on rhythm control.

The researchers conclude that rate control may be the preferable approach to women with persistent AF since it clearly has far fewer adverse effects and does not result in a poorer quality of life than does rhythm control plus cardioversion.

Rienstra, M, et al. Gender-related differences in rhythm control treatment in persistent atrial fibrillation. Journal of the American College of Cardiology, *Vol. 46, No. 7, October 4, 2005, pp. 1298-306*

Kerr, CR and Humphries, K. Gender-related differences in atrial fibrillation. Journal of the American College of Cardiology, *Vol. 46, No. 7, October 4, 2005, pp. 1307-08*

Editor's comment: Although these findings are unlikely to be directly applicable to women with persistent lone AF, they do suggest the possibility that optimum treatment may be different for male and female afibbers.

Results of dronedarone trial

LOS ANGELES, CALIFORNIA. Although amiodarone (Cordarone, Pacerone) is not approved by the FDA for the treatment of atrial fibrillation, it is nevertheless widely prescribed for this condition. It can be very effective in preventing paroxysmal AF, but has the disadvantage of potential

serious adverse effects involving the lungs, kidneys, liver, thyroid, nervous system, and skin. Another disadvantage of amiodarone is its long elimination half-life of 30-55 days. Most of the problems associated with amiodarone are believed to be due to the presence of iodine in the drug. Not surprisingly, this has led to the development of dronedarone, an amiodarone analogue without the iodine component.

Two large clinical trials aimed at evaluating the safety and efficacy of dronedarone have just been completed. One, the EURIDIS trial, involved 612 patients with paroxysmal or persistent AF recruited from 12 European countries. The other, the ADONIS trial, involved 625 afibbers (none with permanent AF) recruited in the USA, Canada, Australia, Argentina, and South Africa. In the combined trials 828 patients were randomized to receive 400 mg twice a day of dronedarone, while the remaining 409 patients received a placebo. All patients were in sinus rhythm at the start of the trial. Patients with congestive heart failure and ventricular dysfunction were excluded from the trial as were those with a resting heart rate below 50 bpm. Trial participants were closely monitored through regular follow-up visits and all were given transtelephonic electrocardiographic monitors for use at regular intervals and when they experienced an afib episode. The main results of the trials were (results combined for the two trials):

- The median time to the first documented recurrence of AF was 116 days in the dronedarone group and 53 days in the placebo group.

- At the end of the trial (12 months from the start) 24.8% of the placebo group were still in normal sinus rhythm as compared to 35.9% in the dronedarone group.

- The majority of documented first recurrences were symptomatic (palpitations, chest pain, dizziness, breathing difficulties, and fatigue), but overall most recorded episodes were asymptomatic (62.3% in the dronedarone group and 54% in the placebo group).

- Patients in the dronedarone group had a slightly lower heart rate (average 103 bpm) during their first recurrence than did those in the placebo group (average 117 bpm).

- Rates of thyroid, liver and lung dysfunction observed over the 12-month trial period were not significantly increased in the dronedarone group. However, there was a substantially higher incidence of elevated serum creatinine levels in the

dronedarone group (2.4% vs. 0.2%), perhaps indicating potential problems with kidney function.

- At the end of the trial 22.8% in the dronedarone and 30.9% in the placebo group had been hospitalized or had died (death accounted for 1% in the dronedarone group and 0.7% in the placebo group).

The researchers conclude that dronedarone is significantly more effective than placebo in maintaining sinus rhythm and in reducing ventricular rate during an afib episode.

Singh, BN, et al. Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. New England Journal of Medicine, *Vol. 357, September 6, 2007, pp. 987-99*
Ezekowitz, MD. Maintaining sinus rhythm – Making treatment better than the disease. New England Journal of Medicine, *Vol. 357, September 6, 2007, pp. 1039-41*

Editor's comment: An effective, safe replacement for amiodarone would certainly be welcome, but short of comparing the two drugs directly, it is difficult to say whether dronedarone can fill this role. Thus, recruitment for a trial to compare dronedarone and amiodarone is currently underway.

Prevention & Treatment with Other Drugs

Magnesium infusions in AF control

TORONTO, CANADA. Magnesium is effective in prolonging the atrial and atrioventricular nodal refractory periods. As afib cannot be initiated during refractory periods, this is clearly a good thing and may explain why many afibbers have experienced substantial benefit from magnesium supplementation. Unfortunately, several studies have shown that 50% or more of patients with atrial fibrillation suffer from hypomagnesemia – that is, a lower than normal blood serum magnesium concentration (less than about 0.8 mmol/L). Serum magnesium concentration is a fairly poor indicator of magnesium status since only about 2% of the body's total magnesium stores are found in the blood. It is thus likely that substantially more than 50% of afibbers are magnesium deficient if intracellular levels are measured.

Researchers at the University of Toronto have just released the results of a meta-analysis of 8 clinical trials involving patients presenting with rapid atrial fibrillation. The trials compared the effect of magnesium infusions with placebo controls and patients given intravenous diltiazem or amiodarone. In the trials 1,200 to 10,000 mg of magnesium (as magnesium sulfate) was infused over a period of 1 to 30 minutes. In four of the studies magnesium infusion was continued for an additional 2 to 6 hours. Adequate rate control (ventricular rate below 100 bpm) was achieved in 61% of patients with magnesium as compared to 35% among controls. Magnesium was found to be as effective as diltiazem and amiodarone in achieving adequate rate control during the first hour. Magnesium was also found to be twice as effective as diltiazem or placebo in restoring sinus rhythm. Overall, the average time to conversion to sinus rhythm was 4 hours for magnesium as compared to 15 hours for placebo. The researchers conclude that magnesium infusions are safe and effective in achieving both rate and rhythm control in patients presenting with rapid atrial fibrillation.

Onalan, O, et al. Meta-analysis of magnesium therapy for the acute management of rapid atrial fibrillation. American Journal of Cardiology, *Vol. 99, June 15, 2007, pp. 1726-32*

Editor's comment: It is hoped that emergency departments will take note of these findings and begin to treat acute cases of afib with magnesium infusions rather than with ineffective infusions of digoxin, verapamil, or diltiazem. It would be tempting to speculate that oral supplementation

with magnesium might be effective in slowing heart rate and restoring sinus rhythm during an acute afib episode. However, I have not come across anything in the medical literature indicating that this would be so. Besides, achieving an intake of 1,200 to 10,000 mg via oral ingestion would be pretty well impossible and likely to lead to massive diarrhea. Using magnesium infusions to help prevent afib episodes and ectopic beats would, however, make sense since it is very difficult to correct hypomagnesemia just by oral supplementation.

Beta-blockers given thumbs down

NEW YORK, NY. The beta-blocker atenolol (Tenormin) is the fourth most-prescribed drug in the US with 44 million prescriptions issued every year. A very large proportion of these prescriptions are for the 50 million Americans who suffer from uncomplicated hypertension. This despite the fact that no clinical trial has ever shown that using beta-blockers for the treatment of hypertension reduces overall mortality, or the risk of a first heart attack. Furthermore, clinical trials have shown that treatment of uncomplicated hypertension with beta-blockers is accompanied by a 16-30% increased risk of stroke when compared to treatment with calcium channel blockers, renin angiotensin aldosterone system blockers, or thiazide diuretics. Beta-blockers have been shown to increase insulin resistance and predispose patients to type 2 diabetes. Among other common adverse effects – drowsiness, lethargy, sleep disturbance, visual hallucinations, depression, nightmares, blurred vision, Raynaud's phenomenon, and erectile dysfunction (impotence). There is also evidence that beta-blockers may reduce exercise capacity in otherwise healthy people by up to 40%.

Beta-blockers have, however, been found effective in the treatment of heart failure and are also likely to be beneficial in patients who have suffered a heart attack. As they downregulate the adrenergic (sympathetic) nervous system, they can also be useful in ameliorating stressful situations such as public speaking and in helping to manage adrenergically-mediated atrial fibrillation. Beta-blockers have been recommended as first-line treatment for uncomplicated hypertension for more than three decades and most physicians, unfortunately, still believe that they are highly effective for this purpose. This state of affairs will hopefully change soon.

In April 2007 the American Heart Association and the European Society of Cardiology decided to cancel their endorsement of beta-blockers as first-line treatment for uncomplicated hypertension. The authors of the report had this to say about why the beta-blocker "myth" has been allowed to exist for so long, *These perceptions or misperceptions (among physicians) are unfortunate and obviously must be considered as long-lasting*

repercussions of deceptive marketing by the pharmaceutical industry that beta-blocker were "cardioprotective".
Bangalore, S, et al. Cardiovascular protection using beta-blockers: A critical review of the evidence. **Journal of the American College of Cardiology**, *Vol. 50, No. 7, 2007, pp. 563-72*

Editor's comment: Although beta-blockers may be helpful in the management of adrenergically-mediated afib, they should not be used on a continuous basis by afibbers with vagally-mediated afib.

Ablation - Procedures

Refinement to Pappone method

WUHAN, CHINA. A satisfactory outcome of a catheter-based pulmonary vein isolation procedure depends on the elimination of electrical conduction between the pulmonary veins and the left atrium. Lesions (usually created by application of radiofrequency energy through an ablation catheter) are placed around the veins guided by either electrophysiologic or electroanatomic mapping. Electrophysiologic mapping is based on locating abnormal electrical potentials, while electroanatomic mapping (CARTO) is based on accurately locating anatomical features of the left atrium, specifically in the area where the pulmonary veins connect to the atrium.

Electrophysiologic mapping is used in an ablation procedure known as segmental pulmonary vein isolation (Haissaguerre method), while electroanatomic mapping is used in the so-called circumferential anatomical pulmonary vein isolation (CAPVI) procedure (Pappone method). In the Haissaguerre method the procedure is complete when conduction between the pulmonary veins (PVs) and the left atrium is eliminated. In the Pappone method the completion of ablation rings around the left and right PVs is usually the endpoint. The inability to induce afib is another endpoint often used in the Haissaguerre method.

Chinese researchers now report that they have successfully used two circular Lasso mapping catheters to ensure that electrical conduction between PVs and the left atrium has been eliminated after completion of a CAPVI. Their study involved 106 patients with paroxysmal (78), persistent (12), or permanent AF (16). As part of the procedure, Lasso catheters were placed in the superior and inferior veins on each side (left and right) and ablation was continued as necessary to ensure elimination of PV potentials. Total abolition of all PV potentials was achieved in 94 patients (88.7%).

Eight-seven patients were followed up for 8 to 15 months. The complete success rate of the procedure (no afib, no antiarrhythmics) was 62% and the partial success rate (no afib, but still on antiarrhythmics) was 9%. The researchers conclude that combining CARTO or CartoMerge mapping with the use of double Lasso catheters to ensure complete PV isolation can achieve an “almost ideal” outcome for the treatment of atrial fibrillation.

They do point out though that afib originating outside the pulmonary veins is unlikely to be cured by this method.

It is interesting to look at the pre-procedure tests done in the Wuhan University People's Hospital. All patients had ECGs, chest x-rays, echocardiogram, transesophageal echocardiography (TEE), and magnetic resonance imaging (MRI) or multislice CAT scan (for merging with CARTO data) prior to their ablation. Echocardiograms, MRI or CAT scans (to check for stenosis) were repeated at 1, 3, and 12 months post-ablation and Holter recording were obtained at 1, 2, 3, 6, 9, 12, 18, and 24 months post-ablation. T3, T4, liver function, and chest x-ray were checked every 3 months after the procedure in patients on amiodarone. The average duration of the ablation procedure was 2.5 hours with fluoroscopy time and ablation time of 33 minutes and 25 minutes respectively.

Jian, MA, et al. Linear ablation of left atrium for the treatment of atrial fibrillation guided by double Lasso catheters and three dimensional electroanatomical mapping. Chinese Medical Journal, *Vol. 119, No. 24, 2006, pp. 2042-48*

Editor's comment: The initial procedure complete success rate of 62% is very close to the rates obtained at the top three institutions (Bordeaux, Cleveland Clinic, and Marin General) covered in our 2006 ablation/maze survey. Unfortunately, only 87 of 106 initially ablated patients were included in the follow-up and there is no indication of the fate of the missing 19 patients. Nevertheless, the addition of the double Lasso catheter protocol is, no doubt, a worthwhile refinement. This new procedure also has the advantage that it can be performed with amiodarone still present in the system.

Ultrasound PVI makes its debut

OKLAHOMA CITY, OK. Although pulmonary vein isolation (PVI) using radiofrequency ablation is now highly successful and safe in experienced hands, it is not necessarily so when less skilled operators perform the procedure. It can be difficult to obtain complete isolation of the pulmonary veins using standard 4 mm or 8 mm ablation catheters and pulmonary vein stenosis, thrombus formation, and penetration of the heart wall (tamponade) are still potential complications. A team of American, British, and German researchers now reports on the first trial of a high-intensity-focused ultrasound (HIFU) balloon catheter.

Their study population involved 19 patients with paroxysmal and 8 patients with persistent afib (21 males and 6 females between the ages of 39 and 68 years). Ten of the patients had structural heart disease and left atrial diameter ranged from 30 – 54 mm. After undergoing a magnetic resonance angiogram or a CT scan to determine pulmonary vein

location and size the patients underwent a PVI procedure using a balloon HIFU catheter with a sonicating ring diameter of 20, 25 or 30 mm depending on the size of the veins. The procedure was performed under heavy sedation or general anesthesia. Complete antrum isolation was achieved in all left superior and inferior veins, in 92% of right superior veins, but in only 11% of right inferior veins. A range of 1 – 26 (median of 3) sonic applications was used to isolate the successfully isolated veins.

The patients were followed for at least 15 months after their procedure. At the 12-month follow-up 56% of the 27 patients were free of afib; however, 20% of the group were only achieving this by the continued use of antiarrhythmics. Thus, the complete success rate (no afib, no antiarrhythmics) at the 12-month checkup was 45%, and the partial success rate was 11%. Another 22% had a better than 50% reduction in the number of episodes while using antiarrhythmics that had previously proven ineffective. No cases of stenosis, stroke or transient ischemic attack (TAI) were observed during or after the procedures; however, one case of (non-permanent) phrenic nerve injury and one case of pulmonary hemorrhage did occur.

Nakagawa, H, et al. Initial experience using a forward directed, high-intensity focused ultrasound balloon catheter for pulmonary vein antrum isolation in patients with atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 18, February 2007, pp. 136-44*

Editor's comment: Although a complete success rate of 45% is not overly impressive it will no doubt improve as further experience is acquired. The lack of success in isolating the right inferior veins is, nevertheless, a concern. Only 11% of these veins were isolated. Recent studies have shown that failure to isolate the right inferior veins is a major cause of late afib recurrence (beyond 12 months).[1]

[1] Mainigi, SK, et al. Incidence and predictors of very late recurrence of trail fibrillation after ablation. Journal of Cardiovascular Electrophysiology, Vol. 18, January 2007, pp. 69-74

Highlights from the Venice EP conference

VENICE, ITALY. During the *VeniceArrhythmias2007* conference a group of world-recognized experts in the field of atrial fibrillation ablation gathered to develop a document expressing the consensus reached by these experts regarding the current state of afib ablation. Among the EPs participating in the discussions leading to the so-called Venice Chart were Dr. Andrea Natale, Pr. Michel Haissaguerre, Dr. Pierre Jais, Dr. Carlo Pappone, Dr. Francis Marchlinski, Dr. Douglas Packer, Dr. Richard Schilling (UK), and Dr. Atul Verma (Canada). The discussions ranged from the detailed anatomy of the pulmonary veins to recommendations for post-ablation anticoagulation. Major highlights are presented below:

- The main anatomical structures, which may initiate ectopic beats resulting in afib, are the pulmonary veins, the vein (ligament) of Marshall, the musculature of the coronary sinus, and the posterior wall of the left atrium.

- Most patients (20-60%) presenting for ablation have 4 distinct pulmonary vein opening (ostia) into the left atrium. However, some have 3, some have 5 and their location relative to other features of the left atrium are, by no means, uniform. This provides the rationale for a CT scan or MRI prior to the ablation so as to be better prepared to deal with an unusual configuration.

- The onset and maintenance of atrial fibrillation, irrespective of the underlying mechanism, requires an event (trigger) that initiates the afib and a predisposing substrate that perpetuates it. Inflammation and autonomic nervous system dysfunction may also act to facilitate initiation and maintenance of AF.

- Most patients (about 90%) with AF have underlying structural heart disease or hypertension. Only about 10% have no evident cardiac disorder (so-called "lone" AF). **Editor's note** – The term "lone" AF as defined by this group of experts does not include a reference to age, but only to the absence of evident cardiac disorder.

- Atrial fibrosis and loss of myocardial tissue are common findings in patients with AF. There is some indication that ACE inhibitors and angiotensin receptor blockers may help prevent AF by inhibiting the angiotensin II promoted formation of collagen.

- There is now evidence that lone AF may be associated with certain gene mutations that reduces the atrial refractory period (AERP).

- Vagal denervation, produced by delivering RF energy to the sites of autonomic ganglia, may help control AF. **Editor's note** – It is also likely that extensive vagal denervation may result in a substantially elevated resting heart rate post-ablation.

- Atrial fibrillation perpetuates itself by electrical and structural remodeling. The electrical remodeling involves a shortening

of AERP. The structural remodeling involves enlargement of the atria and changes to individual myocytes (heart cells) – more specifically, an increase in cell size, accumulation of glycogen, myolysis, changes in mitochondrial shape, and alterations in connexin expression.

- There are currently 5 main approaches to catheter ablation for AF – PV isolation, electrogram-based ablation, linear lesions, ablation of autonomic ganglionated plexi, and the sequential ablation strategy. **Editor's note** – The Venice Chart contains detailed descriptions of these procedures.

- The vast majority of procedures currently use radiofrequency energy to create the lesions. New approaches under development include balloon-shaped catheters powered by cryoenergy, high-intensity-focused ultrasound (HIFU), and laser energy.

- The working group emphasized that adequate support personnel and facilities must be available in hospitals performing ablations. These would include facilities for rapidly testing anticoagulation efficacy (ACT) during the procedure, competence and experience to perform needle pericardiocentesis immediately if needed, anesthesiology expertise to manage procedural sedation/general anesthesia and provide resuscitory support if required, cardiac surgery personnel to perform emergency surgical procedures (including open heart surgery) as needed, and the capacity for urgent bedside echocardiographic examination primarily for diagnosing pericardial tamponade (perforation of the heart wall).

- The EP performing the procedure must have adequate training and experience. Two-thirds of the workshop participants felt that a prospective candidate entering a training program for performing AF ablations should have performed at least 100 other ablation procedures and have attended at least 20 AF ablations before being allowed to assist in doing an actual procedure. More than 50% of the experts felt that a "rookie" EP should have performed at least 40 procedures under the guidance of an experienced EP before he/she could begin doing the procedure on their own.

- The general consensus in regard to anticoagulation prior to the procedure was that patients with stroke risk factors ($CHAD_2$ score equal to or greater than 1) and patients with

persistent afib should receive warfarin for at least 3 weeks with documented INR between 2 and 3. Patients who arrive for the procedure in AF should have a TEE (transesophageal echocardiogram) on the day of the procedure or the day before to rule out the presence of left atrial thrombi. Patients with paroxysmal AF and a $CHAD_2$ score of 0 may be treated with warfarin or aspirin (75-325 mg/day). Warfarin should be continued in all patients for 3-6 months after the procedure.

- There is no consensus as to how the ultimate success of the procedure should be measured. There is general agreement that about 30-50% of patients with documented or symptomatic episodes during the first 3 months post-ablation will ultimately be free of afib. Thus, most experts now consider the first 3 months as a "blanking period" during which the success or failure of a procedure cannot be predicted.

- The most feared complications (approximate incidence in brackets) during AF ablations are stroke (1%), cardiac tamponade (0.1 – 1.0%), severe pulmonary vein stenosis (0.5 – 2.0%), phrenic nerve injury – usually resolving on its own (0.1 – 0.5%), atrio-esophageal fistula (very rare, but usually fatal), periesophageal vagal injury (1%), and catheter entrapment in mitral valve (0.01%).

- Post-ablation left atrial tachyarrhythmias (flutter and inappropriate sinus tachycardia) are quite common (3 – 50%), particularly among patients having undergone the circumferential, anatomically-guided (Pappone) procedure. About 50% of these tachycardias resolve on their own, but others may require repeat ablations if they are highly symptomatic.

- Reports of long-term success rates for AF ablation procedures range from 45% to 95%. In centers with the greatest experience the success rate for a first ablation was recently found to average 80.5% (no afib, no drugs). Repeat ablations added another 5-15% success to this number. Longer term recurrence is usually due to the recovery of electrical conduction between the pulmonary veins and the left atrium. Success rates tend to be lower in patients with structural heart disease and in those with permanent AF.

The Venice Chart, with its 20 fact-filled pages and 169 references, is clearly a must-read for anyone interested in the current status of atrial fibrillation ablation.

Natale, A, et al. Venice Chart international consensus document on atrial fibrillation ablation. Journal of Cardiovascular Electrophysiology*, Vol. 18, May 2007, pp. 560-80*

Guidelines for ablation and surgical treatment of AF

DENVER, COLORADO. American and European heart rhythm societies have developed a consensus statement on ablation and surgical treatment of atrial fibrillation. The statement was presented at the Heart Rhythm Society's 2007 Scientific Sessions held in Denver, CO. Among the highlights of the statement are:

- Catheter ablation may be indicated if the patient has symptomatic afib and has failed at least one class 1 or class 3 antiarrhythmic medication. In rare cases, ablation may be the first-line treatment. Ablation should not be attempted if thrombi are present in the left atrium.

- Surgical ablation (maze) may be indicated in afibbers undergoing cardiac surgery. It may also be considered as a stand-alone procedure for symptomatic patients who prefer the surgical approach, or have failed one or more attempts of catheter ablation.

- Low-molecular-weight or intravenous heparin should be used following ablation until anticoagulation (warfarin) becomes effective (INR in range). Warfarin is recommended for all post-ablation patients for at least two months. Whether or not to continue warfarin after two months should be based solely on the presence of stroke risk factors, not on the presence or types of AF. It is generally not recommended that patients with a $CHAD_2$ score of 2 or greater discontinue warfarin therapy.

- Patients with persistent afib usually require additional lesions over and above a complete pulmonary vein isolation. There is no agreement whether these additional lesions should be done during the initial catheter ablation procedure or in a "touch-up".

At this time, catheter ablation should not be considered as a first-line treatment. However, this may change once the results of the CABANA (Catheter Ablation vs Antiarrhythmic Drug Therapy for Atrial Fibrillation) trial are in. This trial will enroll up to 3000 patients who will be followed for 5 years.

O'Riordan, M. Heart rhythm societies develop consensus statement on catheter and surgical ablation of AF, May 10, 2007
http://www.theheart.org/printArticle.do?primaryKey=789667

Magnetically guided ablation not yet ready for prime time

CLEVELAND, OHIO. In order to meet the rapidly growing demand for catheter ablations for atrial fibrillation, it is imperative that the procedure be made less dependent on operator skill and experience. Only by using procedures, which allow relatively inexperienced EPs to achieve a high degree of success, can this demand be met. There are basically three requirements for a successful ablation – mapping the atrium accurately so that the points or lines to be ablated can be determined; navigating the ablation catheter to the points determined in the mapping; creating lesions or lines at these points that are deep enough to ensure complete electrical disconnection. Mapping can be done effectively through electrical (potentials) or electroanatomic measurements, perhaps combined with an overlay of a CT scan or magnetic resonance image (MRI). Highly effective ablation catheters have also been developed with the open-irrigation tip catheter being the current favourite.

The main remaining challenge involves accurate navigation to the ablation sites. Currently used catheters are relatively stiff and, even in the most experienced hands, are often difficult to maneuver so as to achieve complete electrical isolation of the pulmonary veins. This has led to the recent development of highly maneuverable ablation catheters that are guided by external magnets and theoretically can reach any part of the atrium. As a further refinement these catheters can now be positioned at the ablation site by an operator situated in front of a computer screen in a room away from the actual operating room. The catheter can be manipulated by a special joystick (wand method) or by a combination of a joystick and a mouse (coordinate method).

Electrophysiologists at the Cleveland Clinic recently reported on their evaluation of the Niobe II magnetic navigation system (Stereotaxis). This system uses a radiofrequency-heated, 4-mm, solid-tip, magnetic ablation catheter. After familiarizing themselves with the system in a series of 48 AF patients the EPs did a formal study of the system on 45 afibbers (33% paroxysmal, 38% persistent, and 29% permanent) with an average age of 60 years (60% male). The ablation was performed in a step-wise fashion so that step 2 was only implemented if step 1 did not achieve total electrical isolation of the pulmonary veins, and step 3 was only undertaken if step 2 was not successful. The three steps were as follows:

- Step 1 – Circumferential pulmonary vein isolation (Pappone method) of the right and left pulmonary veins using the Niobe II system and electroanatomical mapping.

- Step 2 – Pulmonary vein antrum isolation (Natale method) using the Niobe II system, electroanatomical mapping and ICE guidance.

- Step 3 – Pulmonary vein antrum isolation (Natale method) using fluoroscopy and ICE guidance and a 3.5-mm tip, open-irrigation catheter. This is the conventional protocol used at the Cleveland Clinic.

Although the Niobe II system was very successful in navigating the ablation catheter to the desired spots (60% success with coordinate method, 100% with wand method), electrical disconnection was only achieved in 4 veins in 4 different patients. In the remaining 41 patients (92%) no disconnection was observed in any veins. The step 3 approach (conventional method) was then applied to all patients in order to achieve isolation. In the first 23 patients all pulmonary veins were successfully disconnected, while in the remaining 22 patients only the right pulmonary veins were isolated (after failed attempts to isolate the left ones with the Niobe II system). After a mean follow-up of 11 months, 78% of the 23 patients who had achieved full isolation were afib-free as compared to only 10% in the group where only the right veins were successfully isolated.

The Cleveland researchers conclude that the Niobe II 4-mm tip ablation catheter is incapable of creating adequate lesions for a successful AF ablation. They also noted frequent charring (33% of patients) at the catheter tip, which could lead to thromboembolic complications (ischemic stroke).

Di Biase, L, et al. Remote magnetic navigation. **Journal of the American College of Cardiology**, *Vol. 50, August 28, 2007, pp. 868-74*
Lindsay, BD. Is pulmonary vein antrum isolation a critical determinant of recurrent arrhythmias after ablation of atrial fibrillation? **Journal of the American College of Cardiology**, *Vol. 50, August 28, 2007, pp. 875-76*

Editor's comment: The Niobe II (Stereotaxis) system is clearly effective in positioning the ablation catheter at any desired point in the left atrium using remote control. Unfortunately, the presently used catheter would seem to be ineffective in creating adequate lesions. Work is underway to develop an open-tip, irrigated catheter for use in the system. This would seem to be a formidable challenge, but if overcome could lead to a new, highly effective ablation protocol that could be used successfully by relatively inexperienced operators.

***Box isolation* effective for paroxysmal AF**

FUKUOKA, JAPAN. There is substantial evidence that most paroxysmal afib episodes are initiated in and around the junctions of the pulmonary veins with the left atrium. However, the back (posterior) wall of the left

atrium is also an important source of ectopics capable of initiating and sustaining full-blown AF. The three most common procedures (Haissaguerre, Pappone and Natale) all aim to isolate the pulmonary veins and may include additional lesions as required. A rare (1 in 1000), but very serious, complication of these procedures is the accidental burn-through to the esophagus creating an atrial esophageal fistula. The esophagus runs very close (2-4 mm away) to the posterior left atrial wall, so achieving complete isolation of the pulmonary veins without ablating close to it is often difficult.

Japanese electrophysiologists now report on their experience with a novel ablation procedure aptly named "Box isolation". The initial purpose of the new technique was to avoid having to create vertical lesions in the neighborhood of the esophagus. Essentially, the procedure involves creating a box-like lesion set encompassing the pulmonary veins and indeed most of the posterior wall of the left atrium. Vertical lesions in the vicinity of the esophagus are avoided and extra precautions are taken when creating the top and bottom lines of the box where they cross the esophagus.

The procedure was evaluated in a group of 91 paroxysmal afibbers (95% with lone AF) who had suffered from afib for an average of 5 years and experienced, on average, 10 episodes a month. All had failed antiarrhythmic drug treatment. The ablation procedure was performed during AF (spontaneous or induced) in 93% of the patients. At the completion of the *box isolation*, AF could no longer be induced in 71% of the patients. Three months after the procedure 90% of the patients were free of afib without the use of antiarrhythmics. Repeat ablations were performed (three months after the first procedure) in 6 patients, and 13 months after the initial procedure 86 (95%) of the patients were free of afib without the use of antiarrhythmics. The remaining 5 patients were also afib-free, but only with the use of antiarrhythmic drugs.

Kumagai, K, et al. A new approach for complete isolation of the posterior left atrium including pulmonary veins for atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 18, October, 2007, pp. 1047-52*

Verma, A. "Thinking outside the box". **Journal of Cardiovascular Electrophysiology**, *Vol. 18, October, 2007, pp. 1053-55*

Editor's comment: Based on this relatively small sample size the *Box isolation* technique would appear to be highly effective (95% success) in primarily lone, paroxysmal afibbers. It is, however, doubtful that it would be equally effective in persistent and permanent AF where maintenance of afib may be related to other areas in the heart such as the superior vena cava, the base of the left atrial appendage, and the interatrial septum.

Ablation - Complications

Bisoprolol + magnesium helps prevent post-operative AF

COLOGNE, GERMANY. Atrial fibrillation is a common post-operative complication following coronary bypass graft surgery (CABG). It is estimated that as many as 40% of patients suffer this complication most often during the first two days after surgery. It is common practice to give patients beta-blockers to prevent post-operative AF, but this approach is generally not very effective.

Now researchers at the University of Cologne report that a combination of bisoprolol, a highly cardio-selective beta-blocker, and intravenous and oral magnesium is highly effective in preventing post-operative AF. Their clinical trial involved 100 patients scheduled for elective CABG surgery. The trial participants were randomized to either the prophylaxis group (n=50) or the control group (n=50). Members of the control group remained on whatever beta-blocker they had been on prior to the operation, while those in the prophylaxis group received 2.5 mg of bisoprolol twice a day starting on the day of the surgery. In addition, they received a single intravenous infusion of 100 mL saline solution containing 2000 mg of magnesium sulfate within 30 minutes of arriving in the ICU following surgery. The magnesium component of the bisoprolol + magnesium combination was changed after the infusion to 600 mg of magnesium oxide three times daily for a week following the operation.

The incidence of new afib during the first week was 42% in the control group as compared to only 20% in the prophylaxis group. The difference was even more startling in those over 65 years of age. In this group 65% in the control group developed post-operative afib as compared to only 17% in the prophylaxis group. The bisoprolol/magnesium combination also had an immediate effect on cost effectiveness in that the average hospital stay in the control group was 9 days versus only 7 days in the prophylaxis group. It is interesting to note that 40% of control group participants were treated with bisoprolol before and after their surgery thus perhaps indicating that magnesium is the most important player in the combination.

Behmanesh, S, et al. Effect of prophylactic bisoprolol plus magnesium on the incidence of atrial fibrillation after coronary bypass surgery. Current Medical Research and Opinions, *Vol. 22, No. 8, 2006, pp. 1443-50*

Editor's comment: This study brings two thoughts to mind. An intravenous infusion of 2000 mg magnesium sulfate in 100 mL saline

solution is obviously safe and effective. Personally, if I experienced intolerable, unmanageable afib this is the first approach I would try. The bisoprolol + magnesium combination is obviously effective in controlling new onset afib. Could it be effective in controlling paroxysmal afib? It certainly would be worth a try for adrenergic and perhaps mixed afibbers, but may not be a good idea for vagal afibbers. The daily oral dose of magnesium (1800 mg magnesium oxide) used in the trial would only have provided about 45 mg/day of absorbable elemental magnesium, so it would certainly be easy to up this amount by using a much more absorbable magnesium compound such as magnesium glycinate or citrate.

Antiarrhythmic drugs after PVI

MADDALONI, ITALY. It is fairly common practice to prescribe antiarrhythmic drugs to patients who have undergone a pulmonary vein isolation (PVI) procedure. These drugs are usually discontinued after 2-3 months if the patient remains afib-free, but may be continued indefinitely if the patient still experiences episodes. Italian researchers recently completed a study to determine if continuing antiarrhythmics beyond the first month is of benefit.

Their study included 107 afibbers (60% paroxysmal and 40% persistent) who had suffered AF episodes for a mean of 4.5 years (64% men). Fifty-seven per cent of the study participants had hypertension. The patients underwent an anatomically-guided (CARTO) PVI procedure and were then divided into two groups. Group A received no post-procedure antiarrhythmics, while group B received either amiodarone (71%), flecainide (19%), propafenone (6%), or sotalol (4%).

During the first month following the PVI, 35% of the members in group A had a recurrence of AF as compared to only 17% in group B. However, during the following 12 months, 34% of group A had experienced one or more AF episodes as compared to 30% in group B. This difference, however, was not statistically significant. The percentage of afibbers with one or more asymptomatic episodes (detected by transtelephonic ECG) was 63% in group B, but only 18% in group A.

The researchers conclude that, while antiarrhythmic therapy may be useful during the first month following the PVI, it would seem unnecessary to continue it beyond the first month in order to attempt the prevention of AF recurrences unless the therapy is effective in alleviating symptoms.

Turco, P, et al. Antiarrhythmic drug therapy after radiofrequency catheter ablation in patients with atrial fibrillation. **PACE**, *Vol. 30, January 2007, Suppl. 1, pp. S112-S115*

Asymptomatic AF after ablation

CLEVELAND, OHIO. The medical literature is inconsistent when it comes to the question – "How frequent are asymptomatic AF episodes after a seemingly successful pulmonary vein ablation?" Some studies have found a high incidence of post-ablation asymptomatic episodes, while others have found low to moderate levels.

EPs at the Cleveland Clinic now report the results of a recent study designed to determine the incidence of post-PVAI (pulmonary vein antrum isolation) AF in a group of 86 afibbers 34% of whom had structural heart disease. All the study participants had previously had a permanent pacemaker implanted to deal with symptomatic sick sinus syndrome often exacerbated by antiarrhythmic or rate-control medications. The patients (71% men) had suffered from afib for an average of 6.9 years and were 57 years of age on average; 65% were paroxysmal and 35% persistent, and all had highly symptomatic episodes.

After undergoing a standard PVAI the patients were followed for 9 months with clinic visits at 1, 3, 6, and 9 months. Following the ablation the mode switching of the pacemaker was set to occur at an atrial sensed rate above 170 bpm (indicative of AF). All patients were also equipped with rhythm transmitters. Antiarrhythmic medication (sotalol, propafenone, flecainide or dofetilide) was continued for 2 months post-ablation. Procedural success was defined as no afib episodes beyond 2 months post-PVAI off antiarrhythmic medication. Prior to the ablation, pacemaker interrogation showed an average of 34 mode switch episodes (MSEs) per month. These MSEs correlated with afib symptoms 91% of the time and their average duration was about 20 hours.

Of the 86 patients, 23% had symptomatic episodes following the PVAI, while 32% experienced asymptomatic episodes as detected by MSEs. The asymptomatic episodes were significantly less frequent than symptomatic episodes and much shorter in duration (0.6 minutes versus 134 minutes average). The incidence of asymptomatic episodes declined markedly with time so that at the 3-month check-up only 3% experienced numerous and sustained asymptomatic episodes.

The researchers conclude that about 30% of patients undergoing PVAI for highly symptomatic afib will have asymptomatic episodes after the procedure. However, most of these episodes are short (less than 60-second duration) and become infrequent within 3 months post-procedure. Sustained, asymptomatic episodes are uncommon.

Verma, A, et al. Incidence of atrial arrhythmias detected by permanent pacemakers post-pulmonary vein antrum isolation for atrial fibrillation. **Journal of Cardiovascular Electrophysiology**, *Vol. 18, June 2007, pp. 601-06*

Editor's comment: The main concern about post-procedure asymptomatic episodes is stroke risk. If asymptomatic episodes are frequent and long-lasting then the decision to discontinue warfarin may be more difficult to make than if asymptomatic episodes are infrequent and short. The Cleveland study supports the common practice of discontinuing warfarin 3 months after a successful ablation.

Atrial flutter ablation often leads to AF

CLEVELAND, OHIO. Typical right atrial flutter and atrial fibrillation (AF) often coexist and likely share common triggers. There is also evidence that they share predisposing conditions such as hypertension, heart disease, hyperthyroidism, sinus node dysfunction, and pulmonary disorders. Atrial flutter is not very responsive to treatment with antiarrhythmics, so the normal way of dealing with it is via a cavotricuspid isthmus ablation. In this radiofrequency ablation procedure a linear lesion is created in the right atrium from the tricuspid annulus to the inferior vena cava thereby interrupting the typical counter-clockwise flutter circuit. Unfortunately, there is growing evidence that a successful flutter ablation may, in a substantial number of cases, lead to the later occurrence of AF.

Electrophysiologists at the Cleveland Clinic now report that the development of afib after a flutter ablation is the rule rather than the exception. Their study involved 363 patients with atrial flutter who had been unsuccessfully treated with at least two antiarrhythmic drugs. None of the patients had been diagnosed with atrial fibrillation as well. Thirty-four percent of these patients had evidence of underlying structural heart disease. The average left ventricular ejection fraction in the group was 47% and the average left atrial diameter was 42 mm.

The study participants underwent cavotricuspid isthmus ablation and were then followed up for an average of 39 months. At the end of the follow-up period, only 13% were in sinus rhythm. A total of 68% had developed drug-refractory AF, 14% had developed a combination of AF and atrial flutter, and the remaining 5% had experienced a recurrence of their flutter. A large left atrium was associated with an increased risk of developing afib following the flutter ablation.

The Cleveland Clinic researchers conclude that 82% of all patients undergoing the standard cavotricuspid isthmus ablation for right atrial flutter later develop atrial fibrillation.

Ellis, K, et al. Incidence of atrial fibrillation post-cavotricuspid isthmus ablation in patients with typical atrial flutter. Journal of Cardiovascular Electrophysiology, *Vol. 18, August 2007, pp. 799-802*

Editor's comment: This is indeed discouraging news for patients with right atrial flutter – clearly most of them can expect to develop afib even after a successful flutter ablation! The Cleveland Clinic findings also, to some extent, support the findings from our 2006 ablation/maze survey that undergoing a right atrial flutter ablation as a first attempt in curing coexisting flutter and afib is almost certainly doomed to fail.

Obesity and ablation risks

LEUVEN, BELGIUM. There is increasing evidence that obesity (body mass index greater than 30 km/m^2) is a risk factor for AF and also increases the risk of recurrence after an ablation. Now Belgian researchers report that obese people also are exposed to a significantly greater level of radiation during a pulmonary vein isolation procedure. This is because fluoroscopy (x-ray imaging) systems use an automatic exposure control, which adjusts the tube voltage and current to provide a clear image irrespective of the depth of flesh that the x-rays have to penetrate.

The Belgian researchers measured radiation exposure in a group of 85 lone afibbers who underwent a segmental PVI (including right atrial flutter ablation). The average procedure time was 4 hours and the average fluoroscopy time (time exposed to x-rays) at 3 frames/second was 83 minutes. The researchers estimate that normal weight patients (BMI less than 25) received an average effective radiation dose of 15 milliSievert (mSv), overweight patients (BMI between 25 and 30) received a dose of 27 mSv, and obese patients a dose of 39 mSv or more than twice as much as the dose received by a normal weight person. These dosages would correspond to an increase in overall lifetime cancer mortality of 0.06%, 0.1%, and 0.15% respectively. [NOTE: The Canadian Centre for Occupational Health and Safety has set an annual maximum exposure level of 1.0 mSv for the general public and a regular CT scan involves an exposure of about 1.1 mSv.]

The researchers point out that repeat ablations will increase the total radiation dose as will the use of multislice CT scans now increasingly used in combination with CARTO mapping (non-fluoroscopic). The multislice CT scan can add as much as 5 to 20 mSv exposure, again, depending on the patient's BMI. The researchers conclude that the benefits and risks of ablation of obese individuals (higher radiation exposure and recurrence rates) should be carefully weighed before proceeding with the procedure. They also suggest that a circumferential PVI using non-fluoroscopic (CARTO) mapping may be a better choice for obese people.

Ector, J, et al. Obesity is a major determinant of radiation dose in patients undergoing pulmonary vein isolation for atrial fibrillation. **Journal of the American College of Cardiology**, *Vol. 50, No. 3, 2007, pp. 234-42*

Editor's comment: The patient exposure determined by the Belgian researchers would appear to be quite high. Reports from Hopital Cardiologique de Haut Leveque in Bordeaux (Haissaguerre/Jais group) estimate their average patient exposure to be about 1.1 mSv during a standard segmental PVI. Dr. Perisinakis and colleagues at the University of Crete reported an average exposure of 8.3 mSv per hour of fluoroscopy. Thus, it would seem that radiation exposure varies from center to center with the likelihood of lower exposures in procedures performed by more experienced electrophysiologists.

Maintenance of sinus rhythm post-ablation

MAYWOOD, ILLINOIS. As the number of patients with atrial fibrillation continues to grow, the number of ablation procedures is increasing as well. It is estimated that 53,000 ablation procedures for AF were performed worldwide in 2006 with 25,000 of those taking place in the United States. Although the majority of procedures are initially deemed successful, the recurrence rate can be high primarily depending on the skill of the electrophysiologist (EP) performing the ablation. Post-ablation treatment has been tried with several drugs, particularly anti-inflammatories, but so far none have been successful.

Researchers at the Loyola University Medical Center now report on their evaluation of statin drugs (such as atorvastatin, lovastatin and simvastatin), ACE inhibitors (such as enalapril, lisinopril and ramipril), and angiotensin receptor blockers (ARBs) (such as candesartan, irbesartan, losartan and valsartan) in the pre- and post-ablation treatment of afibbers. Their study involved 132 paroxysmal and 45 persistent afibbers. The majority (71%) were men, 23% had structural heart disease, and 43% had hypertension. Fifty patients (28%) were on statin drugs for at least one month prior to their ablation procedure and remained on these drugs for the average (mean) follow-up period of 13.8 months. Thirty-one patients (18%) were on ACE inhibitors and 18 patients (10%) were on ARBs during the study period (from one month prior to ablation to 13.8 months post-ablation). The study participants all underwent antral pulmonary vein isolation with right flutter ablation where necessary.

At the end of the follow-up period, 75% of paroxysmal afibbers and 63% of persistent afibbers were free of afib for an overall success rate of 72%. However, 13% of those in sinus rhythm were still taking antiarrhythmic drugs, so the performance was actually:

- Full success (no afib, no drugs) 59%
- Partial success (no afib, but on antiarrhythmics) 13%
- Failure 28%

The main indicator of failure was a low left ventricular ejection fraction prior to the procedure.

The researchers observed no benefits of statin drugs on the maintenance of sinus rhythm. In the group not taking statin drugs 74% of patients remained in sinus rhythm, while only 66% in the group taking statins did so. ACE inhibitor treatment showed no advantage either, with only 55% of patients being in sinus rhythm at the end of the follow-up. The small group (18 patients) on ARBs, however, showed an intriguing trend towards better success. At the end of follow-up, 94% of them were still in normal sinus rhythm. Although this is clearly a very small number of patients upon which to base a conclusion, the researchers suggest that larger, prospective, randomized studies would be in order to follow up on these promising findings.

Chekakie, MO, et al. The effects of statins and renin-angiotensin system blockers on atrial fibrillation recurrence following antral pulmonary vein isolation. Journal of Cardiovascular Electrophysiology, *Vol. 18, September 2007, pp. 942-46*

Deneke, T. ARBs, ACE-Is, or statins after catheter ablation of atrial fibrillation? Journal of Cardiovascular Electrophysiology, *Vol. 18, September 2007, pp. 947-49*

Editor's comment: It is known that the renin-angiotensin system (RAS) exhibits pro-inflammatory actions and plays a direct role in the electrical and structural remodeling that takes place in the left atrium during atrial fibrillation. Thus, inhibiting it pre- and post-ablation seems to make sense. Nevertheless, the purpose of a radiofrequency ablation is to create scar tissue (fibrosis) around the pulmonary veins in order to create a barrier to AF propagation. Treatment with drugs that interfere with fibrosis formation may, in fact, affect the integrity of the ablation line and thus promote afib recurrence. This may explain why statins and ACE inhibitors proved ineffective, or perhaps even slightly detrimental, to maintenance of sinus rhythm. ACE inhibitors and ARBs, on the other hand, have different biological activity, which could explain the superiority of ARBs. The possible benefits of ARBs in post-ablation sinus rhythm maintenance clearly need to be established (or disproved) in larger trials.

Ablation - Outcome

Late recurrence of afib after PVI

PHILADELPHIA, PENNSYLVANIA. About 50% of all afibbers undergoing a pulmonary vein ablation experience recurrence of their afib at some point (less frequent if procedure performed by skilled EP, more frequent if not). Depending on the timing, the recurrence is classified as acute (AF returning within the first 4-6 weeks), late (between 1 to 12 months), and very late (greater than 12 months post-ablation). Some researchers use the term "early" to describe recurrence within the first 6 months after the procedure. Risk factors for early recurrence have been fairly well determined and include older age, hypertension, a large left atrium size, presence of foci outside the pulmonary veins, and number of years the patient has suffered from AF.

Now researchers at the University of Pennsylvania (the Callans/Marchlinski group) report that very late recurrence occurs in about 8% of patients thought to have undergone a successful PVI. Their study involved 342 patients who underwent a PVI using both electrophysiologic, electroanatomic and intracardiac ultrasound mapping. It is of interest to note that a pre-procedure transesophageal echocardiogram (TEE) was only performed in patients with persistent afib and in paroxysmal afibbers who arrived for the procedure in afib and had not been adequately anticoagulated for 4 weeks prior to the hospital admission.

The average age of the patients was 55 years, 79% were men, and 65% had the paroxysmal (intermittent) variety of AF. During the procedure 88% of patients had their right superior vein isolated, 90% the left superior vein, right inferior vein 57%, and left inferior vein 77%. All patients returned to the hospital for follow-up 6 weeks, 3 months and 6 months after the procedure, and then every 6 months.

Four weeks post-procedure 72% of the study participants were afib-free. However, subsequent to the 12-month check-up 27 patients experienced a recurrence of AF. This is 7.9% of the original cohort of 342 patients and 11% of the 246 patients whose procedure had been believed to be successful. The researchers found that the main risk factors for very late recurrence was a weight over 200 pounds, fewer veins completely isolated during the procedure (2.8 vs. 3.3), failure to isolate the right inferior vein (37% vs. 61%), failure to isolate all veins (30% vs. 56%), and

more likely to have triggers outside the pulmonary veins (30% vs. 11%). There was also a statistically non-significant trend for patients on digoxin to have a late recurrence (p=0.10).

Mainigi, SK, et al. Incidence and predictors of very late recurrence of atrial fibrillation after ablation. Journal of Cardiovascular Electrophysiology, *Vol. 18, January 2007, pp. 69-74*

Editor's comment: It is a sobering realization that about 10% of afibbers who thought that they were "home free" after having had a year or more of post-procedural normal sinus rhythm may actually experience late afib recurrence. However, for non-obese afibbers it would seem that very late recurrence is closely tied in with shortcomings in their initial procedure.

Ablation improves left ventricular ejection fraction

PHILADELPHIA, PENNSYLVANIA. The left ventricular ejection fraction (LVEF) is a measure of the heart's pumping capacity with a low value being indicative of heart failure. Researchers at the University of Pennsylvania (Marchlinski/Callans Group) now report that low LVEFs improve markedly in afibbers after pulmonary vein isolation (PVI). Their clinical trial included 366 patients scheduled for a PVI; 67% of these patients had impaired left ventricular function with an average LVEF of 42%. The average LVEF for the remainder of the group was 61%. After one or more ablations 56% of the patients were free of afib and off all antiarrhythmics, another 20% were free of afib, but still on antiarrhythmics, while 10% had experienced a greater than 90% decrease in their afib burden (time spent in afib). The researchers equate this with an 86% success rate. The success rate was similar for patients with and without low LVEF.

A comparison of LVEF on the day after the PVI with the value obtained six months post-procedure showed that the average LVEF in the group with low LVEF had increased from 43% to 56%. The researchers conclude that a PVI may reverse AF-induced ventricular cardiomyopathy in patients with atrial fibrillation and depressed left ventricular function.

Gentlesk, PJ, et al. Reversal of left ventricular dysfunction following ablation of atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 18, January 2007, pp. 9-14*

Editor's comment: This article provides a clear example of the confusion surrounding the definition of ablation success. In our surveys we have consistently categorized the outcome of an ablation (at 6 months post-procedure) as either:

- Complete Success: No afib – no antiarrhythmics
- Partial Success: No afib, but still on antiarrhythmics

- Failure: Continuing afib episodes with or without antiarrhythmics.

In this article the 86% success rate is defined as free of afib with or without antiarrhythmics or at least a 90% reduction in afib burden (time spent in afib). According to our definition 56% of patients had complete success, 20% had partial success and the remaining 24% were failures. The difference between a success rate of 86%, as defined in this article, and the actual 56% complete success rate is substantial and, once again, points out the need to always read "the small print".

Surgical Procedures

Success rate for Cox-Maze IV

ST. LOUIS, MISSOURI. The Cox-Maze procedure is considered to be the gold standard for the surgical treatment of atrial fibrillation. The original procedure used a cut-and-sew technique for creating lesions forming a "maze" that conducts the electrical impulse from the sino-atrial (SA) node to the atrio-ventricular (AV) node, while at the same time interrupting any "rogue" circuits. The cut-and-sew process, however, is difficult and time-consuming to perform so it is not surprising that surgeons have been looking for other means of creating the lesions.

Cardiac surgeons at Washington University School of Medicine, Barnes-Jewish Hospital (Dr. Ralph Damiano belongs to this group) now report the development of the Cox-Maze IV procedure. This procedure uses a bipolar radiofrequency ablation clamp (Atricure) to create most of the lesions. A review of the outcome of 130 Cox-Maze procedures was recently published in the *Annals of Surgery*. One hundred of the patients underwent the full maze procedure, 7 a limited Cox-Maze, and 23 had only their pulmonary veins isolated. All the patients had underlying heart disease and none had lone atrial fibrillation. The maze procedure was carried out in connection with coronary artery bypass grafting, valve replacement, patent foramen ovale closure, or other less common heart problems. Five patients died during the operation, 4 in the full Cox-Maze IV procedure, and 1 in the pulmonary vein isolation group. Post-operative pacemaker implantation was necessary in 10% of the full maze patients (none in the pulmonary vein isolation group), and post-operative tachyarrhythmias occurred in 60% of the full maze group and 70% in the PVI group. The average length of the hospital stay was 11 days.

At the 12-month checkup freedom from afib was observed in 91% of patients having undergone the full maze. However, one-third of the patients needed an antiarrhythmic to remain afib-free. Thus, the complete success rate (no afib, no antiarrhythmics) was actually only 67%. For the 23 patients undergoing pulmonary vein isolation only, the percentage that was afib-free at 12 months was 69% and 25% remained on antiarrhythmics. The percentage of PVI patients who were free of afib at the 12-month checkup was substantially higher for paroxysmal afibbers (75%) than for permanent/persistent ones (60%).

The authors of the study conclude with a statement of particular interest to lone afibbers, "It is a weakness of this study that we did not examine pulmonary vein isolation in patients who had lone AF. Further data are needed to evaluate the efficacy of this procedure in this group. However, our historical results with the cut-and-sew procedure (Cox-Maze III) had higher success rates in patients who had AF associated with concomitant cardiac pathology as opposed to those who had lone AF."

In a subsequent round-table discussion of the report Dr. Damiano also made the following statement, "What they are doing in the Electrophysiology Laboratory is ablating most of the back of the left atrium, which our data would suggest would be successful in a significant number of these patients who do not have organic heart disease and a small left atrium. So I do believe there are certain centers around the world that can get excellent success rates with catheter-based ablation. I personally feel that surgical pulmonary vein isolation would be less effective than catheter ablation because it doesn't ablate as much atrial tissue."

Melby, SJ, et al. A new era in the surgical treatment of atrial fibrillation: The impact of ablation technology and lesion set on procedural efficacy. **Annals of Surgery**, *Vol. 244, No. 4, October 2006, pp. 583-92*

Editor's comment: According to the data presented in this report the complete success rate (no afib, no antiarrhythmics) of the full Cox-Maze IV procedure is 67% with a complete + partial success rate (no afib, but continued need for antiarrhythmics) of 91%. It is, of course, important to note that all patients had underlying heart problems, which probably help explain the high mortality and need for permanent pacemaker implantation accompanying the procedure. Nevertheless, the statement by the authors that the Cox III procedure had a lower success rate in lone afibbers than in afibbers with concomitant heart disease would support my own opinion that the Cox-Maze may not be the optimum procedure for lone afibbers, especially not for vagal afibbers with relatively short paroxysmal episodes. I also feel that it is important to take note of the fact that the authors of this report define success as freedom from afib with or without the use of antiarrhythmic drugs. If one defines complete success as absence of afib without the use of antiarrhythmics, then the 67% success rate of the Cox-Maze IV procedure is not superior to the average complete success rate (after repeats as necessary) of 72% for PVIs performed at the 10 top-rated institutions in the LAFS-9 survey.

Post-maze arrhythmias

CLEVELAND, OHIO. Although the Cox-Maze procedure is considered to be highly successful in curing atrial fibrillation, there are cases where arrhythmias develop or recur after the procedure. Electrophysiologists at

the Cleveland Clinic now report a study of 23 patients who were admitted after experiencing supraventricular (atrial) arrhythmias subsequent to having undergone the cut-and-sew Cox-Maze procedure. Eight patients (35%) underwent the procedure in order to cure lone AF, while the remaining 15 had the procedure in conjunction with bypass surgery or mitral valve surgery. Eight of the 23 patients (35%) presented at the Cleveland Clinic with atrial fibrillation caused by conduction recovery around the lesion lines encircling the pulmonary veins, 5 had focal atrial tachycardia, 4 had right atrial flutter associated with the maze incisions, and 6 (26%) had left atrial flutter again associated with the maze lesions.

Twenty-two of the patients (96%) were treated successfully with catheter-based radiofrequency ablation and at the 12-month follow-up 86% were still in sinus rhythm and taking no antiarrhythmics.

Wazni, OM, et al. Atrial arrhythmias after surgical maze: Findings during catheter ablation. **Journal of the American College of Cardiology**, *Vol. 48, October 3, 2006, pp. 1405-09*

Editor's comment: A study carried out at Barnes-Jewish Hospital in St. Louis (Dr. Damiano's group) concluded that post-procedure atrial tachyarrhythmias are relatively common (43% of patients experiencing them) in the 30 days following the maze procedure, especially about a week after. Late recurrence (more than a year post-procedure) is much less common at about 8% of cases.[1] It is comforting to know that these recurrences can, in most cases, be eliminated by catheter ablation performed by a skillful electrophysiologist.

[1] *Ishii, Y, et al. Atrial tachyarrhythmias after the maze procedure: Incidence and prognosis.* **Circulation**, *Vol. 110, Suppl. II, September 14, 2004, pp. II-164-II-68*

Atrial flutter after modified maze procedure

MAYWOOD, ILLINOIS. A modified maze procedure is often performed in patients with atrial fibrillation as part of corrective valve surgery. The procedure involves the creation of wide area lesions circumferentially encircling the pulmonary veins with the addition of any combination of a posterior wall, roof, mitral isthmus, septal and/or cavo-tricuspid isthmus lines. The lesions may be created with radiofrequency energy, cryothermy or microwave energy. It is now becoming apparent that although the procedure is quick (about 20 minutes) and quite effective in eliminating atrial fibrillation it is often followed by the appearance of other tachyarrhythmias especially right or left atrial flutter.

Electrophysiologists at the Loyola Medical Center now report on a series of nine patients who developed atrial flutter following a modified radiofrequency maze procedure. The researchers found that conventional ECGs were unable to distinguish between right and left atrial flutter. However, by using electrophysiological entrainment mapping they

determined that three of the nine patients had typical counterclockwise right atrial flutter while the remaining six had left atrial flutter. This despite the fact that the maze procedure had included ablation of both the cavo-tricuspid isthmus (right atrial flutter) and the mitral isthmus (left atrial flutter). The researchers observed extensive scaring in both the right (38%) and left (65%) atria and speculate that this could explain the inability of surface electrocardiograms to distinguish between right and left flutter. All 9 patients underwent conventional percutaneous catheter ablation and after a mean follow-up of 8 months eight of the nine patients were back in normal sinus rhythm including three patients who remained on antiarrhythmic drugs.

In an accompanying editorial electrophysiologists at the University of Virginia point out that in the case of three of the patients who developed post-maze flutter, cryoablation was used in ablating the tricuspid and mitral isthmuses during the original maze procedure.

Akar, JG, et al. Surface electrocardiographic patterns and electrophysiologic characteristics of atrial flutter following modified radiofrequency maze procedures. Journal of Cardiovascular Electrophysiology*, Vol. 18, April 2007, pp. 349-55*

Mason, PK and DiMarco, JP. Atrial tachycardias after surgical ablations for atrial fibrillation: an incoming tide. Journal of Cardiovascular Electrophysiology*, Vol. 18, April 2007, pp. 356-57 (editorial)*

Editor's comment: It is becoming increasingly clear that the development of flutter after a modified maze procedure or a circumferentially guided catheter ablation is fairly common and is usually a result of incomplete lesion creation. Incomplete lesions around the pulmonary veins are of course also often responsible for recurrence of atrial fibrillation after a seemingly successful catheter ablation. In a recent study of eight patients who developed atrial tachyarrhythmias after a modified maze procedure German researchers observed that complete linear lesions may be difficult to obtain with cryoablation[1]. Thus, while cryoablation is generally considered very safe, there is now some question as to whether it, at its present stage of development, is uniformly able to create lesions that achieve complete isolation.

[1] Chun, KRJ, et al. Pulmonary vein conduction is the major finding in patients with atrial tachyarrhythmias after intraoperative maze ablation. Journal of Cardiovascular Electrophysiology, Vol. 18, April 2007, pp. 358-63

Stroke Risk Factors

LAA removal and stroke risk

CLEVELAND, OHIO. In afib patients with underlying heart disease stagnation of blood flow in the left atrium, more specifically in the left atrial appendage (LAA) – a small pouch connected to the left atrium – is an important source of blood clots and subsequent stroke. There is no evidence that afibbers with a structurally sound heart and normal left ventricular ejection fraction are abnormally prone to clot formation in the LAA. Because the LAA is believed (wrongly in my opinion) to be a useless appendage, it is often removed or occluded (stapled shut) during cardiac surgery such as mitral valve repair or replacement, and in the maze and mini-maze procedures. It has even been suggested that LAA removal or occlusion would be a viable stroke prevention measure for afibbers that cannot tolerate warfarin.

Researchers at the Cleveland Clinic now cast considerable doubt on the value of LAA removal in stroke prevention. Their study involved 136 patients (61% with AF) who underwent mitral valve repair or replacement during which their LAA was removed. Sixty-two percent of the patients were discharged on warfarin, while the remaining did not receive anticoagulation therapy. During the mean follow-up period of 3.6 years, 12.3% of the patients experienced a stroke, transient ischemic event (TIA) or peripheral embolism. The incidence of thromboembolic events (stroke, TIA, etc) was 10% in the warfarin-treated group and 15% in the non-treated group. NOTE: This difference is not statistically significant with most events (71%) occurring in those who had undergone mitral valve repair.

The Cleveland Clinic researchers conclude that LAA removal in patients undergoing mitral valve repair does not provide adequate protection against later thromboembolic events. They point out that blood clots formed in the LAA are not the only source of stroke in AF patients. Other sources like left atrial thrombi and debris originating in the aorta or carotid arteries may be equally important sources. They also suggest that isolating (occluding) the LAA during cardiac surgery may not be an effective stroke prevention measure as several studies have shown that the closure is often incomplete, thus actually increasing the risk of clot formation caused by blood stagnation.

Almahameed, ST, et al. Left atrial appendage exclusion and the risk of thromboembolic events following mitral valve surgery. **Journal of Cardiovascular Electrophysiology,** *Vol. 18, April 2007, pp. 364-66*

Editor's comment: The conclusion of the Cleveland Clinic study is clearly that LAA removal or occlusion is not an effective stroke prevention measure in afibbers.

The LAA is a known incubator of thrombi in afibbers with underlying heart disease, but there is no evidence that this is also the case for lone afibbers. Nevertheless, the LAA is now routinely removed during maze and min-maze procedures irrespective of whether the patient has underlying heart disease or not.

Is this a good idea? Some researchers think not. A comprehensive study by British researchers concluded, "The removal of the LAA may result in unfavourable hemodynamic and hormonal effects"[1], while a study by German researchers conclude, "Elimination of the LAA may impede thirst in the case of hypovolemia, may impair the hemodynamic response to volume or pressure overload, may decrease cardiac output, and may promote heart failure."[2]

It is clear that further studies are urgently required to clearly establish the benefits and disadvantages of LAA removal and equally clear that such studies, to be of value, must distinguish between afibbers with heart disease and those without.

[1] Al-Saady, NM, et al. Left atrial appendage: structure, function, and role in thromboembolism. Heart, Vol. 82, 1999, pp. 547-55

[2] Stollberger, C, et al. Elimination of the left atrial appendage to prevent stroke or embolism? Chest, Vol. 124, December 2003, pp. 2356-62

Stroke Prevention

Aspirin in primary stroke prevention

BIRMINGHAM, ALABAMA. Although there is substantial evidence that aspirin is beneficial in protecting against a second heart attack (secondary prevention), it is still controversial whether the daily aspirin "ritual" helps protect against a first stroke or heart attack (primary prevention). Researchers from the University of Alabama now present the results of a meta-analysis of 6 large trials aimed at evaluating the benefits of aspirin in primary prevention of cardiovascular events (heart attack and stroke) and coronary heart disease.

The trials involved a total of 47,293 aspirin users and 45,580 controls not on aspirin who had no prior indication of cardiovascular disease. The dosage of aspirin involved in the trials varied from 75 mg/day to 500 mg/day. The researchers conclude that regular aspirin use reduces the relative risk of experiencing a first non-fatal heart attack by 24%, that of developing coronary heart disease by 23%, and reduces the risk of any cardiovascular event by 15% (relative). No risk reduction was observed for stroke, cardiovascular mortality or all-cause mortality. The authors conclude that their analysis supports the current recommendation for the use of aspirin for primary prevention in patients with a high risk of cardiovascular disease (10-year risk of 6% or higher). Unfortunately, they completely ignore the downside of aspirin usage – a substantially increased risk of hemorrhagic stroke and major gastrointestinal bleeding. NOTE: This study was funded by Bayer, the major manufacturer of aspirin.

Bartolucci, AA and Howard, G. Meta-analysis of data from the 6 primary prevention trials of cardiovascular events using aspirin. American Journal of Cardiology, *Vol. 98, September 15, 2006, pp. 746-50*

Editor's comment: It is noteworthy that long-term aspirin usage had no effect on the risk of stroke in patients without prior cardiovascular disease. On the other hand, a meta-analysis of 5 of the 6 trials discussed above clearly showed that long-term aspirin usage increases the relative risk of hemorrhagic stroke (stroke caused by a burst blood vessel) by about 40% and the risk of major gastrointestinal bleeding by 70%. Thus, it would seem prudent to keep in mind the conclusion of the U.S. Preventive Services Task Force, "Patients at low risk for coronary heart disease probably do not benefit from and may even be harmed by aspirin because the risk for adverse events may exceed the benefits of chemoprevention."[1]

[1] Hayden, M, et al. Aspirin for the primary prevention of cardiovascular events. Annals of Internal Medicine, Vol. 136, January 15, 2002, pp. 161-72

Possible new warfarin replacement

GOTHENBURG, SWEDEN. Hip and knee replacement surgery is associated with a significant incidence of deep vein thrombosis, pulmonary embolism, and stroke. Effective post-operative anticoagulation is therefore essential. Because of its slow onset of action, need for frequent monitoring, numerous drug interactions, and undesirable side effects warfarin is far from being an ideal candidate for use in hip and knee replacement procedures. Thus, it is common practice to use low-molecular-weight heparins like enoxaparin (Lovenox) for prevention of thromboembolism. The drug is usually injected (0.4 ml providing 40 mg) prior to surgery, 6-8 hours after, and then once a day in the evening for 5 to 9 days after the procedure.

A team of British, Danish, Dutch, and German researchers now reports that rivaroxaban (BAY 59-7939) may be a suitable oral anticoagulant equally as effective as enoxaparin and with similar or fewer side effects. rivaroxaban inhibits coagulation Factor X, has a rapid onset of action, can be given in one daily dose, and does not require titration and frequent monitoring.

The phase II randomized, double-blind clinical trial involved 852 patients who were assigned to receive various doses of rivaroxaban (5, 10, 20, 30 or 40 mg) or 40 mg of enoxaparin 6-8 hours after completion of surgery and then once a day in the evening for the next 5-9 days. An enoxaparin injection was also given on the evening before surgery for the patients in the enoxaparin group.

Thromboembolic complications occurred in 25.2% of patients receiving enoxaparin and in 6.4% to 14.9% of those receiving rivaroxaban. Major postoperative bleeding (the major adverse effect of both drugs) was observed in 1.9% of patients receiving enoxaparin and in 0.7% to 5.1% of those receiving rivaroxaban. Detailed results are presented below:

		Thromboembolic	Major Bleeding
Drug	Dosage, mg	Events, %	Events, %
Enoxaparin	40	25.2	1.9
Rivaroxaban	51	4.9	2.3
Rivaroxaban	10	10.6	0.7
Rivaroxaban	20	8.5	4.3
Rivaroxaban	30	13.5	4.9
Rivaroxaban	40	6.4	5.1

The researchers conclude that 10 mg/day of rivaroxaban may be the optimum dose when considering both efficacy and safety. A large phase III trial is being planned. About 4% of patients in the rivaroxaban group experienced an increase in aminotransferase levels indicating possible liver toxicity. NOTE: This study was funded by Bayer, the developer of rivaroxaban.

Eriksson, BI, et al. A once-daily, oral, direct Factor Xa inhibitor, rivaroxaban (BAY 59-7939), for thromboprophylaxis after total hip replacement. Circulation, *Vol. 114, November 28, 2006, pp. 2374-81*

Mahaffey, KW and Becker, RC. The scientific community's quest to identify optimal targets for anticoagulant pharmacotherapy. Circulation, *Vol. 114, November 28, 2006, pp. 2313-16*

Editor's comment: It is encouraging to see continued research on finding a worthy successor to warfarin, but the results for rivaroxaban are not very impressive and I doubt that it will prove suitable for long-term use unless the liver toxicity problems are eliminated. Thus, it is not likely to be the "white knight" many afibbers are eagerly awaiting. Another agent, dabigatran, has also shown promising results and is now undergoing phase III trials. Dabigatran belongs to the same class of anticoagulants as ximelagatran, so potential liver toxicity will no doubt be monitored closely.

Warfarin + aspirin – Not a good idea!

COLUMBIA, MISSOURI. Patients at high risk for cardiovascular events are sometimes prescribed a combination of warfarin and aspirin in an attempt to provide added protection. Now a team of researchers from Canada, Finland, France, and the United States reports that the combination does not confer added stroke protection among patients with atrial fibrillation, but does increase the incidence of major and minor bleeding events.

The study involved 7300 patients who participated in the SPORTIF III and V trials comparing the efficacy and safety of warfarin and ximelagatran for stroke prevention in AF patients. (NOTE: The trial participants were not lone afibbers, but afibbers with a high risk of ischemic stroke). The trial protocol discouraged the concomitant use of aspirin, but doses up to 100 mg/day were allowed at the discretion of participating physicians. Those prescribed aspirin were significantly more likely to have diabetes, coronary artery disease, and left ventricular dysfunction.

Trial participants were followed for an average of 16.5 months during which time INR was closely controlled between 2.0 and 3.0 and all strokes (ischemic or hemorrhagic), transient ischemic attacks (TIAs), and major and minor bleeding events were recorded. Bleeding events were

defined as major if fatal, involving a critical anatomical site, or requiring transfusion of 2 units of blood or more.

The researchers found no significant difference in the incidence of stroke between patients taking warfarin and those taking warfarin + aspirin nor was there any difference between patients taking ximelagatran and those taking ximelagatran + aspirin. Overall, annual ischemic stroke rates ranged from 1.2% to 1.7%. The incidence of major bleeding events was, however, significantly higher for patients taking warfarin + aspirin (3.9%/year) than for those taking warfarin alone (2.3%/year). The rate of minor bleeds was also significantly higher when aspirin was added with a rate from warfarin alone of 37% vs. 63% with warfarin + aspirin. The most common site for major bleeds was the gastrointestinal tract.

The researchers conclude that the results suggest that the risks associated with addition of aspirin to anticoagulation in patients with atrial fibrillation outweigh the benefits.

Flaker, GC, et al. Risks and benefits of combining aspirin with anticoagulation therapy in patients with atrial fibrillation: An exploratory analysis of stroke prevention using an oral thrombin inhibitor in atrial fibrillation (SPORTIF) trials. American Heart Journal, *Vol. 152, November 2006, pp. 967-73*

Vitamin B6 helps protect against stroke

UDINE, ITALY. Italian researchers now confirm that low blood levels of vitamin B6 (pyridoxine) are a strong risk factor for heart attack, angina, and ischemic stroke. Their study involved 1021 healthy middle-aged subjects (490 men and 531 women) who were followed for 12 years after having undergone a baseline medical examination complete with extensive blood sampling. During the follow-up members of the group experienced 30 heart attacks (of which 15 were fatal), 36 cases of unstable angina, 29 ischemic strokes, and 14 transient ischemic attacks (TIAs) for a total of 109 coronary and cerebrovascular events (0.9% a year).

The researchers found that study participants with a vitamin B6 level of 40 nmol/L had a 31% lower risk of a cardiovascular or cerebrovascular event than did patients with a level of only 15 nmol/L. They also observed that an elevated homocysteine level (14 micromol/L) was associated with a 34% greater risk than a level of 9.8 micromol/L. There was no indication that the blood level of folate and vitamin B12 had any correlation with the risk of stroke or heart attack, nor was there any indication that the plasma concentration of C-reactive protein did. A combination of low vitamin B6 and high homocysteine levels was found to be particularly dangerous with this combination conferring an 18 times greater risk of experiencing an event than the risk associated with a low homocysteine level and a high vitamin B6 level.

The researchers conclude that high homocysteine and low vitamin B6 plasma levels are long-term independent risk factors for coronary and cerebrovascular events.

Vanuzzo, D, et al. Both vitamin B6 and total homocysteine plasma levels predict long-term atherothrombotic events in healthy subjects. **European Heart Journal,** *Vol. 28, 2007, pp. 484-91*

Editor's comment: A daily intake of 40 mg of vitamin B6 (pyridoxine) will result in a plasma level of about 230 nmol/L. Most well-formulated multivitamins contains about 25-30 mg of B6 so should provide adequate protection.

New antiplatelet/anticoagulation combination for AF patients

MADRID, SPAIN. Triflusal is an antiplatelet agent similar to aspirin, but not derived from acetylsalicylic acid. Several clinical trials in Europe have found it equivalent to aspirin in its ability to prevent cardiovascular events, but less likely to cause internal bleeding. Clinical trials have shown that 600 mg/day of triflusal is equivalent to 300 mg/day of aspirin as far as clinical efficacy is concerned.

Spanish researchers have just completed a clinical trial aimed at comparing the efficacy and safety of full-dose warfarin therapy (INR = 2.0-3.0) and a combination of triflusal (600 mg/day) with a reduced warfarin dose (INR = 1.25-2.0 or 1.4-2.4 if classified as high-risk). The trial involved 967 patients with atrial fibrillation, about 40% of which had hypertension and 10% had ischemic heart disease. The majority (77%) of trial participants were younger than 75 years of age. The researchers noted that older patients needed significantly less warfarin (1.9 mg/day vs. 2.1 mg/day) than younger patients to stay within INR range in the warfarin only group of the trial as well as in the triflusal/warfarin group (1.45 mg/day vs. 1.7 mg/day).

At the end of the trial the researchers made the following observations:

- For trial participants with no prior embolism, the total percentage of serious adverse events (fatal and non-fatal ischemic or hemorrhagic stroke/TIA, systemic embolism, heart attack, sudden death, and death from bleeding) in the elderly group (75 years of age or older) receiving warfarin alone was 4.6%/year vs. 1.8%/year in the younger group. The corresponding numbers for patients on the combination (triflusal + warfarin) were substantially lower at 1.1%/year and 0.8%/year respectively.

- For trial participants with prior embolism, the event rate in the warfarin only group was 11.1%/year in the older group vs. 4.6%/year in the younger group. Corresponding numbers for the combination were 5.0%/year and 3.4%/year.

- Survival of elderly patients was substantially higher in the combination group. This was largely due to the fact that those in the warfarin group experienced more intracranial bleeding events (hemorrhagic stroke) than did those in the combination group (3.1% vs. 0.2%). Elderly warfarin group participants also suffered more fatalities from internal bleeding (2.1%/year vs. 0.3%/year in combination group). The non-fatal gastric bleeding rate was, however, higher in the combination group. The authors of the study point out that, in their experience, patients treated with warfarin alone tend to have more, usually fatal, intracranial bleeding complications, while those receiving combined therapy tend to experience more non-fatal upper gastrointestinal bleeding.

The Spanish researchers conclude that combination therapy (triflusal + low-dose warfarin) significantly reduces vascular events and bleeding mortality in elderly patients.

Perez-Gomez, F, et al. Antithrombotic therapy in elderly patients with atrial fibrillation: Effects and bleeding complications. European Heart Journal, *Vol. 28, 2007, pp. 996-1003*

Editor's comment: It is interesting to note that, while the percentage of events (outcome rate) for patients on combination therapy is fairly low (2.3% and 1.5%) in both older and younger patients, the outcome rate is quite different for those on warfarin. Here the outcome rate is 7% for the older patients versus 2.5% for younger ones, again proving that warfarin alone is a poor choice for older afibbers. Triflusal, unfortunately, is not available in North America.

Folic acid reduces risk of stroke

BEIJING, CHINA. There is substantial evidence that high levels of the amino acid homocysteine increase the risk of atherosclerosis and ischemic stroke. Homocysteine levels can be reduced by supplementation with B vitamins, specifically folic acid, vitamin B6, and vitamin B12. It is, however, not clear whether B vitamin supplementation as such decreases the risk of stroke and cardiovascular disease. Now a group of Chinese researchers report that folic acid supplementation is indeed effective in reducing the risk of ischemic stroke.

The researchers analyzed data from 8 randomized clinical trials involving almost 17,000 participants. The trials compared folic acid

supplementation (with or without combination with vitamins B6 and B12) with either a placebo, a lower does of folic acid, or usual care for a minimum duration of 6 months. The researchers conclude that folic acid supplementation reduces stroke risk by 18% overall. Longer term supplementation (more than 3 years) results in a greater (29%) reduction in stroke risk as does a homocysteine reduction of 20% or more. The beneficial effect of folic acid supplementation was found to be greater in countries where folic acid fortification of grains is not mandatory indicating perhaps that once an adequate folate status has been achieved, no further benefit is obtained by additional supplementation. The researchers also observed no benefit of supplementation in study participants who had already suffered a previous stroke. They conclude that folic acid supplementation is effective in the prevention of a first stroke (primary prevention).

Wang, X, et al. Efficacy of folic acid supplementation in stroke prevention. **The Lancet**, *Vol. 369, June 2, 2007, pp. 1876-82*

The warfarin conundrum

BOSTON, MASSACHUSETTS. Anticoagulation with warfarin is currently recommended for afibbers with one or more risk factors for ischemic stroke (hypertension, heart failure, diabetes, prior stroke, prosthetic heart valve, and age above 75 years). Warfarin therapy, unfortunately, is associated with an increased risk of major hemorrhage (internal bleeding) generally estimated at about 2%/patient-year. Major hemorrhage is defined as internal bleeding that is fatal, requires hospitalization with blood transfusion, or involves a critical site such as the brain. Although the indications for warfarin therapy generally increase with age, there is some concern that the risk of major hemorrhage may increase even more with age. Researchers at the Boston University School of Medicine now report that the rate of warfarin-related serious internal bleeding is much higher among afibbers 80 years or older than previously thought.

Their study included 472 afibbers most of whom (91%) had one or more risk factors for stroke and 35% of whom had coronary artery disease. Thirty-two percent were 80 years of age or older and 40% overall were on aspirin. All afib patients were started on warfarin (INR 2.0 – 3.0) at discharge from hospital and followed for a year. Management of warfarin therapy was done at the Massachusetts General Hospital. Highlights from the study are as follows:

- Only 58% of total time on warfarin was spent within the recommended window of 2.0 – 3.0 INR.

- Patients with the highest risk of ischemic stroke also experienced most of the bleeding.

- 13% of patients aged 80 years or older experienced a major hemorrhage during the first year of therapy as compared to 4.75% in the group younger than 80 years. The first 90 days of therapy were associated with a 3-fold increased risk.

- By the end of the first year, 134 patients (28%) had been taken off warfarin either because they had regained sinus rhythm or because they had suffered serious bleeding. In the age group 80 years and above, 81% of warfarin discontinuations were due to safety concerns.

The researchers conclude that previously published rates of bleeding during warfarin therapy underestimate the incidence actually experienced in clinical practice, particularly in the age group 80 years and above.

Hylek, EM, et al. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation, *Vol. 115, May 29, 2007, pp. 2689-96*

Wyse, DG. Bleeding while starting anticoagulation for thromboembolism prophylaxis in elderly patients with atrial fibrillation. Circulation, *Vol. 115, May 29, 2007, pp. 2684-86*

Editor's comment: As is common in trials and studies involving warfarin, there was no comparison group in this study. Thus, it is not clear whether the benefit (avoidance of ischemic stroke) of warfarin outweighs the risks (major hemorrhage including often fatal hemorrhagic stroke) especially in older afibbers. As Dr. George Wyse of the University of Calgary states in an accompanying editorial, "It would be extremely useful if one were able to estimate a net benefit comparing the risk of bleeding and the risk of thrombotic stroke."

Complication of *Watchman* implantation

VIENNA, AUSTRIA. The left atrial appendage (LAA) is believed to be the main source of blood clots (thrombi) involved in ischemic stroke among AF patients with underlying heart disease. Because of this, the LAA is often removed or sewn/stapled shut during cardiac surgery such as in the maze and mini-maze procedures. Another approach to avoiding stroke due to LAA thrombi is by blocking the opening to the left atrium itself. This is done by inserting a self-expanding, teflon-coated nitinol cage in the LAA opening so as to block it completely. The expanded cage is about 30 mm in diameter and is delivered to the LAA (in collapsed form) via a catheter threaded through a vein in a procedure similar to that used in radiofrequency ablation. Two blocking systems are currently in use – the PLAATO device and the WATCHMAN device.

Austrian cardiologists now report a case of a 78-year-old AF patient who had a *Watchman* device implanted in November 2005. About 10 minutes

after implantation the device worked itself loose and became lodged in the aortic valve. Attempts to remove it destroyed the valve and a prosthetic valve had to be implanted during open heart surgery, which included sewing the LAA shut. The operation was followed by numerous complications including pleural effusions, bradycardia and complete heart block necessitating the implantation of a permanent pacemaker. The patient now has heart failure and is on warfarin, carvedilol, enalapril, furosemide and aspirin.

The authors of the report speculate that the closure of the LAA may have been responsible for some of the post-surgical complications; they point out that the LAA releases natriuretic hormones and has other important functions including the prevention of elevated intra-atrial pressure and accompanying pulmonary congestion.

Stollberger, C, et al. Serious complications from dislocation of a Watchman left atrial appendage occluder. Journal of Cardiovascular Electrophysiology, *Vol. 18, August 2007, pp. 880-81*

Editor's comment: This report adds to the growing evidence that tampering with the left atrial appendage in order to avoid stroke may not be a good idea. There certainly would be no justification for doing so in the case of lone afib where LAA thrombi have never been observed.

A vitamin C + vitamin E combination may help prevent stroke

BOSTON, MASSACHUSETTS. Despite the fact that antioxidants such as vitamin C and vitamin E exert their beneficial effects by delaying the **ONSET** of certain age-related diseases, the medical community continues to attempt to disprove their benefits by applying them to patient populations who are already sick. This is disingenuous at best, blatantly dishonest at worst. Dietary antioxidants (in commonly used doses) are effective in **PRIMARY** prevention of disease, **NOT** in **SECONDARY** prevention, i.e. for patients already suffering from disease (heart disease, cancer, etc).

Researchers at the Brigham and Women's Hospital and the Harvard Medical School recently reported yet another clinical study designed to prove the worthlessness of dietary antioxidants. The patient population consisted of 8171 female health professionals above the age of 40 years. The majority (64%) had been diagnosed with cardiovascular disease and the remaining 36% had 3 or more risk factors for cardiovascular disease (hypertension, high cholesterol level, diabetes, or a family history of heart attack). About 77% of the group was overweight with 48% being obese.

The women were randomized to receive placebo, vitamin C (500 mg/day of synthetic ascorbic acid), vitamin E (600 IU every second day of d-alpha-tocopherol acetate), or a combination of vitamins C and E. A subgroup

also received 50 mg every other day of synthetic beta-carotene either with or without vitamins C and E. During an average follow-up of 9.4 years, 274 of the women experienced a heart attack (myocardial infarction), 889 underwent angioplasty or bypass surgery, and 395 died from cardiovascular events.

There was no difference in the overall incidence of cardiovascular events among women who had supplemented with vitamin C and those who had been given placebos. However, patients who had been given vitamin E (and had stuck with the regimen) experienced a statistically significant 13% reduction in cardiovascular events over the follow-up period, a 22% reduction in heart attacks, and a 27% reduction in stroke. Overall, the incidence of heart attack, stroke and cardiovascular death was reduced by 23% in the group of vitamin E supplementers who continued their supplementation throughout the trial period. Furthermore, participants who had been randomized to take both vitamin C and vitamin E experienced a statistically significant 31% reduction in stroke incidence.

The researchers conclude that, "*There were no overall effects of ascorbic acid, vitamin E, or beta-carotene on cardiovascular events among women at high risk for CVD*". They also conclude that, "*We found no detrimental effects of any of these agents on total or CVD mortality*". In other words, while antioxidant supplementation may be of no value, it is at least not likely to cause any harm. The researchers also make the following interesting comment:

"*For vitamin E, there have been suggestions that gamma tocopherol is a more powerful antioxidant. Supplementation with alpha tocopherol depletes gamma tocopherol, which may explain the lack of effect seen in vitamin E trials*".

In other words, they used the least effective form of vitamin E in their trial, one that will, in addition, deplete the level of the most effective form.

Cook, NR, et al. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women. **Archives of Internal Medicine**, *Vol. 167, August 13/27, 2007, pp. 1610-18*

Editor's comment: This is clearly another hatchet job on antioxidants. Only by including participants who had not been following the study protocol (i.e. those who had NOT been taking antioxidants as directed) were the researchers able to "prove" that antioxidants have no benefit in SECONDARY prevention. When those participants who had not followed the protocol were censored out, vitamin E proved to be highly effective, and a combination of vitamin C and E actually reduced stroke incidence by 31% - a performance significantly better than that of aspirin.

Odds and Ends

Resting heart rate and lifespan

ZURICH, SWITZERLAND. Resting heart rate (RHR) usually averages 60-80 beats a minute (bpm), but can occasionally exceed 100 bpm in unconditioned, sedentary individuals and be as low as 30 bpm in highly trained endurance athletes. It has long been known that patients with coronary heart disease and an elevated RHR have a shorter life expectancy than do those with a normal or low RHR.

Swiss researchers now suggest that an elevated RHR may also be associated with a reduced lifespan in the general population. They point out that among mammals RHR is generally inversely proportional to life expectancy – small animals have a higher RHR and shorter lifespan than do larges ones. As a matter of fact, the average number of heartbeats per lifetime in most mammalians is pretty well constant at about 7×10^8. The researchers provide the fascinating comparison of a shrew (weighing 2 g) and having a heart rate of 1000 bpm with a blue whale (weighing 100,000 kg) and having a heart rate of 6 bpm. The lifespan of the shrew is 1 year, while that of the blue whale is 118 years. Interestingly, the total lifetime oxygen consumption of the two species is very similar at about 37,000 litres/kg/lifetime.

For some unknown reason, humans deviate from the normal semi-logarithmic relationship between RHR and life expectancy in that they (barring any fatal diseases or accidents) are good for about 30×10^8 heartbeats per lifetime. The researchers provide pretty compelling arguments for their hypothesis and pose the fascinating question, "Does RHR causally determine lifespan and if so, what can be done to maximize it?"

It is estimated that a high RHR is genetically ordained in about 21-26% of cases. A high body mass index, hypertension, smoking, alcohol consumption, and the metabolic syndrome probably account for at least another 20%. Some very recent research postulates a common link between an elevated RHR and the metabolic syndrome, namely, a lack of nitric oxide, which modulates the autonomic control of RHR. It is also an established fact that regular endurance training increases parasympathetic activity and decreases sympathetic activity in the human heart resulting in a significant reduction in RHR.

Unfortunately, it is not clear whether the use of beta-blockers or calcium channel blockers to lower an elevated RHR will actually increase the lifespan of people without heart disease. However, it is known that preventing anxiety and stress, and avoiding toxics (caffeine, alcohol, nicotine, amphetamines, cocaine) can all reduce RHR – as can pet ownership. The search for new drugs that will reduce RHR without the side effects of beta- and calcium channel blockers is ongoing with one of the more promising candidates being ivabradine (Procoralan) which acts specifically on the sinus node to reduce RHR.

The researchers conclude their intriguing article by calling for large clinical trials to determine if any drug-induced reduction in RHR will indeed extend the life expectancy of healthy people.
Cook, S, et al. High heart rate: a cardiovascular risk factor? European Heart Journal, *Vol. 27, 2006, pp. 2387-93*

Editor's comment: I found this article absolutely fascinating but, you may well ask, what has it got to do with lone atrial fibrillation? Several related questions immediately come to mind:

1. Can afibbers with asymptomatic permanent afib (without underlying heart disease) and uncontrolled RHR expect a shorter lifespan?
2. Can permanent afibbers (with no underlying heart disease) with RHR controlled by beta- or calcium channel blockers expect a shorter lifespan?
3. Many afibbers experience an elevated RHR for months, if not years, post-ablation or maze procedure. Will this, albeit temporary, rapid depletion of their lifetime heartbeat "capital" reduce their lifespan? Would medication with beta- or calcium channel blockers prevent the effects of this depletion? Should endurance exercise be "prescribed" for this group of afibbers?
4. There is some evidence that non-inherited elevated RHR is associated with a defect in the bioavailability of nitric oxide (NO). Would taking NO-generating medications such as NO-ASA (nitroxy-butyl-acetylsalicylate) or the amino acid, l-arginine, help reduce an elevated RHR experienced after an ablation or maze procedure?

These are all vital and intriguing questions. Hopefully, future medical research will address them.

Hospital data now on the Internet

The US Department of Health and Human Services has added mortality data to their web site, which compares the performance of 4800 hospitals in the USA. The web site can be found at http://www.hospitalcompare.hhs.gov

New exercise guidelines

DALLAS, TEXAS. An expert panel of physicians, epidemiologists, exercise scientists, and public health specialists has released updated recommendations for the level of physical activity required to achieve and maintain optimum health. These recommendations are endorsed by the American College of Sports Medicine and the American Heart Association, and apply to all healthy adults between the ages of 18 and 65 years. There is compelling evidence that lack of regular physical activity substantially increases the risk of cardiovascular disease, hypertension, ischemic stroke, diabetes, osteoporosis, obesity, colon cancer, depression, and anxiety. Despite this, a 2005 survey concluded that less than half of the US adult population meets the recommended physical activity levels.

The expert panel recommends that all healthy adults aged 18 to 65 years engage in at least 30 minutes of moderate-intensity aerobic physical activity on 5 days each week, or vigorous-intensity aerobic activity for a minimum of 20 minutes on 3 days of the week. Combinations of moderate and vigorous exercise are also acceptable and the 30 minutes of moderate physical activity can be met, for example, by 3 individual bouts of 10 minutes each. The panel emphasizes that physical exercise over and above the recommend minimum can be expected to lead to reduced premature mortality and further health improvements, particularly in regard to cardiovascular health. The panel also recommends activities that maintain and increase muscular strength for a minimum of 2 days each week. Such activities would include stair climbing, weight training, and weight-bearing calisthenics.

The intensity of physical exercise is usually expressed in terms of energy expenditure which, in turn, is expressed in **metabolic equivalents** (MET). One MET represents an individual's energy expenditure while sitting quietly for 1 minute (equivalent to about 1.2 calories/minute for a person weighing 160 lbs). Moderate activity is associated with a MET equivalent of 3-6 METs per minute, while vigorous exercise is associated with METs greater than 6. METs for some common activities are given below:

- Walking at 3 mph (5.0 km/h) 3.3 MET
- Walking at very brisk pace of 4 mph (6.4 km/h) 5.0 MET

- Bicycling on flat surface at 10-12 mph (16-19 km/h) 6.0 MET
- Bicycling fast at 14-16 mph (22-26 km/h) 10.0 MET
- Golfing (walking and pulling clubs) 4.3 MET
- Swimming (leisurely) 6.0 MET
- Swimming (moderate to hard) 8.0-11.0 MET
- Hiking at moderate pace with light or no pack 7.0 MET
- Hiking at steep grades and heavy pack 7.5-9.0 MET
- Jogging at 5 mph (8 km/h) 8.0 MET
- Cross-country skiing (slow) 7.0 MET
- Cross-country skiing (fast) 9.0 MET
- Competitive soccer 10.0 MET

Thus, 30 minutes of walking at 3.0 mph would accumulate 99 METs (3.3x30) and jogging for 20 minutes at 5 mph would accumulate 160 METs (8x20). The panel suggests a minimum weekly MET accumulation of 450 to 750 METs be achieved through specific physical exercise.

The panel makes the interesting observation that exercise is relatively ineffective in achieving weight loss, but that a very much increased level of activity is required to maintain a weight loss achieved by other means. They also acknowledge that the risk of musculoskeletal injury increases substantially with increased physical activity and can affect as many as 55% of people involved in jogging programs and US Army basic training. The risk of cardiac arrest and heart attack also increases during vigorous physical exercise, especially among infrequent exercisers. Nevertheless, the panel concludes that, in the case of healthy individuals, the benefits of regular moderate to vigorous physical activity far outweighs the risks. They also suggest that healthy men and women do not need to consult with a physician or other healthcare provider prior to embarking on a regular exercise program. However, those with cardiovascular disease, diabetes, or other chronic diseases should clearly do so.

I an accompanying article Miriam Nelson of Tufts University and other members of a separate panel outline physical activity recommendations for those above the age of 65 years and adults aged 50-64 years with clinically significant chronic disease conditions or functional limitations. The recommendations are identical to those discussed above, except that the definition of *moderate* and *vigorous* exercise is tailored to the individual's basic fitness level rather than given as specific MET targets. The guidelines also include specific recommendations for flexibility and balance exercises which are especially important for older individuals. The researchers provide the following sobering statistics in regards to chronic disease prevalence among Americans over the age of 65 years:

- Arthritis 49%
- Hypertension 40%

- Heart disease 31%
- Osteoporosis (women) 26%
- Diabetes 13%

Haskell, WL, et al. Physical activity and public health. Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation, *Vol. 116, August 28, 2007*
Nelson, ME, et al. Physical activity and public health in older adults. Updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation, *Vol. 116, August 28, 2007*

Specialized centers benefit AF patients

The University of Virginia (Charlottesville) and the Oregon Health and Science University (Portland) have both opened special centers for afib patients. The centers provide education, check the appropriateness of previously prescribed medications, address other medical issues such as sleep apnea, and arrange for catheter ablation if necessary. A survey carried out at the University of Virginia found that 76% of afibbers admitted to the center were on the wrong kind or dosage of medications. The patients spent an average of 39% of their time in afib when joining the center program. This was reduced to 15% when appropriate medications were prescribed. About 20% of those undergoing ablation procedures experienced recurrence, but nevertheless reduced their AF burden considerably.
http://www.theheart.org/printArticle.do?primaryKey=789831

Research Reports

Aspirin: Friend or Foe?

Hans R. Larsen

It is estimated that more than 50 million Americans now take a daily aspirin (acetylsalicylic acid) for prevention of cardiovascular disease. This translates into roughly 10 billion to 20 billion tablets consumed annually in the US alone[1].

The 2006 *Guidelines for the Management of Patients with Atrial Fibrillation* recommends that afibbers with no risk factors for ischemic stroke (hypertension, diabetes, heart failure, left ventricular ejection fraction below 0.35, heart disease, rheumatic heart disease, thyrotoxicosis, prior heart attack, stroke or TIA, or presence of prosthetic heart valves) take 81 to 325 mg of aspirin daily for stroke prevention[2]. This research report will examine whether this is a reasonable recommendation.

Stroke Risk in Lone Atrial Fibrillation

Several major clinical trials and epidemiologic studies have concluded that atrial fibrillation is associated with an increased risk of ischemic stroke. Although this conclusion is likely valid for afibbers with heart disease and other risk factors, there is no evidence that lone afibbers with none of the above risk factors have an increased risk[3]. Medical experts are pretty unanimous on this point. Dr. Rodney Falk, MD of Boston University, a world-renowned expert on atrial fibrillation, says that the stroke risk in patients with lone atrial fibrillation is minimal[4]. Professor Michael D. Ezekowitz, MD of the Veterans Administration says, "patients with lone atrial fibrillation are not at higher risk for thromboembolism than the general population and can be managed without anticoagulation or anti-platelet therapy"[5]. Dr. Stephen L. Kopecky of the Mayo Clinic did the first study regarding stroke risk in patients with lone atrial fibrillation. He found that lone afibbers under the age of 60 years had an exceptionally low stroke risk (0.55%/person-year) and that this risk varied little whether the fibrillation was paroxysmal or permanent[6].

More recently, researchers at the Mayo Clinic published a study regarding the correlation between lone atrial fibrillation (LAF) and stroke risk and overall mortality. The study is remarkable in that it followed the participants for 30 years and thus gives a good indication of the long-term prognosis for untreated LAF. The study involved 46 residents of Olmsted County who were diagnosed with LAF at an average age of 45.8 years (range of 34-58 years). None of the participants had coronary artery disease, hypertension, diabetes, mitral valve prolapse, congestive heart

failure, or any other condition that would increase their risk of ischemic stroke (cerebral infarction). None of the participants were treated with warfarin. They were followed until death or July 1, 2002. At time of last follow-up the average age was 74 years (range of 63-85 years). At the beginning of the study 76% of participants had paroxysmal afib and 24% had the persistent variety; this changed to 59% paroxysmal and 41% persistent by the end of the study period. All participants were Caucasians and 83% were men.

The Mayo researchers made the following important observations:

1. The observed mortality rate among the afibbers over a 25-year period was substantially lower (15.9%) than the mortality expected in a group of age- and sex-matched white Minnesotans (32.5%).

2. The incidence of ischemic stroke (cerebral infarction) in the afib group was no greater (0.5%/person-year) than in the general population. The researchers conclude that, "This observation indicated that the pathophysiological mechanisms responsible for the development of a cerebrovascular event were unrelated to the continued presence of AF." In other words, LAF as such is not associated with an increased risk of stroke[7].

So why should lone afibbers, with no risk factors for stroke, worry about an increased risk of ischemic stroke? They probably should not, but the authors of the latest guidelines obviously believe that they should.

Ischemic Stroke

There are two types of ischemic stroke – thrombotic and embolic. Both involve the obstruction and subsequent stoppage of the blood supply to an area of the brain (infarction). However, the mechanism by which the obstruction occurs differs.

A thrombotic stroke involves the formation of atherosclerotic plaque and subsequent narrowing and clot (thrombus) formation at the point of obstruction. In an embolic stroke, on the other hand, the obstruction is caused by the lodging of an embolus (blood clot or atherosclerotic plaque) formed in the heart or in an artery outside the brain. Cardiogenic emboli (blood clots originating in the heart) can form on heart valves, particularly prosthetic ones, or as a result of mitral stenosis. Cardiogenic emboli can also originate from the walls of the heart as a result of a heart attack (myocardial infarction), atrial fibrillation or congestive heart failure or from a benign atrial tumour (myxoma).

By far, the majority of strokes occurring in atrial fibrillation are cardioembolic. Anticoagulation with warfarin provides significant protection against this type of stroke, while antiplatelet therapy with aspirin has very limited effect[8]. This should come as no great surprise since thrombi originating in the left atrium tend to be rich in fibrin rather than in platelets[9]. The magic number of 22% reduction in ischemic stroke, eg. from about 2.8%/year to 2.2%/year in a 70-year-old male with hypertension, is often mentioned in connection with aspirin prophylaxis. However, there is now some doubt whether this observed risk reduction is related to AF at all. Dr. Gregory Lip of the University of Birmingham recently made the following observation in an editorial discussing the merits of prescribing aspirin for patients with atrial fibrillation:

> *"Since AF frequently co-exists with vascular disease, it is likely that we are seeing an effect of aspirin on vascular disease, rather than on stroke associated with AF per se. Also, thrombogenesis in AF is largely coagulation-related and the platelet abnormalities in AF, where present, are not much more than that seen with the associated vascular disease alone."*[10]

He also questions the soundness of the 2006 Guidelines with the following statement:

> *"Many guidelines still recommend aspirin for 'low-risk' patients with AF, but the recent Japanese Atrial Fibrillation stroke trial even questions this approach, showing that aspirin was no better (or perhaps worse) than placebo in low-risk AF patients. Indeed, the use of aspirin may be to treat (or reassure) the prescriber, rather than the patient."*[10]

Aspirin in Stroke Prevention

There is no evidence that daily aspirin consumption protects against a first ischemic stroke[11]. As a matter of fact, there is now evidence that it may do more harm than good in low-risk patients with atrial fibrillation. In a 2005 study of 871 low-risk AF patients Japanese researchers conclude that daily aspirin therapy (150-200 mg/day) in this group is neither effective nor safe. They actually observed more cardiovascular deaths, strokes and TIAs in the aspirin group than in the placebo group. In addition, fatal or major bleeding was found to be more frequent in the aspirin group than in the placebo group. Overall, the incidence of strokes, deaths and other adverse events was 42% greater in the aspirin group than in the placebo group. The trial was stopped early since the

probability that aspirin would prove superior to placebo in stroke prevention, if it continued, was deemed to be vanishingly small[12].

Aspirin in Prevention of Heart Attacks

In 2003, five clinical trials designed to determine the benefits of aspirin therapy in the prevention of a first heart attack were reviewed in a study funded by Bayer, the manufacturer of aspirin[13]. Two of the trials, the Physicians Health Study and the British Doctors Trials, involved a total of 27,210 healthy men aged 40-84 years. The participants were followed for a mean of 5 and 6 years respectively. The rate of nonfatal heart attack was 0.28% per year in the aspirin group and 0.40% per year in the placebo group; that is, an absolute risk reduction of 0.12% or a relative risk reduction of 30%. Two other studies involving men and women at high risk for cardiovascular disease revealed an incidence rate of 0.53% per year for nonfatal heart attack in the aspirin group versus 0.76% in the placebo group; that is, an absolute risk reduction of 0.23% or a relative risk reduction of 31%.

Considering that the risk of hemorrhagic stroke and fatal bleeding is about 0.2% per year, and that of major gastrointestinal bleeding is about 0.5% per year, it is clear that long-term aspirin therapy for the prevention of a first heart attack (primary prevention) is not appropriate. This is recognized in the FDA's 2003 decision not to approve aspirin for long-term use in the **primary prevention** of heart attacks[14].

More recently, researchers at the University of Alabama performed a meta-analysis of six clinical trials involving 47,293 aspirin users and 45,580 controls not on aspirin who had no prior indication of cardiovascular disease. This study differed from the previously discussed one in that it included data from the recently completed Women's Health Study. The dosage of aspirin involved in the trials varied from 75 mg/day to 500 mg/day. The researchers conclude that regular aspirin use reduces the relative risk of experiencing a first non-fatal heart attack by 24%, that of developing coronary heart disease by 23%, and reduces the risk of any cardiovascular event by 15% (relative). No risk reduction was observed for stroke, cardiovascular mortality or all-cause mortality. The authors conclude that their analysis supports the current industry recommendation for the use of aspirin for primary prevention in patients with a high risk of cardiovascular disease (10-year risk of 6% or higher). Unfortunately, they completely ignore the downside of aspirin usage – a substantially increased risk of hemorrhagic stroke and major gastrointestinal bleeding. (NOTE: This study was funded by Bayer, the major manufacturer of aspirin).[11]

A meta-analysis of 5 of the 6 trials discussed above clearly shows that long-term aspirin usage increases the relative risk of hemorrhagic stroke (stroke caused by a burst blood vessel) by about 40% and the risk of major gastrointestinal bleeding by 70%. Thus, it would seem prudent to keep in mind the conclusion of the U.S. Preventive Services Task Force, "Patients at low risk for coronary heart disease probably do not benefit from and may even be harmed by aspirin because the risk for adverse events may exceed the benefits of chemoprevention."[15]

Aspirin does, however, have a significant role to play in preventing death when a first heart attack is actually experienced. Several large-scale trials have shown that taking as aspirin as soon as possible after feeling the first symptoms of a heart attack can reduce the risk of dying by 23%. Medical doctors at the Texas Southwestern Medical School have found that the aspirin should be chewed rather than swallowed whole in order to minimize the time it takes for it to take effect. Aspirin works by blocking the synthesis of thromboxane, a metabolite of arachidonic acid, which is involved in the formation of blood clots. Aspirin enters the blood stream very quickly and swallowing a chewed tablet with water was found to inhibit thromboxane formation by 50% after 5 minutes and by 90% after 14 minutes[16].

There are several useful tools available on the Internet for determining your risk of future coronary heart disease. You can find two at
http://www.intmed.mcw.edu/clincalc/heartrisk.html
http://www.med-decisions.com

Optimum Dosage of Aspirin

Although people with low risk for future coronary heart disease events would likely not benefit from a daily aspirin, there are groups of patients who would indeed do so, especially patients who have already suffered a thrombotic stroke or a heart attack. An obvious question is how much aspirin is required on a daily basis to achieve optimum protection? A recent review by a team of French and American physicians provides a plausible answer.

One 300-mg dose of aspirin irreversibly destroys the ability of platelets to form the aggregates that are involved in thrombotic, ischemic stroke. The platelets recover their ability to aggregate at a rate of about 10% a day. Thus, a prophylactic regimen of a one-time, 325-mg dose (standard dosage) followed by a daily dose of 81 mg (baby aspirin) or even half a baby aspirin would provide the full beneficial effect of aspirin as far as prevention of secondary cardiovascular events is concerned. Limited data suggest that 100 mg of aspirin every other day is also effective in suppressing platelet function.

The 300-mg loading dose, if taken in oral form, is effective within about an hour of ingestion. However, absorption and complete destruction of platelet activity can be achieved in half this time by chewing the tablet, or by taking the aspirin in the form of Alka-Seltzer[1].

The authors of this study point out that no clinical trial has ever demonstrated that taking large doses of aspirin on a daily basis is more effective than smaller doses over the range of 30 mg to 1300 mg a day[1].

Safety of Aspirin

Aspirin is not innocuous. It can cause serious bleeding in the gastrointestinal tract and can aggravate existing ulcers. The estimated death rate from gastrointestinal (GI) bleeding ranges from 8-12% of all cases. Researchers at Oxford University have released the results of a very large study aimed at establishing the magnitude of aspirin-related bleeding incidents. They carefully studied the results of 24 major randomized clinical trials involving almost 66,000 participants. They conclude that when treated for a year 2.47% of aspirin users develop GI bleeding as compared to 1.42% among placebo users. Put in terms of the 50 million Americans now taking aspirin this means that the excess incidence of GI bleeding attributable to aspirin would be 525,000 and the excess mortality would be 50,000 every year. The researchers also investigated whether lower dosages of aspirin would be safer. They found that they were not. The incidence of GI bleeding among low-dose aspirin users was 2.30% compared with 1.45% for placebo users. Somewhat surprisingly, the study also found that enterically-coated or otherwise modified formulations were no safer than standard aspirin. The increase in GI bleeding among users of modified formulations was 93% as compared to 68% for all aspirin users and 59% for low-dose users. The researchers conclude that patients and their physicians need to consider the trade-off between the benefits and harms of long-term aspirin use. Dr. Martin Tramer of the Geneva University Hospitals in Switzerland wholeheartedly agrees with this conclusion and adds, “It may be more appropriate for some people to eat an apple rather than an aspirin a day.”[17,18]

A study of 1225 patients with indications of adverse drug reactions admitted to two large British hospitals found that 18% of these reactions was associated with aspirin usage and most frequently involved gastrointestinal bleeding or peptic ulceration. The mortality among patients admitted with aspirin-related adverse events was 8%[19].

Although the above-mentioned Oxford study found no reduction of adverse events comparing low-dose aspirin vs. regular dose, other studies

have found that low-dose is safer. The Dutch TIA study observed a bleeding incident rate of 2.6% in patients taking 30 mg/day vs. 3.2% in those taking 283 mg/day. The CURE trial observed a bleeding incident rate of 1.56% for daily doses of less than 100 mg vs. 2.29% for doses greater than 100 mg[1].

Overall, the evidence and common sense tend to support the conclusion that less is safer. The combined data from the TIA and CURE trials indicate that about 350,000 major bleeding events could be avoided every year in the US alone by using 81 mg/day instead of 325 mg/day for long-term prophylaxis.

The Oxford study discussed above also noted that neither enteric-coated nor buffered aspirin formulations decreased bleeding risk. This outcome was also reported in a study carried out by researchers at Boston University School of Medicine. The researchers conclude that the increase in risk (comparing aspirin and non-aspirin users) of major upper gastrointestinal bleeding was 2.6-fold for plain aspirin, 2.7-fold for enteric-coated aspirin, and 3.1-fold for buffered aspirin. They did not observe any significant differences in risk attributable to the three aspirin forms according to bleeding site (gastric vs. duodenal). Their conclusion was, "*Use of low doses of enteric-coated or buffered aspirin carries a three-fold increase in the risk of major upper gastrointestinal bleeding. The assumption that these formulations are less harmful than plain aspirin may be mistaken*."[20]

Alternative Options for Stroke Prevention

As discussed above, aspirin is largely ineffective in preventing the formation of fibrin-rich thrombi (clots) such as those involved in cardioembolic, ischemic stroke. Thus, if the aim is to prevent this kind of stroke, then the emphasis should be on supplementing with agents that reduce fibrinogen level or increase fibrinolytic activity (fibrin breakdown) rather than with agents that inhibit platelet aggregation. The most important of such supplements are niacin (vitamin B3), fish oils, vitamin C, and nattokinase.

Niacin

A clinical trial involving patients with peripheral arterial disease who supplemented with niacin for one year (2 x 1500 mg daily) observed a significant decrease (18%) in fibrinogen level and a remarkable 60% decrease in prothrombin Fragments 1 and 2. Corresponding numbers for warfarin therapy was 0% drop in fibrinogen level and a 48% drop in prothrombin Fragments 1 and 2[21].

Fish Oils

Studies carried out in 1994 by South African researchers concluded that fish oil (6 grams/day) reduces the level of coagulation factors V and VII in healthy men and women and also reduces factor X and fibrinogen levels in women[22]. Researchers at the University of Oslo have found that fish oil supplementation is effective in reducing fibrinogen levels in men. Their study involved 64 healthy men between the ages of 35 and 45 years. The men were randomized to receive olive oil capsules or fish oil capsules daily for 6 weeks. The fish oil capsules supplied a daily intake of EPA (eicosapentaenoic acid) of 3.6 grams and a daily intake of DHA (docosahexaenoic acid) of 2.9 grams. At the end of the study period, the average fibrinogen levels had dropped by 13% (from 2.73 g/L to 2.37 g/L). The researchers conclude that the antithrombotic (blood clot preventing) effect of fish oils may be due to their ability to lower fibrinogen levels[23].

Vitamin C

A clinical trial involving 40 patients who had suffered a previous heart attack examined the effect of vitamin C supplementation on fibrinolytic activity. An intake of 1000 mg of ascorbic acid twice a day resulted in an increase in serum ascorbic acid of 96% and a 45% increase in fibrinolytic activity. A second group of patients with acute myocardial infarction (recent heart attack) were also given 2 x 1000 mg of vitamin C daily with the result that serum ascorbic acid level rose by 94%, while fibrinolytic activity increased by 63%[24]. NOTE: Vitamin C should be taken in combination with the bioflavonoids with which it normally occurs in nature.

Nattokinase

Nattokinase is a potent enzyme that is highly effective in dissolving blood clots (thrombi). It works both by dissolving the blood clot directly and by inactivating plasminogen activator inhibitor type 1 (PAI-1), a strong inhibitor of fibrinolysis[25]. Nattokinase is a highly purified extract from natto, a traditional fermented cheese-like food that has been used in Japan for centuries. Dr. Hiroyuki Sumi discovered nattokinase in 1980 and established that it was highly effective in dissolving blood clots[26].

Animal experiments have shown that nattokinase is about four times as effective as the body's endogenous "blood clot dissolver" plasmin[27]. Other research has clearly shown that nattokinase prevents the formation of blood clots on injured artery walls[28,29]. Some researchers believe it is superior to conventional clot-dissolving drugs such as urokinase. Other researchers have found that it contains ACE inhibitors and, in large doses, is highly effective in lowering blood pressure in hypertensive individuals[30]. The beneficial effects of nattokinase persist for 18 hours

or more and positive effects have been observed with as little as 50 mg[31].

A clinical trial involving 204 airline passengers at high risk for venous thrombosis was recently carried out to determine if a combination of nattokinase and pycnogenol (a water extract from the bark of the French maritime pine) would prevent venous thrombosis. The incidence of venous thrombosis in the nattokinase/pycnogenol group was 0% as compared to 7.6% in the control group[32].

These findings add to the evidence of nattokinase's effectiveness in preventing thrombosis. Deep vein thrombosis is caused by blood stagnation in the veins, particularly in the legs. There is evidence that a significant source of blood clots in permanent afibbers with cardiovascular disease is the left atrial appendage where blood tends to stagnate during atrial fibrillation. It would seem likely that nattokinase might also be effective in preventing the formation of cardioembolic clots in the left atrial appendage.

Optional Supplements

It would make little sense to just focus on a natural stroke prevention program that only addresses the risk of embolic stroke when thrombotic stroke is actually more prevalent. So, it would be prudent to add natural platelet aggregation inhibitors to the above regimen. These would include folic acid, vitamin B6 and vitamin B12 for homocysteine reduction as well as vitamin E, potassium, magnesium and ginkgo biloba.

Conclusion

The recommendation (2006 *Guidelines for the Management of Patients with Atrial Fibrillation)* that lone afibbers with no risk factors for stroke should be treated with 81 to 325 mg/day of aspirin does not stand up to closer scrutiny and is not supported by clinical evidence. As a matter of fact, there is now evidence that following the recommendation may do more harm than good.

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Afib Reduction/Elimination
LAF Survey 14

Afib Reduction/Elimination
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SUMMARY

The findings and conclusions of LAF Survey 14 are based on the responses from 224 afibbers who had attempted to reduce or eliminate their afib burden through means other than ablation or surgical procedures, and who had been on their program for at least 6 months. More than half the respondents believed they had found a way to materially reduce or completely eliminate their afib episodes. The successful protocols used to eliminate afib were evenly split between the use of pharmaceutical drugs and the use of alternative approaches such as trigger avoidance, supplementation, dietary changes, stress management, and elimination of underlying conditions such as GERD (gastroesophageal reflux disease), sleep apnea and hypoglycemia.

The survey cannot accurately predict what proportion of the total afib population will be able to materially reduce or eliminate their afib through means other than ablation or surgery. Nevertheless, it is likely that a substantial proportion of those who give it a sincere try will be able to substantially improve their condition. A detailed protocol for effective afib reduction/elimination is presented in Appendix A.

INTRODUCTION

LAF Survey 14 was conducted in September/October 2007 and received a total of 248 responses. The purpose of the survey is two-fold:

- To determine the proportion of afibbers who have been successful in managing their afib through means other than ablation or surgical procedures.

- To obtain and share information about successful protocols.

Success in managing afib was defined as a 50% reduction in afib burden over the most recent 6-month period as compared to a 6-month period prior to starting on the protocol that ultimately proved successful. Other terms used in the survey are defined as follows:

- **Afib burden** – The number of episodes over a 6-month period multiplied by their average duration.
- **Paroxysmal LAF** – Episodes occurring intermittently and tending to terminate spontaneously, usually within 48 hours.

- **Persistent LAF** – Episodes lasting longer than 7 days and not terminating spontaneously, but can be terminated with chemical or electrical cardioversion.

- **Permanent LAF** – Constant (chronic, 24/7) afib not amenable to effective termination by cardioversion.

- **Adrenergic LAF** – Episodes occurring almost exclusively during daytime, often in connection with exercise, or emotional or work-related stress.

- **Vagal LAF** – Episodes tend to occur during rest, at night, or following a heavy meal. Alcohol and cold drinks are common triggers.

- **Mixed (random) LAF** – Episodes occur anytime and do not consistently fit the adrenergic or vagal pattern.

- **PAC-Tamer** – Homemade potassium drink. See http://www.afibbers.org/conference/session38.pdf

- **Waller water** – Homemade magnesium drink. See http://www.afibbers.org/Wallerwater.pdf

- **Ectopic beat** – A heartbeat that is initiated at a location other then the sinoatrial node (feels like an extra beat).

- **PAC** – A premature ectopic beat originating in the atrium.

- **PVC** – A premature ectopic beat originating below the atrioventricular (AV) node, often in the ventricular muscle itself.

Statistical Terms

- **N** – Number of respondents in sample.

- **Mean** – The average value for a group of data, i.e. the sum of the values of all data points divided by the number of data points.

- **Median** – The value in the middle of a group of data, i.e. the value above which half of all individual values can be found and below which the remaining 50% can be found.

- **Statistical significance** – In this study average values are considered different if the probability of the difference arising by chance is less than 5 in 100 using the two-tailed t-test. This is expressed as "p" being equal to 0.5 or less. Lower values of p are indicative of a greater certainty that observed differences are truly significant.

All statistical tests were carried out using the *GraphPad Instat* program (GraphPad Software Inc., San Diego, CA).

BACKGROUND OF RESPONDENTS

A total of 248 afibbers (189 males and 59 females) responded to the survey. Their baseline characteristics are presented in Table 1.

Table 1
Baseline Characteristics

Variable	Male	Female	Total
Gender distribution	76%	24%	100%
Median age*	59	60	60
Age range*	26-78	34-80	26-80
Median age at 1st episode	50	51	50
Age range at 1st episode	10-75	7-75	7-75
Median no. of years of afib	7	6	7
LAF confirmed by diagnosis	86%	92%	87%
Underlying heart disease	3.7%	1.6%	3.2%
Median weight, lbs/kg	183/83.0	147/66.7	175/79.5
Median height, ft/meters	5'11"/1.80	5'5"/1.65	5'10"/1.78
Median BMI	25.2	23.6	25.1
Median birth weight, kg	3.620	3.365	3.410
Median rest. heart rate, bpm	60	68	60
Median blood pressure	120/75	117/70	120/75
Blood type O	42%	39%	41%
Blood type A	37%	41%	38%
Blood type B	15%	10%	13%
Blood type AB	6%	10%	7%

* At time of completing survey

There were no significant differences in the base characteristics between males and females except for the expected differences in weight and height, which were highly significant ($p < 0.0001$). The difference in BMI was also significant, but somewhat less so ($p = 0.04$), as was the

difference in birth weight (p = 0.03). The difference in resting heart rate, 60 bpm vs. 68 bpm, was very significant at p < 0.0001.

Afib Type

A total of 218 respondents had provided detailed information about their type of afib prior to starting their quest to reduce or eliminate their afib burden. The distribution is shown in Table 2.

Table 2
Type of Afib

Type of Afib	Male,%	Female,%	Total,%
Adrenergic	7	6	6
Mixed	32	34	33
Vagal	51	46	50
Total paroxysmal	90	86	89
Persistent	5	2	5
Permanent	5	12	6
Total	100	100	100

Type of afib did not correlate with age at diagnosis, blood type, height, or presence of heart disease. However, a correlation was observed between afib type and weight and BMI with mixed afibbers having a lower weight and BMI than persistent afibbers. Birth weight was significantly higher for permanent afibbers than for mixed and vagal afibbers.

Afib Burden

A total of 190 paroxysmal afibbers had provided data about their episode frequency and duration over a 6-month period prior to beginning their quest to eliminate or reduce their afib burden. This information is summarized in Table 3.

Table 3
Afib Burden

Type of Afib	N	Median # of Episodes	Med.Duration hours	Med. Burden hours
Adrenergic	12	7	12	164
Mixed	63	15	6	96
Vagal	93	7	6	48
Not known	22	12	5	79
Total paroxysmal	190	10	6	84

Mixed afibbers experienced significantly more episodes over the 6-month period than did vagal afibbers (p = 0.0002). Adrenergic afibbers experienced the highest overall burden of afib and this was significantly higher than the burden experienced by vagal afibbers (p = 0.03).

Paroxysmal afib burden prior to program implementation did not correlate with age at diagnosis, years of afib, weight, height, BMI, birth weight, resting heart rate, blood type, or presence of heart disease.

OVERVIEW OF INTERVENTION PROGRAM RESULTS

A total of 248 respondents participated in the LAF-14 Survey. Of these, 6 (2.4%) had made no attempt to reduce their afib burden by means other than ablation and surgical procedures. Eighteen respondents (7%) had been on their intervention program for less than 6 months leaving 224 respondents for further evaluation. These respondents had been on their program for a median of 36 months.

In answer to the question, "**Did you ultimately find a program that was successful in materially reducing or eliminating your afib burden?**", 144 respondents (64%) answered "YES" and 80 (36%) answered "NO". A total of 29 NO-responders went on to have an ablation/maze procedure, of which, 19 (66%) were deemed to be successful. Five of the NO responders stated that their intervention program had been partially successful, but they decided to undergo an ablation or maze procedure anyway.

Seven YES responders had undergone an unsuccessful ablation/maze procedure, but had ultimately found a non-ablation, non-surgical approach to manage or eliminate their afib. Another YES responder had managed their afib successfully with drugs, but decided to have an ablation (successful) to be able to discontinue the drugs. Finally, one YES responder had found a successful protocol, but had undergone a maze procedure in connection with open-heart surgery for other heart-related problems.

Among the respondents who had not tried to reduce their afib burden with means other than ablation/surgery, two had undergone a successful ablation, and finally, among afibbers who had been on their protocol for less than 6 months, five had undergone an ablation, of which, two were successful.

Overall, 45 of the 248 respondents (18%) had undergone an ablation/maze procedure with 25 or 56% being successful.

Characteristics of YES and NO Responders

Baseline characteristics of the 224 afibbers who had tried to manage or eliminate their afib for 6 months or longer is presented in Table 4.

Table 4
Baseline Characteristics of YES and NO Responders

Variable	YESResponders	NO Responders
Number in sample	144	80
% female	22.2	22.5
% male	77.8	77.5
Median age*	60	59
Age range*	26-80	35-77
Median age at first episode	51	50
Age range at first episode	7-75	10-71
Median no. of years of afib	6	8
LAF confirmed by diagnosis	85%	93%
Underlying heart disease	3.5%	3.8%
Median weight, kg	79.5	80.2
Median height, meters	1.78	1.80
Median body mass index (BMI)	25.1	24.9
Median birth weight, kg	3.410	3.475
Median resting heart rate, bpm	60	60
Median blood pressure	120/75	120/75
Blood type O	39%	45%
Blood type A	41%	33%
Blood type B	12%	17%
Blood type AB	8%	5%

* At time of completing survey

There were no statistically significant differences in baseline characteristics between YES and NO responders.

Afib Type

The types of afib encountered in the two groups prior to beginning the intervention protocol are shown in Table 5.

Table 5
Afib Type

Type of Afib	YES Responders	NO Responders
Adrenergic	9%	3%
Mixed	27%	45%
Vagal	56%	38%
Total paroxysmal	92%	86%
Persistent	6%	1%
Permanent	2%	13%
TOTAL	100%	100%
Not sure	16 respondents	9 respondents

The difference in percentage of mixed and vagal afibbers (27% vs 45% and 56% vs 38%) between the YES and NO responders was statistically

significant (p = 0.03). This difference would indicate that vagal afib is comparatively easier to manage than is mixed afib.

Afib Burden

Ninety-six YES responders and 42 NO responders had provided data to allow a comparison of the paroxysmal afib burden experienced prior to the start of the intervention protocol. This data is summarized in Table 6.

Table 6
Afib Burden

Afib Burden*	YES Responders	NO Responders
Median no. of episodes	11	8
Median duration, hrs	6	8
Median burden, hrs	90	78

* during a 6-month period prior to beginning intervention program

There was no significant difference in afib burden prior to program implementation when comparing YES responders to NO responders indicating that initial afib burden, as such, is not a determinant of ultimate success in reducing or eliminating afib.

Intervention Modalities

A summary of the percentage of YES and NO responders who had used different modalities in their quest to relieve or eliminate their afib burden is presented in Table 7. Please not that percentages do not add up to 100 since most respondents had tried more than one modality.

Table 7
Main Components of Intervention Programs

Component	YES Responders	NO Responders	Total
Trigger avoidance	86%	93%	88%
Dietary changes	51%	63%	55%
Supplementation	81%	91%	84%
Drug therapy	79%	78%	79%
Other therapies	51%	61%	55%
Disease treatment	35%	39%	37%
Ablation/maze	6%	36%	17%
Total in group	144	80	224

Most (85%) of NO respondents had tried more than one modality with 46% trying four or more, 21% trying three, and 18% trying two. Among YES respondents 78% had tried more than one modality with 37% trying four or more, 20% trying three, and 22% trying two. Thus, there was no

indication that NO responders had been less persistent in their search for a protocol that worked. Of course, it is not possible to conclude anything about the diligence with which the various options were pursued in the two groups.

PROGRAM DETAILS

Trigger Avoidance

A total of 124 YES responders (86%) and 74 NO responders (93%) had attempted to reduce or eliminate their afib through trigger avoidance. The percentage of afibbers who had practiced avoidance of some common triggers is shown in Table 8.

Table 8
Trigger Avoidance

Trigger	YES Responders	NO Responders	Total
Monosodium glutamate MSG	32%	39%	34%
Aspartame	36%	43%	38%
Alcohol	52%	64%	56%
Caffeine	64%	74%	67%
Tyramine-containing foods	5%	11%	7%
High glycemic index foods	22%	24%	22%
Cold drinks	17%	36%	24%
Heavy evening meals	38%	50%	42%
Dehydration	33%	54%	40%
Stress	32%	38%	34%
Physical overexertion	40%	34%	38%
Sleeping on left side	35%	60%	44%
Other	21%	18%	20%
Total in group	144	80	224

Among other triggers avoided wheat, gluten, sugars, bending over, and lack of sleep figured prominently. Caffeine was clearly the most common trigger factor avoided followed by alcohol (especially red wine), sleeping on the left side, heavy evening meals, dehydration, physical overexertion, and aspartame and other food additives.

Among YES responders 36% believed that trigger avoidance on its own had reduced their afib burden by at least 50% over the most recent 6-month period after beginning the protocol. Another 14% believed it had made little or no difference, and 50% believed that trigger avoidance, in combination with other measures, had resulted in at least a 50% reduction in afib burden. Among NO responders 24% felt that trigger avoidance had improved their condition somewhat, but not by 50% or more.

Over half of all respondents (58%) who had embarked on trigger avoidance had noted other benefits as detailed in Table 9.

Table 9
Other Benefits of Trigger Avoidance

Better overall health	10%
Weight loss	9%
Improved mood, less anxiety, calmer	6%
Fewer ectopic beats	5%
Better sleep	4%
Better digestion, less bloating	4%
More energy, less tired	3%
Fewer colds and infections	2%

NOTE: Percentages are based on the total group of 194 respondents who had practiced trigger avoidance.

Dietary Changes

A total of 74 YES responders (51%) and 50 NO responders (63%) had attempted to reduce or eliminate their afib through diet changes. The percentage of those who had tried various approaches is shown in Table 10.

Table 10
Dietary Changes

Change	YES Responders	NO Responders	Total
Eliminated gluten	11%	16%	13%
Eliminated wheat	13%	15%	14%
Eliminated/reduced dairy	9%	21%	13%
Changed to Paleo diet	8%	11%	9%
Changed to Zone diet	5%	6%	5%
Changed to Atkins diet	1%	1%	1%
Reduced sugar intake	4%	6%	5%
Increased veggies/fruits	0%	6%	2%
Eating smaller portions	3%	1%	3%
Other changes	26%	13%	21%
Total in group	144	80	224

Among the YES responders 30% believed that dietary changes had reduced their afib burden by at least 50% over the most recent 6-month period after beginning the protocol. Another 15% believed it had made little or no difference, and 55% believed that dietary changes, in combination with other measures, had resulted in at least a 50% reduction in afib burden.

Eliminating wheat, eliminating gluten, or switching to the Paleo diet or Zone diet all have one thing in common – the elimination of wheat. Thus,

it would be of interest to determine if the baseline characteristics of those afibbers who benefited from wheat elimination are different from those who did not. Twenty-seven respondents had observed no benefit from wheat elimination (including 10 who had switched to the Paleo diet), while 26 respondents had observed a benefit (including 10 who had switched to the Paleo diet). The percentage of vagal afibbers in the successful group was substantially higher than in the unsuccessful group (62% vs. 29%, p = 0.04). The percentage of females in the successful group was also substantially higher than in the unsuccessful group (50% vs. 19%, p = 0.04). This same ratio also applied to the Paleo diet on its own.

In other words, women (especially vagal afibbers) who try the Paleo diet or wheat elimination are far more likely to be successful than are men. The reason could well be that most women still do the meal preparation and may be more inclined to be strict in their adherence to the diet if they have afib themselves than if it is the husband's problem. Also, men are probably more inclined to ignore the possible benefits of strict adherence and be less diligent.

The fact that vagal afibbers experienced more success with wheat elimination supports the contention that vagal afib is easier to manage than are the mixed, adrenergic, and permanent types. Of course, the possible influence of genetic differences between the sexes cannot be ruled out, but it seems unlikely to be a major cause in the difference in success with wheat elimination.

Any adverse effects from diet changes were minor with the need for adjustment of fiber content being the most significant. Fifty-nine per cent of respondents who had embarked on diet changes felt that their changes had made a significant overall positive impact on their health and wellbeing, quite apart from any effects on their afib. The major benefits are detailed in Table 11.

Table 11
Other Benefits of Dietary Changes

Weight loss	23%
Better overall health	10%
Improved digestion	10%
More energy	8%
Less anxiety and depression	2%

NOTE: Percentages are based on the total group of 124 respondents who had made diet changes.

Supplementation

A total of 117 Yes responders (81%) and 73 NO responders (91%) had attempted to reduce or eliminate their afib burden through supplementation with vitamins, minerals, and herbs. The percentage of those who had tried various supplements and the percentage of those who had found them beneficial are given in Table 12.

Table 12
Supplementation

	YES responders		NO responders		ALL responders	
Supplement	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
Fish oil	68	25	74	7	71	18
Magnesium glycinate	62	71	71	17	65	48
Coenzyme Q10	60	24	60	9	60	18
Potassium	52	21	60	11	55	17
Vitamin C	44	10	56	5	49	8
Vitamin E	44	15	42	6	44	12
B-vitamins	43	18	45	6	44	13
Multivitamin	40	6	42	6	41	6
Taurine	38	51	49	8	43	32
Low-sodium V8 juice	25	34	23	12	24	26
L-carnitine	20	17	29	5	23	11
Zinc	20	4	18	0	19	3
Magnesium oxide	19	41	30	9	23	25
Calcium	18	5	27	0	22	2
Selenium	17	5	19	0	18	3
Probiotics	15	24	26	5	19	14
Digestive enzymes	10	33	19	7	14	19
L-arginine	9	9	15	9	12	9
Sea salt	9	9	16	0	12	4
Melatonin	5	0	8	0	6	0
Waller water	3	25	11	13	6	17
Ribose	3	100	1	0	2	75
Magnesium infusions	2	50	8	0	4	13
PAC-Tamer drink	1	0	3	0	2	0

One or two respondents had found the following supplements beneficial – celery juice, hawthorn, niacin, flax oil, and a lysine/proline combination.

The average number of supplements tried by each respondent was 7. The most popular one was fish oil, which had been tried by 71% of all respondents. Only 25% of YES responders, and 7% of NO responders had found it beneficial as far as reducing their afib burden was concerned. Fish oil supplementation, of course, has many other benefits independent of any effect on afib, most notably, stroke prevention. The second-most popular supplement was magnesium glycinate, which had been tried by 65% of all respondents and found beneficial by 71% of YES responders

and 17% of NO responders. Coenzyme Q10 had been tried by 60% of all responders and found beneficial by 18%, while potassium had been tried by 55% and found beneficial by 17%. Taurine had been tried by 43% of all respondents and found beneficial by 51% of YES responders.

Other supplements which had been found beneficial by 50% or more of the YES responders who had tried them include magnesium infusions and ribose; however, as only 3 and 2 respondents had tried them nothing can be concluded about their effectiveness in a larger population, particularly since 6 NO responders had tried infusions and none had found them beneficial. Nevertheless, the ribose results look promising and it is to be hoped that this supplement will receive a more thorough evaluation. Somewhat surprisingly, 19% of YES responders had tried magnesium oxide supplements and 41% had found them beneficial (vs. only 9% among NO responders). This may indicate a placebo effect, or that magnesium oxide is better absorbed than reported in the medical literature. Low-sodium V8 juice, probiotics, digestive enzymes, and Waller water had been found beneficial by 34%, 24%, 33%, and 25% respectively of the YES responders who had tried them.

Among the YES responders 25% believed that supplementation had reduced their afib burden by at least 50% over the most recent 6-month period after starting their protocol. Another 22% believed it had made little or no difference, and the remaining 53% believed that supplementation, in combination with other measures, had resulted in at least a 50% reduction in afib burden. In contrast, 82% of NO responders felt that supplementation had been of no benefit. The remaining 18% felt that they had achieved some benefit, but not enough to reduce their afib burden by 50%. It is of interest that 92% of those claiming some benefit had been supplementing with magnesium. Among YES responders who claimed that supplementation had helped, 56% had been supplementing with magnesium glycinate.

Comparing baseline characteristics of those who had benefited from magnesium glycinate supplementation and those who had not revealed that those who had benefited had experienced afib for only 3 years vs. 7 years for those who had not benefited ($p = 0.04$). This could perhaps indicate that magnesium supplementation is more likely to be successful if started early in one's afib career. There was a strong correlation between having made successful dietary changes and supplementing with magnesium glycinate ($p = 0.04$) and a trend for blood type 0 to be more common among those who had not benefited from magnesium supplementation ($p = 0.06$). Finally, it is worth noting that about 50% of those supplementing with magnesium glycinate also supplemented with potassium and taurine.

Seventeen percent of the 190 respondents had noted adverse effects from taking supplements. The most prevalent of these are listed in Table 13.

Table 13
Adverse Effects of Supplementation

Loose stools and diarrhea*	5%
Upset stomach, bloating	2%
Niacin flush	1%
Carnitine and Q10 causing afib	1%

* Mostly from magnesium supplementation

Among other less frequent adverse effects (mentioned by one respondent each) were an increased frequency of afib or ectopics caused by B-vitamin, potassium + zinc, l-arginine and magnesium.

Thirty-nine percent of the 190 respondents had noted further beneficial effects of their supplementation program. The most prevalent of these are listed in Table 14.

Table 14
Benefits of Supplementation

Increased energy	8%
Better general health	6%
Fewer ectopic beats	6%
Less severe afib symptoms	3%
Cholesterol reduction	3%
Improved digestion	3%
Elimination of leg cramps	2%
Reduction of blood pressure	2%

Other benefits mentioned by one or two respondents included improved mood, better weight control, fewer colds/flu, softer skin (vitamin C), and the heart feeling calmer.

Use of Pharmaceutical Drugs

A total of 114 YES responders (79%) and 62 NO responders (78%) had attempted to reduce or eliminate their afib burden through the use of prescription drugs (antiarrhythmics, beta-blockers or calcium channel blockers). The percentage of those who had tried various drugs and the percentage who had found them beneficial in reducing their afib burden are given in Table 15.

Table 15
Pharmaceutical Drug Use

Drug	YES responders Tried.%	YES responders Benefit.%	NO responders Tried.%	NO responders Benefit.%	ALL responders Tried.%	ALL responders Benefit.%
Beta-blocker	49	45	55	21	51	36
Flecainide	38	74	39	33	38	60
Sotalol	20	43	24	13	22	32
Cal. channel block.	20	35	34	19	25	27
Propafenone	17	47	21	15	18	34
Digoxin	14	13	16	10	15	12
On-demand flecainide	13	53	10	33	12	48
ACE inhibitors	12	36	6	0	10	28
Amiodarone	9	70	11	57	10	65
Proton pump inhib.	8	67	6	25	7	54
Tranquilizers	7	50	11	43	9	47
Disopyramide	6	43	0	0	4	43
Rythmol SR	6	29	10	33	7	31
On-demand propaf.	5	50	5	0	5	33
Angiotensin II block.	4	60	5	0	5	38
Antidepressants	4	25	5	0	4	14
Dofetilide	3	67	5	33	3	50
On-demand beta-block.	3	0	10	17	5	11
Aldosterone blockers	1	100	2	0	1	50
Procainamide	1	0	2	0	1	0

The average number of drugs tried by each respondent was 2.5 and there was no indication that NO responders had tried fewer drugs than had YES responders. The most popular drugs were beta-blockers, which had been tried by 51% of all respondents and found beneficial by 36% (Yes responders 45%, NO responders 21%). The second-most popular drug was flecainide (Tambocor), which had been tried by 38% and found beneficial by 60% (74% among YES responders and 33% among NO responders). In third place came calcium channel blockers, which had been tried by 25% and found beneficial by 27% (35% among YES responders and 19% among NO responders). Sotalol (Betapace) had been tried by 22% of all respondents and 32% of them had found this drug beneficial (43% of YES responders and 13% of NO responders). Amiodarone had been tried by 10% of all respondents and had been found beneficial by 65% (70% of YES responders and 57% of NO responders). Although only tried by 7% of respondents, proton pump inhibitors (omeprazole, etc) had been found effective by 54%. Finally, 6 respondents had tried dofetilide (Tikosyn) with half of those finding it beneficial.

Beta-blockers and propafenone (Rythmol) were the most effective drugs for adrenergic afibbers; for mixed it was dofetilide (Tikosyn), propafenone, amiodarone, and flecainide that were the most effective, while for vagal afibbers amiodarone, flecainide, and calcium-channel blockers were most effective. The most effective drug overall was amiodarone, while the least effective was digoxin (Lanoxin). Somewhat surprisingly, 30% of vagal afibbers who had tried beta-blockers on a continuous basis had found them effective. NOTE: Half of them were taking the beta-blocker in combination with flecainide or amiodarone.

One respondent had eliminated his afib by correcting a low serum potassium level (3.2 mEq/l) with 50 mg/day of the aldosterone blocker, eplerenone, plus 2000 mg/day of potassium. He also took 50 mg of flecainide before bedtime. This protocol brought his potassium level up to 4.2 mEq/l.

Among the YES responders 56% believed that the use of prescription drugs had reduced their afib burden by at least 50% over the most recent 6-month period after beginning their protocol. Another 19% believed it had made no difference, and the remaining 25% believed that the use of drugs, in combination with other measures, had resulted in at least a 50% reduction in afib burden.

Thirty-five percent of the 176 respondents had noticed adverse effects from their medications. The most prevalent of these are listed in Table 16.

Table 16
Adverse Effects of Drugs

Tiredness, fatigue	15%
Hypotension (low blood pressure)	3%
Sexual dysfunction	2%
Constipation	2%
Increase in ectopics	2%
Thyroid problems*	1%
Headaches	1%
Dizziness/lightheadedness	1%
Problems with sleeping	1%

* Associated with amiodarone

Flecainide users (34%) were the most likely to report adverse events followed by amiodarone (29%) and sotalol (26%) users.

Eleven percent of the 176 respondents had noted further benefits from their medications. These are listed in Table 17.

Table 17
Additional Benefits of Drugs

Reduction in blood pressure	4%
Fewer ectopic beats	2%
Lower heart rate	2%
Fewer migraine attacks	1%
Decrease in GERD symptoms	1%
Calmer	1%

Use of Alternative Protocols

A total of 74 YES responders (51%) and 49 NO responders (61%) had attempted to reduce or eliminate their afib burden through the use of stress management or other alternative therapies. The percentage of those who had tried various protocols and the percentage who had found them beneficial in reducing their afib burden are given in Table 18.

Table 18
Alternative Therapies

	YES responders		NO responders		ALL responders	
Alternative Therapy	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
Relaxation therapy	39	52	43	10	41	34
Breathing exercises	38	57	47	17	41	39
Acupuncture	15	18	18	0	16	10
Chiropractic	5	25	4	0	5	17
Chinese herbal med.	7	40	12	0	9	18
Meditation	32	42	27	23	30	35
Yoga	20	60	16	38	19	52
Qi Gong	5	75	6	33	6	57
Tai Chi	5	50	6	0	6	29
Cognitive thinking	12	67	8	0	11	46
Amalgam remov/detox.	14	50	6	0	11	38

It was mostly adrenergic afibbers who benefited from relaxation therapy.

Relaxation therapy had been tried by 41% of respondents and found beneficial by 34% (mostly adrenergic afibbers). Breathing exercises had also been tried by 41% and found beneficial by 39%. Meditation had been tried by 30% and found beneficial by 35%. The most effective therapy was Qi Gong, which had been tried by 6% of respondents and found beneficial by 57%. Yoga and cognitive thinking therapy were also found effective at 52% and 46% success rates respectively.

Among the YES responders 19% believed that the use of stress management and other alternative therapies had reduced their afib burden by at least 50% over the most recent 6-month period after

beginning their protocol. Another 28% believed it had made no difference, and the remaining 53% felt that the use of alternative therapies, in combination with other measures, had resulted in at least a 50% reduction in afib burden.

Only 2 respondents (2%) reported adverse effects of their alternative therapy program and both were related to vigorous exercise. In contrast, 26% of respondents who had tried alternative therapies reported additional benefits over and above the effect on afib burden. The most prevalent of these benefits were an increased sense of mental and physical wellbeing (7%), feeling calmer and more relaxed (7%), more flexible due to yoga training (3%), and more energy (2%).

Treatment of Underlying Diseases

A total of 52 YES responders (36%) and 30 NO responders (38%) had attempted to reduce or eliminate their afib burden by dealing with underlying disease conditions. Table 19 shows the most prevalent conditions dealt with and the degree of success attained in doing so.

Table 19
Elimination of Diseases

	YES responders		NO responders		ALL responders	
Disease	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
GERD	42	41	43	0	43	26
Digestive problems	33	53	47	0	38	29
Food allergies	12	50	13	0	12	30
Sleep apnea	21	27	13	0	18	20
Hyperthyroidism	2	100	3	0	2	50
Hypothyroidism	10	20	10	0	10	13
Hypoglycemia	10	20	3	0	7	17

Other conditions treated were constipation, tooth abscesses, hypokalemia (one each).

GERD (gastroesophageal reflux disease) and digestive problems affected a total of 36 or 44% of the 82 respondents. Half of them (22%) had reduced their afib burden by effectively dealing with these conditions. Sleep apnea affected 18% of respondents and was dealt with successfully in 20% of cases. Food allergies were reported by 12% and effectively treated by 30%.

Somewhat surprisingly, only about 10% of GERD patients had used proton pump inhibitors (Nexium, Prilosec) in treating their problem. The remaining had used diet (58%) or probiotics and digestive enzymes (33%)

to help alleviate GERD. Sleep apnea sufferers were generally overweight or obese and most had used a CPAP machine to alleviate their problem.

Among the YES responders 35% believed that dealing with underlying disease conditions had reduced their afib burden by at least 50% over the most recent 6-month period after starting their regimen. Another 21% believed it had made no difference, and the remaining 44% felt that dealing with underlying conditions, in combination with other measures, had resulted in at least a 50% reduction in afib burden. In contrast, 83% of NO Responders felt that attempting to deal with their underlying conditions had made no difference.

An impressive 63% of the 82 respondents who had dealt with underlying disease conditions in an attempt to reduce their afib burden had observed additional benefits, the most common of which are summarized in Table 20.

Table 20
Additional Benefits from Treatment of Underlying Disease Conditions

Improved digestion and bowel function	17%
No more acid reflux (heartburn)	17%
Better sleep	16%
Overall better health and wellbeing	6%
More energy	4%
No more fluctuations in blood sugar	4%
Weight loss	4%

Ways of Shortening Episodes

A total of 110 respondents (49% - YES and NO respondents combined) had found one or more ways of shortening their episodes. The number and percentage of those who had found effective protocols are presented in Table 21.

Table 21
Means of Shortening of Episodes

Effective Protocol	Number	Percent
On-demand flecainide	27	25
Light exercise	26	24
Resting	23	21
Vigorous exercise	19	17
On-demand beta-blocker	17	15
Tranquilizers	11	10
On-demand propafenone	11	10
Hydrotherapy	9	8
Meditation	8	7
Valsalva maneuver	7	6
Increase supplements*	7	6
On-demand cal. channel blocker	5	5
Acupuncture/acupressure	3	3
Increase regular medication	3	3
Drinking lots of water	3	3
Stand up (when resting at onset)	2	2
Coughing	2	2
Sleeping in cool room	2	2
Warm bath	1	1

* Especially magnesium, taurine and potassium

Twenty-five percent of the 110 respondents had found the on-demand (pill-in-pocket) approach with flecainide to be effective in hastening conversion to normal sinus rhythm. This approach was equally effective for mixed and vagal afibbers, but significantly more effective for YES responders than for NO responders.

Twenty-four percent had found light exercise to be effective, 23% had benefited from resting (equal benefit for all afib types), 19% from vigorous exercise, 17% from on-demand beta-blockers, and 11% from tranquilizers. The most effective therapies for women were hydrotherapy, meditation, tranquilizers and resting, while the most effective therapy for men was vigorous exercise. NOTE: 80% of respondents who had found vigorous exercise beneficial were male, vagal afibbers.

Ways of Prevention Ectopics

Sixty-eight respondents (33%) had found one or more means of preventing ectopics (premature beats, PVCs, PACs), 21% did not experience ectopics, and the remaining 46% had not found a way of preventing ectopics. The number and percentage of respondents who had found effective protocols are presented in Table 22.

Table 22
Prevention of Ectopics

Effective Protocol	Number	Percent
Supplementation with magnesium*	30	44
Supplementation with potassium*	29	43
Low-sodium V8 juice	18	26
Supplementation with taurine*	16	24
Beta-blocker	10	15
Tranquilizers	7	10
Additional supplements**	7	10
Additional antiarrhythmics	4	6
PAC-Tamer drink	1	1

* Mostly in combination (magnesium/potassium/taurine)
** Specifically potassium and coenzyme Q10

By far the most effective way of preventing ectopics is by supplementing with magnesium and/or potassium, preferably in combination with taurine. Forty-four percent of all respondents had found this approach to be effective, while 26% had found drinking low-sodium (high potassium) V8 juice to be effective in preventing ectopics. Beta-blockers and tranquilizers were also found to be somewhat effective. In my own experience the most effective way of preventing or eliminating ectopics is by drinking (over a 10-minute period) 8 ounces of lukewarm water containing the following:

- 1 pouch of *Emergen-C*
- 1 teaspoon of magnesium citrate (*Natural Calm*)
- 1 teaspoon of potassium gluconate
- 1000 mg of taurine (may be taken separately in capsule form)

This drink will provide, besides 1000 mg of vitamin C, 740 mg of elemental potassium and 265 mg of elemental magnesium in a highly absorbable form.

Other suggestions for preventing ectopics include avoiding trigger factors such as caffeine, sugar, and sleeping on the left side.

Overall Results of Intervention Protocols

One hundred and forty-four respondents (64% of the total) answered YES to the question, "**Did you ultimately find a program that was successful in materially reducing or eliminating your afib burden?**" The average time these respondents had been on their successful program varied from 6 to 120 months with a median of 22 months. Ninety-one YES

responders had kept track of the number of episodes and duration during their time on the program as well as before they started. Results are compared in Table 23.

Table 23
Overall Results

Burden over 6 months	Before Protocol	After Implementation
No. of episodes	10	0.8
Average duration, hrs	6	1
Afib burden, hrs	72	2

NOTE: Permanent afib is counted as 24 hours a day for 180 days, ie. 4320 hours over 6 months.

The differences in the two columns were all statistically extremely significant. Perhaps even more impressive is the fact that almost a third of the 91 respondents had experienced no episodes at all since implementing their protocol. Nevertheless, 45 of the respondents still needed to avoid triggers, while 30% did not. The remaining 25% still needed to avoid triggers, but much less so.

Ninety-five percent of respondents would recommend their program to fellow afibbers, but 5% would not, primarily because their programs involved the use of amiodarone or drastic measures such as early retirement.

Overall, 157 respondents who had not undergone ablation and had been on their program for 6 months or longer had kept records of their afib burden prior to implementing their program and for the most recent 6 months while on the program. These respondents can be assigned to 4 different groups:

- Worsened or no improvement — 40 respondents
- Less than 50% improvement — 11 respondents
- Better than 50%, but not eliminated — 57 respondents
- No episodes in most recent 6 months — 42 respondents

In addition, 7 persistent afibbers either completely eliminated their afib (4 respondents) or became paroxysmal. Thus, out of the group of 157 respondents with complete data, 68% had reduced their afib burden by 50% or more, and 29% had experienced no episodes in the most recent 6 months.

It clearly would be of interest to determine the relevant differences between the group of 46 respondents (Group A) who managed to completely eliminate their afib for at least a 6-month period (including

former persistent afibbers) and the group of 40 respondents (Group B) whose condition worsened or remained the same. To do so is the purpose of the following section.

COMPARISON BETWEEN GROUPS A AND B

In this section the baseline characteristics and actions taken will be compared for a group of 46 afibbers (Group A) who experienced no afib episodes over the latest 6-month period and a group of 40 afibbers whose condition worsened or remained the same (Group B).

Table 24
Comparison of Baseline Characteristics

Variable	Group A	Group B
% female	24	33
% male	76	67
Median age @completion	60	58
Age range @ completion	33-77	40-77
Median age at first episode	50	52
Age range at first episode	16-69	20-71
Median no. of years of afib	7	7.5
LAF confirmed by diagnosis	89%	93%
Underlying heart disease	4.8%	2.5%
Median weight, kg	81.6	78.8
Median height, meters	1.78	1.80
Median body mass index (BMI)	25.8	25.0
Median birth weight, kg	3.280	3.700
Median resting heart rate, bpm	60	62
Median blood pressure	120/75	120/73
Months on program	36	48
Blood type O	39%	47%
Blood type A	42%	30%
Blood type B	14%	17%
Blood type AB	5%	6%
Adrenergic	10%	3%
Mixed	24%	42%
Vagal	63%	45%
Paroxysmal	98%	90%
Permanent	2%	10%
Total	100%	100%

There were no statistically significant differences in baseline characteristics between the two groups except for median birth weight which was almost a pound (420 grams) higher in Group B.

The afib burden 6 months prior to beginning the protocols and for the most recent 6-month period are shown in Table 25.

Table 25
Afib Burden

Afib Burden	Before Intervention Group A	Before Intervention Group B	After Intervention Group A	After Intervention Group B
Median no. of episodes	4	6	0	24
Median duration, hrs	6	8	0	12
Median burden, hrs	33	56	0	208

There was no statistically significant difference between the pre-intervention afib burden of Groups A and B. However, the difference in pre- and post-intervention burden was highly significant for both groups with Group B getting much worse and Group A eliminating afib altogether, at least for a 6-month period.

Intervention Modalities

A summary of the percentage of Group A and B members who had used different modalities in their quest to relieve or eliminate their afib burden is presented in Table 26. Please note that percentages do not add up to 100 since most respondents had tried more than one modality.

Table 26
Main Components of Intervention Program

Component	Group A	Group B
Trigger avoidance	85%	93%
Dietary changes	41%	70%
Supplementation	70%	90%
Drug therapy	72%	75%
Other therapies	54%	63%
Disease treatment	41%	36%

There was no indication that members of Group B had tried fewer interventions than had those of Group A – quite the contrary. Most surprising was the finding that only 41% of those in Group A had made dietary changes as compared to 70% in Group B ($p = 0.02$). Trigger sensitivity was not significantly different between the two groups, except that those in Group B had found sleeping on the left side to be more detrimental than had those in Group A (53% vs 28%, $p = 0.05$).

Dietary Changes

Seventy percent of Group B and 41% of group A had tried changing their diet. The percentage of those having tried different approaches and their rate of success is presented in Table 27.

Table 27
Dietary Interventions

Intervention	Group A % Tried	Group A % Success*	Group B % Tried	Group B % Success*
Elimination of gluten	13	33	20	0
Elimination of wheat	13	33	18	0
Reduced dairy	11	60	20	0
Changed to paleo diet	9	75	5	0

* % of those who had tried the intervention and believed it had reduced their afib burden by 50% or more.

There clearly was a substantial difference in the degree of success experienced in the two groups. Group B had no luck at all, while Group A found that diet changes had reduced their afib burden by 50% or more in from 33 to 75% of cases. The major difference between the two groups was that there were no mixed afibbers in Group A, while the proportion of mixed afibbers in Group B was 55%. It was also noted that 75% of Group A members who had found diet changes beneficial were women.

Supplementation

Ninety percent of Group B and 70% of Group A had tried supplementation. The percentage of those having tried different supplements and their rate of success is presented in Table 28.

Table 28
Supplement Interventions

Supplement	Group A (N=46) Tried,%	Group A (N=46) Benefit,%	Group B (N=40) Tried,%	Group B (N=40) Benefit,%	Total Tried,%	Total Benefit,%
Magnesium glycinate	39	67	81	21	55	38
Magnesium infusions	2	100	6	0	3	33
Potassium	28	54	58	5	40	24
Taurine	20	67	50	0	31	22
Magnesium oxide	20	44	28	0	22	21
Low-sodium V8 juice	7	67	22	0	13	18
Digestive enzymes	13	33	14	0	13	18
Coenzyme Q10	37	24	67	13	48	17
Fish oil	48	23	75	7	57	14
Probiotics	11	0	28	0	17	0

The most beneficial supplement was magnesium glycinate (chelated magnesium), which had been tried by 55% of all 86 responders and found beneficial by 38%. Thirty-nine percent of Group A had tried magnesium glycinate and two-thirds had found this supplement beneficial. Potassium and taurine were also found to be effective with 24% and 22% of those

having tried them finding them beneficial (54% and 67% respectively in Group A). Fish oil was the most popular supplement, but only 14% (23% in Group A) had found it beneficial as far as afib was concerned.

It is not surprising that magnesium turned out to be highly beneficial. Magnesium has proven antiarrhythmic properties and magnesium sulfate injections have been found to shorten episode duration. It is also worth noting that 80% of the US adult population (excluding those who supplement) do not get the recommended daily allowance of 420 mg/day for men and 320 mg/day for women from their diet.[1] Furthermore, there is also evidence that magnesium intake is inversely proportional to the level of the inflammatory marker C-reactive protein.[1] This all adds up to the conclusion that magnesium is likely the most effective supplement for lone afibbers. It also points to the possibility that the massive extent of magnesium deficiency in the USA, and likely in Canada and western Europe as well, may be at least partly responsible for the afib epidemic.

In the experience of many afibbers a combination of magnesium, potassium, and taurine is even more effective than magnesium alone. A commonly used combination is:

- 3 x 100-200 mg/day of elemental magnesium from magnesium glycinate
- 3 teaspoons/day of potassium gluconate powder providing 3 x 540 mg/day of elemental potassium
- 3 x 1000 mg/day of taurine

When the above combination is first started it is a good idea to begin just with magnesium and taurine as there is evidence that it is difficult to remedy a low potassium level without first ensuring an adequate level of magnesium. Also, it is advisable to gradually increase magnesium over a couple of weeks (3x100 mg/day to 3x200 mg/day) so as to avoid any stomach upset. The above supplements are best taken in juice or in a protein shake. NOTE: *Natural Calm* magnesium citrate can also be used, but needs to be started slowly to avoid loose stools.

[1] King, DE, et al. Dietary magnesium and C-reactive protein levels. Journal of the American College of Nutrition, Vol. 24, No. 3, 2005, pp. 166-71

Coenzyme Q10 had been tried by 48% of all respondents and found beneficial by 17% (24% in Group A). However, some afibbers have found that coenzyme Q10 is too excitatory and worsens their condition. Experimentation is definitely required here.

Pharmaceutical Drugs

Seventy-five percent of Group B and 72% of Group A had tried pharmaceutical drugs. The percentage of those having tried the various drugs and their extent of success is presented in Table 29. NOTE: Only drugs, which had been tried by at least 5% of the total group, are included here.

Table 29
Pharmaceutical Interventions

	Group A		Group B		Total	
Drug	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
Amiodarone	7	100	3	100	5	100
Tranquilizers	7	33	8	100	7	67
Proton pump inhibitors	11	60	3	0	7	50
Flecainide	28	69	25	20	27	48
Beta-blocker	37	41	38	40	37	41
Calcium-channel blocker	17	38	23	33	20	35
Sotalol	22	40	20	25	21	33
ACE inhibitors	11	40	8	0	9	25
Propafenone	13	33	8	0	10	22
Digoxin	13	17	13	0	13	9

Amiodarone, although only tried by 4 afibbers, had a 100% success rate, but was accompanied by a 50% rate of adverse effects involving thyroid problems. Tranquilizers (Ativan, Xanax, Valium) were found quite effective for mixed afibbers and proton pump inhibitors (PPI) were effective for those with GERD or digestive problems. Flecainide had been tried by 27% of the total group of 86 respondents and had been found effective by 48%. Beta-blockers had been tried by 37% and found effective by 41%; however, 84% of those who had found beta-blockers successful were taking antiarrhythmics as well. Sotalol had been tried by 21% and found effective by 33%. There was no indication that sotalol was any less effective for vagal afibbers than for mixed.

Use of Alternative Protocols

Seventy-five percent of Group B and 54% of Group A had tried to reduce their afib burden with the use of stress management techniques and other alternative therapies. The percentage of those having tried the various protocols and their success rates are presented in Table 30.

Table 30
Alternative Protocols

	Group A		Group B		Total	
Alternative Therapy	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
Breathing exercises	26	58	28	18	27	39
Relaxation therapy	17	38	33	31	24	33
Meditation	20	44	25	30	22	37
Yoga	9	75	10	25	9	50
Acupuncture	7	0	13	0	9	0
Amalgam remov/detox	7	67	3	0	5	50
Cognitive thinking	2	0	8	0	5	0
Qi Gong	2	100	3	100	2	100
Chiropractic	2	0	3	0	2	0
Tai Chi	2	0	3	0	2	0

Breathing exercise was the most popular protocol; it had been tried by 27% of the total group and found beneficial by 39%. Relaxation therapy had been tried by 24% and found beneficial by 33%, while meditation had been tried by 22% and found beneficial by 37%. Yoga had been found beneficial by half of the 9% of the group who had tried it. Two afibbers had tried Qi Gong and both had found it beneficial.

Treatment of Underlying Disease

A total of 18 Group A members (39%) and 14 Group B members (35%) had attempted to reduce or eliminate their afib burden by dealing with underlying disease conditions. Table 31 shows the most prevalent conditions dealt with and the degree of success in eliminating afib by doing so.

Table 31
Elimination of Diseases

	Group A		Group B		Total	
Disease	Tried,%	Benefit,%	Tried,%	Benefit,%	Tried,%	Benefit,%
Sleep apnea	9	75	5	0	7	50
GERD	20	33	15	17	17	27
Digestive problems	11	60	18	0	14	25
Food allergies	9	50	10	0	9	25
Hypoglycemia	9	25	3	0	6	20
Hypothyroidism	4	0	3	0	3	0

Treatment of sleep apnea (with a CPAP machine) was the most effective of the disease elimination protocols with an overall success rate of 50% (75% in Group A). The most common disease condition was GERD (gastroesophageal reflux disease), which 17% of the 32 afibbers had attempted to eliminate with a 27% success rate as far as reduction or

elimination of afib is concerned. Fourteen percent had tried to eliminate digestive problems and 25% (60% in Group A) had been able to eliminate or reduce (by 50% or more) their afib by doing so.

Preventing Ectopics

Thirty percent of Group A did not experience ectopics, while only 17% of Group B were free of this annoyance. One third of Group A had found an effective means of dealing with ectopics, while only 15% of Group B had done so. The most effective way of preventing ectopics was through supplementation with potassium (including low-sodium V8 juice) which 60% of Group A had found beneficial. Forty percent had found magnesium supplementation beneficial either on its own or in combination with potassium, and 20% (all vagal) had found the use of tranquilizers to be beneficial for ectopics.

Trigger Avoidance

Forty-five percent of Group A no longer had to avoid triggers, while 28% still had to do so, but to a lesser extent.

Review of Successful Protocols

The main modalities used by Group A were almost evenly split between the use of pharmaceutical drugs and the use of other approaches. Ultimately, 22 Group A respondents (no afib episodes in the last 6 months) had managed to achieve their afib-free status through the use of antiarrhythmic drugs (mostly flecainide). Fourteen had relied solely on drugs, while 4 had combined drugs, supplements (mostly magnesium), and alternative protocols. Four had combined antiarrhythmics with trigger avoidance, dietary changes, and elimination of GERD.

The remaining 24 respondents had managed to remain afib-free for at least 6 months through the use of protocols not involving pharmaceutical drugs. Trigger avoidance had been successfully practiced by 14 Group A members, but was usually accompanied by other protocols such as supplementation (10 respondents), dietary changes (4 respondents), and stress management and other alternative therapies (6 respondents). Diet changes had been made by 9 respondents, 8 of whom had also used supplementation (mostly magnesium) and 3 had also used other alternative methods. One respondent had managed to become afib-free through dietary changes alone. Seventeen (71%) of the 24 respondents had used supplementation with 3 relying on supplementation alone. It is interesting that no mixed afibbers had been successful in using dietary changes to eliminate their afib burden. The most successful – based on

this albeit very small sample – were female, vagal afibbers who switched to a paleo diet.

CONCLUSIONS

A total of 248 afibbers (189 males and 59 females) participated in LAF Survey 14. The majority (89%) had paroxysmal afib with 50% having the vagal type and 33% the mixed. Mixed afibbers experienced significantly more episodes than did vagal ones, but adrenergic afibbers carried the highest overall afib burden (# of episodes x average duration) prior to the implementation of their programs.

A total of 224 respondents had attempted to reduce or eliminate their afib using means other than ablation or surgical procedures and had been on their program for 6 months or longer (36 months on average).

In answer to the question, "**Did you ultimately find a program that was successful in materially reducing or eliminating your afib burden?**", 144 respondents (64%) answered "YES" and 80 (36%) answered "NO". A total of 29 NO responders went on to have an ablation/maze procedure, of which, 19 (66%) were deemed to be successful. Five of the NO responders stated that their intervention program had been partially successful, but they decided to undergo an ablation or maze procedure anyway. Overall, 45 of the 248 respondents (18%) had undergone an ablation/maze procedure with 25 or 56% being successful.

There were no significant differences in baseline characteristics between YES and NO responders. The division into the two groups is clearly subjective since it is based on the respondents' feeling about the benefits of their chosen protocols. Nevertheless, some interesting differences stand out.

- The difference in percentage of mixed and vagal afibbers (27% vs 45% and 56% vs 38%) between the YES and NO responders was statistically significant ($p = 0.03$). This difference would indicate that vagal afib is comparatively easier to manage than is mixed afib.

- There was no significant difference in afib burden prior to program implementation when comparing YES responders to NO responders indicating that initial afib burden, as such, is not a determinant of ultimate success in reducing or eliminating afib.

- The most popular intervention program was trigger avoidance engaged in by 88% of all respondents. This was followed by supplementation (84%), therapy with pharmaceutical drugs (79%), dietary changes (55%), and other therapies (55%).

- Avoidance of caffeine had been found useful by 67% of respondents, alcohol avoidance by 56%, and avoidance of aspartame and MSG by 38% and 34% respectively. Altogether, respondents had identified 17 important triggers.

- The most important dietary changes were elimination of wheat, gluten and dairy products, and a switch to the Paleo diet. These changes were significantly more successful among females and vagal afibbers.

- Eighty-five percent of responders had tried supplementation. The most effective supplement was magnesium glycinate, which had been found beneficial by 48% of those who had tried it. Potassium supplementation (including low-sodium V8 juice) had been tried by 79% of all respondents and found beneficial by 43%. Taurine had been tried by 43% and found beneficial by 32%. About half of those supplementing with magnesium also took potassium and taurine.

- The most successful pharmaceutical drug was amiodarone, which had been tried by 10% and found beneficial by 65%. Flecainide (Tambocor) was the most popular antiarrhythmic. It had been tried by 38% of all respondents and been found successful by 60%.

- Breathing exercises and relaxation therapy were the most commonly tried stress reduction measures and had been found successful by 39% and 34% respectively. Yoga had been tried by 19% and found beneficial by 52%.

- Dealing with GERD, digestive problems, and food allergies had benefited 26-30% for those who dealt with these conditions. This clearly indicates that digestive problems are an important component of afib.

- The percentages of YES responders who believed that the various therapies had been beneficial on their own, or in combination with other measures, are given below:

	Sole Therapy	Combined
Trigger avoidance	36%	50%
Dietary changes	30%	55%
Supplementation	25%	53%
Drug therapy	56%	25%
Other therapies	19%	53%
Disease treatment	35%	44%

- About 50% of respondents had found a way of shortening their episodes. On-demand (pill-in-pocket) flecainide had been found effective by 25%, light exercise by 24%, and resting by 21%. The most effective therapies for women were hydrotherapy, meditation, tranquilizers and resting, while the most effective therapy for men was vigorous exercise. This is not surprising since vigorous exercise will increase adrenergic tone and 80% of respondents who had found vigorous exercise beneficial were male, vagal afibbers.

- A third of respondents had found ways of preventing ectopics with supplementation with the magnesium/potassium/taurine combination being the most popular followed by the consumption of low-sodium V8 juice.

- A comparison between 46 afibbers (Group A) who had managed to completely eliminate their afib episodes over the most recent 6 months and 40 afibbers (Group B) whose condition had worsened or remained constant revealed the following:

    - The median birth weight in Group A was substantially lower than in Group B.
    - There was no indication that members of Group B had tried fewer interventions than had those members in Group A.
    - Group B had achieved no improvement at all through dietary changes, while Group A had achieved significant benefits, especially by changing to the Paleo diet (75%), avoiding dairy (60%), and eliminating wheat and gluten (33%).
    - Group A had achieved very significant benefits from supplementing with magnesium, potassium and taurine, while Group B had seen little or no benefit from supplementing.
    - Amiodarone was the most effective antiarrhythmic, but its use, in 50% of cases, was accompanied by adverse effects, notably thyroid problems. Tranquilizers (Ativan,

Xanax, Valium) were found to be quite effective for mixed afibbers. Flecainide had been found effective by 41% of those who had tried it.

- The treatment of sleep apnea and GERD had benefited 50% and 27% respectively.

Overall, it would appear that Groups A and B and indeed, YES and NO responders, are markedly different in that practically nothing worked for NO responders and those in Group B, while several different protocols worked quite well for YES responders and those in Group A.

It is not apparent what the difference is since there is no indication that NO responders were less diligent in their approach than were YES responders. It is possible that the statistically significant lower birth weight in Group A could contain a clue, but it is certainly not obvious what that clue might be, especially since a higher birth weight is generally associated with better cardiovascular health.

I have discussed the birth weight finding with Pat Chambers, MD and he points out that a higher birth weight such as found in Group B is associated with increased baroreflex sensitivity[1] and that an increased baroreflex sensitivity, in turn, is associated with more difficulty in dealing with sudden changes in autonomic tone that could lead to an afib episode. Thus, it may well be that lone afibbers can be divided into two groups - those (like in Group A) whose main underlying problems are magnesium deficiency, wheat sensitivity, etc. and those (like in Group B) whose main underlying problem is an increased baroreflex sensitivity. Clearly, it would be much easier to correct a magnesium deficiency than an increased baroreflex sensitivity, perhaps explaining why "nothing worked" for Group B. It is also intriguing to speculate that the reason why mixed type afibbers (neither pure adrenergic nor pure vagal) have a more difficult time reducing their afib burden could be that they have increased baroreflex sensitivity. Hopefully, medical researchers will some day cast more light over this finding.

[1] Leotta, G, et al. Effects of birth weight on spontaneous baroreflex sensitivity in adult life. *Nutrition, Metabolism and Cardiovascular Diseases*, Vol. 17, May 2007, pp. 303-10

Appendix A
Protocol for Afib Reduction/Elimination

The following 12-step program is based on the findings of LAF Survey 14, numerous Bulletin Board postings, especially from "The List", and with supporting information from my first book *Lone Atrial Fibrillation: Towards a Cure – Volume 1*.

1. Ensure that your condition is indeed lone atrial fibrillation (no underlying heart disease) and rule out known causes such as thyroid disorders, hypoglycemia, hyperaldosteronism (Conn's Syndrome) and pheochromocytoma.

2. Ensure that your liver and kidney functions are normal before embarking on an abatement program based on pharmaceutical drugs or supplements. This would involve BUN, creatinine and liver enzyme tests. It is also a good idea to establish your baseline electrolyte concentrations. This can be done through a simple blood test. Although the results are not very indicative of the concentration where it matters, namely in the myocytes (heart muscle cells) they will alert you to serious deficiencies. If the potassium level is below 4.5 mEq/L then supplementation is likely necessary to bring the daily intake up to the recommended 4500 mg/day. Magnesium level is best determined in red blood cells (RBCs) or in scrapings from the mouth (Exatest). NOTE: Probably close to 90% of lone afibbers test low for magnesium when using the Exatest. Finally, it would also be advisable to determine if systemic inflammation is present. A high-sensitivity C-reactive protein (hs-CRP) level above 1.0 mg/L (0.1 mg/dL) may indicate the need for supplementation with an effective anti-inflammatory such as beta-sitosterol or Zyflamend.

3. If not already doing so start keeping a detailed journal of the timing, duration and likely triggers of your afib episodes. This is essential in helping you determine the nature of your afib (adrenergic, mixed or vagal) and in establishing a successful abatement program.

4. Determine what your triggers are and scrupulously avoid them. If you are not yet sure what they are try avoiding caffeine, alcohol, MSG, aspartame, wheat, tyramine-containing foods, sugar and sleeping on your left side and see if that improves your situation.

5. Unless your magnesium and potassium levels are excessive begin supplementing with the magnesium, potassium, taurine combo to see if that is beneficial in your specific case. If your sun exposure

is limited supplement with vitamin D as well to ensure optimum absorption of magnesium.

6. Eliminate wheat and gluten-containing grains from your diet. Rice is OK and oats and rye may be as well, but this needs to be determined on an individual basis. Also avoid high glycemic load foods, *trans*-fatty acids and tyramine-containing foods. Avoid large meals and if hypoglycemia is a problem have a light snack mid-morning and mid-afternoon. Ensure adequate hydration; daily water intake, in addition to that supplied by food, should be 1-1.5 liters (32-48 oz.)

7. Determine if you have any disease conditions associated with atrial fibrillation such as sleep apnea, GERD (gastroesophageal reflux disease), hyperthyroidism or hypoglycemia and take appropriate steps to deal with them. Also ensure that your digestive process is functioning properly. Bloating and gas formation in the stomach often cause ectopics and in some cases, atrial fibrillation. If this is a problem supplementation with pancreatic enzymes and betaine hydrochloride may be helpful. If bloating and gas occur close to bedtime an 80 mg simethicone tablet may help (best taken about 45 minutes prior to bedtime).

8. Find a relaxation therapy or other alternative protocol helpful in relieving stress that works for you and practice it daily.

9. If following steps 1-8 does not provide relief switch to a strict paleo diet. This combined with magnesium/potassium/taurine supplementation is probably the most effective step you can take, but it does require a very significant commitment, persistence, self-discipline and full cooperation from your spouse or significant other.

10. Try the on-demand (pill-in-pocket) approach to terminating episodes quickly with flecainide crushed and swallowed with lukewarm water at the start of an episode (200 mg for people weighing less than 70 kg (154 lbs) and 300 mg for people weighing more than 70 kg). In the case of a heart rate exceeding 100 bpm taking a beta-blocker first may be advisable. Propafenone (Rythmol) can also be used for the on-demand approach (450 mg for people weighing less than 70 kg and 600 mg for people weighing over 70 kg).

11. Consider going on an antiarrhythmic drug full time. Flecainide (Tambocor), possibly in combination with a beta-blocker, would appear to be most successful and should generally be tried first

(50-100 mg every 12 hours). Only as a last resort should amiodarone or amiodarone+flecainide be tried.

12. If steps 1-11 have been faithfully followed and doing so has brought no relief get in line for an ablation or maze procedure with a highly skilled and experienced electrophysiologist or cardiac surgeon.

Why not go directly to an antiarrhythmic or ablation you may ask!? Because, there is no guarantee of success and both have the potential for serious adverse effects, while improving your diet, eliminating wheat and supplementing with magnesium only have positive effects.

Ablation/Maze Survey – 2007

2007 Ablation/Maze Survey

The 2007 Ablation/Maze Survey produced 303 responses, 120 of which were updates to responses submitted in the 2006 survey. Combining the 335 respondents to the 2006 survey with the 183 new respondents contributing their experience in 2007 results in a total database of 516 patients having undergone a total of 798 procedures.

The first part of the survey findings cover radiofrequency ablation procedures and the general background of respondents. Part 2, to be published in the February 2008 issue, will cover the maze and mini-maze procedures, cryoablation, right and left flutter ablations, and other less common procedures.

This report has been divided into six major sections: –

- Definition of Terms
- Evaluation of Background Data
- Initial Procedure Results – RF Ablation
- Procedure Outcome – RF Ablation
- Patient Outcome
- Performance Rating

Definition of Terms

Types of Atrial Fibrillation

- **Paroxysmal –** Episodes occurring intermittently and tending to terminate spontaneously - usually within 48 hours.
- **Persistent** – Episodes lasting longer than 7 days and not terminating spontaneously, but can be terminated with chemical or electrical cardioversion.
- **Permanent** – Constant (chronic, 24/7) afib not amenable to effective termination by cardioversion.
- **Adrenergic** – Episodes occurring almost exclusively during daytime, often in connection with exercise or emotional or work-related stress.

- **Vagal** – Episodes tending to occur during rest, at night or after a meal. Alcohol and cold drinks are common triggers.
- **Mixed (random) –** Episodes occur anytime and do not consistently fit the adrenergic or vagal pattern.

Procedures

- **Focal ablation** – The original radiofrequency (RF) ablation procedure in which specific active foci of aberrant impulses are located and ablated.
- **Pulmonary vein ablation (PVA) –** An ablation procedure in which a ring of scar tissue is placed just inside the pulmonary veins where they enter the left atrium. The original PVA carries a high risk of pulmonary vein stenosis, so it is rarely used in its original form anymore. Thus, the term PVA is now associated with ablation around the pulmonary veins when a more specific description (SPVI, CAPVI or PVAI) is not used by the EP or the exact type of pulmonary vein isolation procedure is not known by the respondent.
- **Segmental pulmonary vein isolation (SPVI or Haissaguerre procedure) –** In this procedure electrophysiological mapping (using a multipolar Lasso catheter) is used to locate the pathways taken by aberrant impulses from the pulmonary veins and these pathways are then eliminated by ablation around the veins approximately 5 to 10 mm from the ostium of the veins.
- **Circumferential anatomical pulmonary vein isolation (CAPVI or Pappone procedure) –** In this procedure anatomical mapping (CARTO) is used to establish the exact location of the pulmonary veins. Two rings of lesions are then created in the left atrium - one completely encircling the left pulmonary veins and another completely encircling the right pulmonary veins; the two rings are usually joined by a linear lesion.
- **Pulmonary vein antrum isolation (PVAI or Natale procedure) –** This procedure is a variant of the Haissaguerre procedure. It involves locating aberrant pathways through electrophysiological mapping (using a multipolar Lasso catheter) and ablating these pathways guided by an ultrasound (ICE) catheter. The ablation is performed as close as possible to the outside edge (antrum) of the junction between the pulmonary veins and the atrial wall. All four pulmonary veins as well as the superior vena cava (if indicated) are isolated during the procedure.

- All three variants of the PVI procedure may be followed by focal ablations involving other areas of the atrium wall or creation of linear lesions in order to eliminate sources of afib located outside the pulmonary veins.
- **Cryoablation –** In this procedure a nitrogen-cooled, rather than electrically-heated, catheter is used to create the ablation lesions.
- **Maze procedure** – The original surgical procedure, the full maze or Cox procedure, used a cut-and-sew protocol for creating lesions forming a "maze" that conducted the electrical impulse from the SA to the AV node, while at the same time interrupting any "rogue" circuits. The cut-and-sew method has now largely been replaced by the use of RF-powered devices, but cryosurgery, microwave application, and high-intensity focused ultrasound (HIFU) have all been tried as well and are preferred by some surgeons. Creating the full set of maze lesions usually requires open-heart surgery and the use of a heart/lung machine.
- **Mini-maze procedure –** The so-called mini-maze procedure also involves lesions on the outside of the heart wall, but access to the heart is through incisions between the ribs rather than via open-heart surgery. The mini-maze may involve the creation of the full maze set of lesions, but usually focuses on pulmonary vein isolation. The procedure does not involve the use of a heart/lung machine and lesions are created by the application of RF energy or cryoablation.
- **Right atrial flutter ablation –** This procedure involves the application of radiofrequency energy to create a block of the cavotricuspid isthmus in the right atrium so as to interrupt the flutter circuit. A right atrial flutter ablation is usually successful in eliminating the flutter, but rarely helps eliminate atrial fibrillation and may even, in some cases, cause the development of atrial fibrillation.
- **Left atrial flutter ablation –** Left atrial flutter is a common complication of ablation for atrial fibrillation. It most often resolves on its own, but if not it may be necessary to re-enter the left atrium, locate the offending circuit, and block it via radiofrequency catheter ablation.
- **AV node ablation + pacemaker –** In this procedure the AV node (the ventricular beat controller) is isolated from any extraneous impulses through cauterization of surrounding tissue, and the ventricles are fed their "marching order" through an implanted pacemaker. The procedure does not eliminate atrial fibrillation, but makes it substantially less noticeable. Patients who have undergone AV node ablation

and pacemaker installation are entirely dependent on the pacemaker and are usually on warfarin for life.

Statistical Terms

- **N** – The number of respondents in a sample.
- **Mean** – The average value for a group of data, i.e. the sum of the values of all data points divided by the number of data points.
- **Median** – The value in the middle of a group of data, i.e. the value above which half of all individual values can be found and below which the remaining 50% can be found.
- **Statistical significance** – In this study average values are considered different if the probability of the difference arising by chance is less than 5 in 100 using the two-tailed t-test. This is expressed as "p" being equal to 0.5 or less. Lower values of p are indicative of a greater certainty that observed differences are truly significant.

All statistical tests were carried out using the *GraphPad Instat* program (GraphPad Software Inc, San Diego, CA).

Definition of Success

The success of the procedures is (unless otherwise noted) judged at least 6 months after the last reported ablation (initial or touch-up). It is defined in two ways:

Subjectively – The afibber's own opinion as to whether the procedure was completely successful, partially successful, or not successful at all

Objectively – The following criteria are used to define success objectively:

- Complete success – No afib episodes, no antiarrhythmics, consistent sinus rhythm
- Partial success – No afib episodes, but on antiarrhythmics
- Failure – Afib episodes still occurring
- Uncertain – Cases where insufficient data was available or where less than 6 months had gone by since the procedure.

Afib burden – The number of episodes over a 3-month period multiplied by their average duration.

Overview of Procedures

The procedures used to cure atrial fibrillation can be divided into two groups: – **catheterization procedures** and **surgical procedures**. Both types involve the creation of lesions on the heart wall (right and/or left atrium) in order to stop the propagation of impulses not involved in conducting the heart beat "signal" from the sino-atrial (SA) node to the atrio-ventricular (AV) node.

Catheterization procedures create the lesions from the inside via an ablation catheter threaded through the femoral vein and are performed by electrophysiologists (EPs). Surgical procedures create the lesions from the outside and access is either through incisions between the ribs or may involve open-heart surgery and the use of a heart/lung machine. Surgical procedures are carried out by cardiothoracic surgeons.

The overwhelming majority of catheterization procedures use radiofrequency (RF) energy to create the lesions, but some EPs prefer the use of nitrogen-cooled catheters (cryoablation) rather than RF-powered ones due to their reduced risk of creating pulmonary vein stenosis.

The original surgical procedure, the full maze or Cox procedure, used a cut and sew protocol for creating lesions forming a "maze" that conducted the electrical impulse from the SA to the AV node, while at the same time interrupting any "rogue" circuits. The cut and sew method has now largely been replaced by the use of RF-powered devices, but cryosurgery, microwave application, and high-intensity focused ultrasound (HIFU) have all been tried as well and are preferred by some surgeons.

The so-called mini-maze procedure also involves lesions on the outside of the heart wall, but access to the heart is through incisions between the ribs rather than via open-heart surgery. The mini-maze may involve the creation of the full maze set of lesions, but usually focuses on pulmonary vein isolation. The procedure does not involve the use of a heart/lung machine.

Most of the rogue electrical impulses that create afib originate in the area where the pulmonary veins join the left atrium. Thus, all catheterization procedures aimed at curing afib involve electrical isolation of the pulmonary veins from the left atrium wall. Depending on the origin of the afib, catheterization procedures may also involve ablations of the superior vena cava and coronary sinus (thoracic veins), linear ablation of the left atrial roof, and a standard cavotricuspid isthmus (right flutter) ablation.

Surgical procedures, except for the full maze, also focus on isolating the pulmonary veins, but in addition may involve lesion creation at specific spots located by mapping, removal of the left atrial appendage, and disconnection of the ligaments of Marshall – a potent source of vagal input.

Evaluation of Background Data

Distribution of Procedures

Five hundred and sixteen afibbers responded to the survey and provided data for a total of 798 procedures distributed as follows:

TABLE 1

	Number of Procedures				
RF Ablation Procedures	1st	2nd	3rd	Further	Total
Focal ablation	37	23	3	0	63
Pulmonary vein ablation (PVA)	38	47	12	1	198
Segmental pulmonary vein ablation	54	30	8	0	92
Circumferential pulmonary vein ablation	49	23	5	4	81
Pulmonary vein antrum isolation	89	23	7	2	121
Combination PVI*	3	0	0	0	3
Ablation for SVT	0	2	1	0	3
Ablation procedure not specified	48	23	6	11	88
Total RF ablation procedures	**418**	**171**	**42**	**18**	**649**
Other Procedures					
Cryoablation	6	3	1	0	10
Maze procedure	16	3	1	2	22
Mini-maze procedure	26	3	6	1	36
Right atrial flutter	37	12	4	1	54
Left atrial flutter	6	6	3	0	15
AV node ablation + pacemaker	7	2	1	2	12
Total other procedures	**98**	**29**	**16**	**6**	**149**
GRAND TOTAL	**516**	**200**	**58**	**24**	**798**

* Combination of segmental and circumferential procedures

The majority of procedures (81%) were radiofrequency (RF) ablation procedures aimed at curing atrial fibrillation. Thirty-nine percent of the 516 respondents underwent a second procedure, 11% a third procedure, and 5% underwent further procedures. The most widely used AF ablation procedure was the generic pulmonary vein ablation (PVA) followed by the pulmonary vein antrum isolation (Natale), the segmental PVI (Haissaguerre), and the circumferential PVI (Pappone).

General Background of Respondents

TABLE 2

Demographics	Male	Female	Total
Gender distribution	78%	22%	100%
Average (median) age*, yrs	58	59	58
Median age at diagnosis, yrs	47	49	48
Age range at diagnosis, yrs	5-74	10-79	5-79
Years since diagnosis (median)	8	8	8
Years since diagnosis (range)	1-45	1-44	1-45
Underlying heart disease	9%	8%	8%
AF confirmed by diagnosis	93%	92%	93%
Median age at last procedure, yrs	56	56	56
Age range (last procedure), yrs	26-81	26-85	26-85

* At time of completing survey

There are no significant differences between males and females as far as demographic variables are concerned.

Afib Type

A total of 434 respondents had provided detailed information regarding their type of AF (adrenergic, mixed, vagal) prior to their procedure. The distribution was as follows:

TABLE 3

Type of AF	Male	Female	Total
N (no. of respondents)	339	95	434
Adrenergic, %	5	5	5
Mixed, %	49	54	50
Vagal, %	25	18	23
Total paroxysmal, %	78	77	78
Persistent, %	4	7	5
Permanent, %	18	16	17
TOTAL	100	100	100

The majority of respondents (78%) had paroxysmal or persistent AF, while 17% were in permanent AF. Mixed (random) AF was the most common paroxysmal type for both sexes followed by vagal, permanent and adrenergic.

Afib Frequency and Burden

Four hundred and seventy-eight respondents had provided information about their episode frequency. The distribution was as follows:

TABLE 4

Afib Frequency*	Male	Female	Total
N (no. of respondents)	374	104	478
Permanent, %	16	14	16
Daily, %	24	27	24
Twice weekly, %	26	25	26
Weekly, %	13	13	13
Twice a month, %	10	7	9
Monthly, %	5	7	6
Every 2 months, %	1	1	1
Every 3 months, %	2	4	2
Every 6 months, %	2	1	2
Once a year, %	0.5	1	1
Less than once a year, %	0.5	0	0.4

* Prior to first procedure

The majority of respondents (79%) experienced episodes at least once a week and 40% were in afib every day (including permanent afibbers). Only 6% of those seeking a cure through ablation or surgical procedures had episodes less frequent than once a month. This indicates that most afibbers only opt for a procedure when the frequency of episodes becomes intolerable or permanent AF becomes a reality.

The median duration of paroxysmal episodes was 9 hours with a wide range of from a few minutes to 120 hours. There was no statistically significant difference in afib burden between paroxysmal afibbers taking antiarrhythmics or blockers and those taking no medications on a continuous basis.

An estimate of total afib burden for the three types of paroxysmal afib is given below.

TABLE 5

Type of Afib	N	Med. # of Episodes	Med. Duration hours	Med. Burden hours
Adrenergic	20	26	5	104
Mixed	197	26	10	208
Vagal	96	26	8	163
Not known	63	26	8	180
Total paroxysmal	376	26	9	180

NOTE: Episodes per 3 months estimated as follows: –

Daily episodes = 90	One episode every 2 months = 1.5
Twice-weekly episodes = 26	One episodes every 3 months = 1
Weekly episodes = 13	One episode every 6 months = 0.5
Twice-monthly episodes = 6	One episodes every year = 0.25
Monthly episodes = 3	

Burden = median no. of episodes over 3 months multiplied by median duration in hours

It is clear that mixed afibbers have longer episodes and a heavier afib burden than do adrenergic and vagal ones, and these differences are statistically significant. This finding adds to the evidence that mixed afib is the most difficult to deal with.

Comparison of Baseline Characteristics

It would be of interest to compare baseline characteristics between afibbers who decided to undergo an ablation or surgical procedure and those who were able to eliminate their afib through medications or alternative protocols (for at least 6 months). Such a comparison is presented in the table below.

TABLE 6

	Ablation/Maze Respondents[1]	Meds/Alternative Respondents[2]
Male, %	78	76
Female, %	22	24
Present age (median), yrs.	58	60
Age at diagnosis, yrs	48	50
Years since diagnosis	8	7
Paroxysmal – mixed, %	50	24
Paroxysmal – vagal, %	23	63
Permanent, %	17	2
3-mos. parox. median burden, hrs.	180	16

[1] Respondents to LAFS-12
[2] Group A in LAFS-14

It is clear from this comparison that afibbers who opted for an ablation/maze procedure carried a much heavier afib burden prior to their procedure (an average of 180 hours over a 3-month period) than did afibbers who were able to eliminate their afib (for at least a 6-month period) through alternative protocols, or the use of medications (an average of 16 hours over a 3-month period).

It is also clear that the ablation/maze group included significantly more permanent afibbers (17%) than did the medication/alternative group (2%). Finally, in the medication/alternative group 63% of respondents had vagal afib versus only 23% in the ablation/maze group. Vagal afib is generally easier to manage than is mixed.

Use of Antiarrhythmics and Blockers

The majority of respondents (86%) were taking one or more drugs on a continuous basis to reduce their episode frequency and duration, or ameliorate the effects of their permanent AF. The popularity of the various drugs among the 493 afibbers who had provided information about AF type and drug use is presented below.

TABLE 7

Drug	Adrenergic	Mixed	Vagal	Persist.	Perm.	Unknown	Total
	%	%	%	%	%	%	%
Beta-blockers	10	16	11	9	19	10	14
Calcium chan. block.	0	4	6	14	16	6	7
Amiodarone	0	7	5	27	12	12	9
Digoxin	0	0	0	0	1	1	1
Disopyramide	5	2	3	5	1	0	2
Dofetilide	0	5	5	9	8	7	6
Flecainide	29	27	29	9	8	22	23
Propafenone	0	13	13	9	5	7	10
Sotalol	29	12	12	5	8	15	12
Combination A	5	0	2	0	0	0	1
Combination B	0	0	1	0	3	3	1
Other (incl. combs.)	5	0	0	0	1	0	0
No drugs	19	13	12	14	15	15	14
TOTAL, %	100	100	100	100	100	100	100
Number in group	21	212	98	22	73	67	493

Combination A – antiarrhythmic + beta-blocker
Combination B – antiarrhythmic + calcium channel blocker

Flecainide (Tambocor) was the most prescribed antiarrhythmic and was used on a continuous basis by 23% of respondents. Beta-blockers were the second most popular drugs followed by sotalol, propafenone and

amiodarone. About 35% of permanent afibbers were, as would be expected, solely on beta-blockers or calcium channel blockers. However, a rather astounding 45% were on antiarrhythmics, which would not be expected to benefit permanent afibbers unless they were awaiting cardioversion. It is encouraging to see the low usage of digoxin (Lanoxin), which should never be used by lone afibbers. The usage of digoxin was only 0.6% in this survey as compared to 7% in LAF Survey 1 conducted in February 2001.

Almost 50% of vagal afibbers (paroxysmal or persistent) were on drugs with beta-blocking properties (beta-blockers, propafenone, amiodarone and sotalol) on a continuous basis. These drugs are generally contraindicated for vagally-mediated AF. Flecainide was the most prescribed drug for vagal afibbers followed by propafenone, sotalol, beta-blockers, and amiodarone. Sotalol and flecainide were the most popular drugs for adrenergic afibbers, while flecainide was the most prescribed drug for mixed afibbers. Fourteen percent of all respondents used no drugs to manage their afib.

As would be expected in a group of afibbers awaiting ablation or maze procedure, the drugs were clearly not effective in preventing episodes or in lessening the overall burden of the afib. The following table shows the average values for afib frequency, duration and burden (frequency x duration) for a group of 223 paroxysmal afibbers during the 3-month period preceding their first procedure.

Sixty of 405 paroxysmal afibbers (15%) were using the on-demand (pill-in-the-pocket) approach in an attempt to shorten their episodes. Median episode duration with flecainide was 10 hours (range of 1 – 72 hours), 15 hours with propafenone (range of 2 – 90 hours), and 8 hours with other approaches. This compares to a median episode duration of 8 hours (range of 0.1 – 96 hours) when not using the on-demand approach. Thus, in this group of afibbers, 86% of whom were using antiarrhythmics or blockers on a continuous basis, the use of the on-demand approach did not seem to confer any benefit.

Initial Procedure - RF Ablation

Demographics

A total of 418 afibbers underwent a RF ablation for atrial fibrillation as their first procedure. The majority of the 409 respondents who knew their type of afib had the paroxysmal form (80%), 5% had persistent afib, while the remaining 15% were in permanent afib. Among the 279 paroxysmal afibbers who were aware of the initiating circumstances for their episodes, 62% characterized themselves as mixed, 32% were vagal, and 6% were adrenergic.

The median age of respondents at the time they completed the questionnaire was 58 years with a range of 26 to 86 years. The median age at diagnosis was 47 years with a range of 5 to 79 years. The median age at the latest procedure was 56 years with a range of 26 to 85 years. The average (median) number of years between diagnosis and last procedure was 8 years with a range of 1 to 44 years.

Twenty-three percent of respondents were female. Six percent of respondents had been diagnosed with heart disease.

Respondents with reported heart disease were diagnosed with afib significantly later in life than those without heart disease (52 versus 46 years of age) and underwent their ablation later (59 versus 55 years of age).

Initial Procedure Results

Only afibbers who had undergone their first RF ablation at least 6 months prior to completing the survey questionnaire were considered in this evaluation in order to avoid making premature conclusions as to success. Thus, 365 afibbers who knew the outcome of their first ablation were included. Results are presented in the table below.

TABLE 8

	# in Group	Complete Success,%	Partial Success,%	Failure,%
Ablation Results				
Adrenergic	15	44	6	50
Mixed	157	35	6	58
Vagal	71	33	3	64
Not sure	52	24	7	69
Total paroxysmal	295	33	6	61
Persistent	14	46	8	46
Permanent	56	42	5	53
Grand total	**365**	**35**	**6**	**59**
Other Possible Variables				
Underlying heart disease	24	29	4	67
Outcome for males	281	36	4	60
Outcome for females	84	31	13	56
Demographics		years	years	years
Age at diagnosis, med.	365	49	45	46
Years since diagnosis	365	9	8	8

The overall rate of complete success (no afib, no antiarrhythmics) for a first RF ablation was 35%. The rate of partial success (afib controlled with antiarrhythmics) was 6%, and the overall failure rate was a disappointing 59%. There was no statistically significant difference in failure rate for the 3 types of AF (adrenergic, mixed and vagal). The failure rate for permanent afibbers tended to be slightly lower than for paroxysmal afibbers, while the failure rate for afibbers with underlying heart disease was somewhat higher than the average. However, none of these differences reached statistical significance.

The seeming anomaly that ablations for permanent and persistent afib have lower failure rates can perhaps be explained by the fact that 80% of these ablations were carried out by top-rated EPs.

The difference in outcome for male and female afibbers was not statistically significant, nor did present age, age at diagnosis, or years since diagnosis correlate with success/failure.

The overall success rate (35%) observed in this survey is clearly disappointing. However, as previous surveys have shown, success rates are mostly dependent on the skill and experience of the EP performing the procedure.

Success Rate vs. AF Severity

It is conceivable that the success rate might be affected by the severity of the AF (frequency and duration of episodes).

TABLE 9

Parameters	# in Group	Complete Success,%	Partial Success,%	Failure,%
Episode frequency				
Permanent	55	42	5	53
Daily	81	30	5	65
Weekly or twice-weekly	138	32	4	64
Monthly or twice-monthly	54	41	11	48
Less than once a month	23	43	4	53
Episode duration				
Less than 10 hrs	129	34	3	63
10 - 24 hrs	99	33	8	59
Longer than 24 hrs	41	37	7	56
Permanent	55	42	5	53

Episode duration, somewhat surprisingly, did not play a statistically significant role in determining the outcome of the first ablation. The risk of failure did, however, increase with increasing episode frequency. Afibbers who experienced episodes every week or more frequently had a 65% risk of failure, while those with less frequent episodes had a failure risk of 49%. This difference is statistically significant ($p = 0.03$) and may indicate that ablation should be considered if episodes frequency approaches once a week. However, in assessing the validity of any possible correlation such as this, it should always be kept in mind that the overriding factor in any evaluation of ablation success is the EP performing the procedure.

Second and Third Procedure Results

Only afibbers who had undergone their second and third ablations at least 6 months prior to completing the survey were included in this tabulation in order to avoid making premature conclusions as to success. Results are presented in the table below.

TABLE 10

	# in Group	Complete Success,%	Partial Success,%	Failure,%
Procedure outcome				
1st procedure	365	35	6	59
2nd procedure	141	34	6	60
3rd procedure	34	32	15	53
Total/Average	**540**	**35**	**6**	**59**

The outcome of the second and third procedures is not significantly different from those of the first procedure, thus supporting the claim by many EPs that a follow-up procedure is not materially different from the

initial procedure. The remainder of this section will thus combine the results for all RF ablation procedures for which the outcome is known (including fourth, fifth and sixth procedures).

Procedure Outcome - RF Ablation

Popularity of Procedures

TABLE 11

Procedure	1998-2003,%	2004-2005,%	2006-2007,%	1998-2007,%
Focal ablation	19	7	8	10
PV ablation (PVA)	40	28	28	31
Segmental PVI	8	17	16	14
Circumferential PVI	7	14	15	12
Antrum PVI	8	22	22	19
Combination PVI*	0	0	1	0
Ablation for SVT	0	0	1	0
Unspecified	18	12	13	14
Total # in period	146	276	277	649

* Combination of segmental and circumferential procedures

It is clear that focal ablation as such has declined over the years in the group surveyed. The popularity of the various procedures aimed at isolating the pulmonary veins has, on the other hand, increased. The most reported procedure is the generic PV ablation (PVA), which likely includes elements of the Haissaguerre, Natale and Pappone methods. This is followed by the PV antrum (Natale) method at 19%, the segmental ablation (Haissaguerre) method at 14%, and the circumferential PVI (Pappone) at 12% over the period 1998-2007.

All three procedures have shown substantial growth since the 1998-2003 period. Of course, the procedure distribution may be quite different if another population group was surveyed.

Outcome of Procedures

TABLE 12

	1998-2004			2005-2007			1998-2007		
Procedure	Comp. Succ.	Part. Succ.	Fail.	Comp. Succ.	Part. Succ.	Fail.	Comp. Succ.	Part. Succ.	Fail.
Focal ablation	14	6	81	32	5	63	20	6	75
PV ablation (PVA)	23	5	72	28	7	65	25	5	69
Segmental PVI	30	0	70	47	2	51	43	1	56
Circumferent. PVI	32	14	54	27	7	67	29	10	62
Antrum PVI	51	16	32	64	3	33	59	8	33
Unspecified	13	5	82	37	13	50	25	9	66
Average, %	26	7	67	41	6	54	**34**	**7**	**59**

The average complete success rate for 549 individual RF ablation procedures performed during the period 1998-2007 was 34%. The partial success rate was 7% and the failure rate 59%.

Complete success rates have improved markedly from the average 26% observed for the 1998-2004 period to 41% for the 2005-2007 period. Failure rates also declined from 67% to 54%.

By far the most successful procedure was the pulmonary vein antrum isolation procedure (Natale method) as primarily practiced at the Cleveland Clinic and the Marin General Hospital. Complete success rate for the period 1998-2007 was 59% and the failure rate was 33%. The complete success rate increased from 51% in 1998-2004 to 64% in 2005-2007.

The second most successful procedure was the segmental PVI (Haissaguerre method) as practiced in Bordeaux and several other clinics. Average complete success rate for the period 1998-2007 was 43% and an average failure rate of 56%. The circumferential PVI (Pappone method) had an average complete success rate of 29% and an average failure rate of 62% over the period 1998-2007. There was no improvement in success rate from the 1998-2004 period to the 2005-2007 period. However, the failure rate increased from 54% to 67%, perhaps indicating an influx of relatively inexperienced operators.

In interpreting these results it should be kept in mind that 60% of the pulmonary vein antrum isolation procedures were performed by Dr. Andrea Natale, a recognized world leader in RF ablation.

Adverse Events

The 2007 ablation/maze survey did not specifically enquire about adverse events. However, the 2006 survey did and since the incidence of adverse events is an important consideration in deciding on an ablation, I have repeated the results of the 2006 survey.

The table below shows the incidence of adverse events that occurred during or shortly following 358 RF ablation procedures performed during the period 1998-2006. Fifty-nine percent of all procedures were not accompanied by an adverse event, while 41% were associated with one or more events.

TABLE 13

	1998-2004			2005-2006			1998-2006		
	Comp.	Part.		Comp.	Part.		Comp.	Part.	
Events, %	Succ.	Succ.	Fail.	Succ.	Succ.	Fail.	Succ.	Succ.	Fail.
No adverse event	74	63	55	69	30	48	71	50	52
One or more	26	38	45	31	70	52	29	50	48
Total, %	100	100	100	100	100	100	100	100	100

It is clear that the risk of adverse events is substantially higher in the case of a failed ablation (48%) than in the case of a successful one (29%). This difference is statistically very significant (p=0.002). About 70% of all adverse events reported were fully resolved at the time the survey was completed.

The following table shows the distribution of events. The percentage of events relates to the number of procedures (not the total number of events). Thus, the sum of adverse events and no adverse events may not always equal 100% since some procedures were accompanied by more than one adverse event.

TABLE 14

	1998-2004			2005-2006			1998-2006			
	Comp. Succ.	Part. Succ.	Fail.	Comp. Succ.	Part. Succ.	Fail.	Comp. Succ.	Part. Succ.	Fail.	Total Evnts
None, %	74	63	55	69	30	48	71	50	52	**59**
Hematoma	13	13	19	14	10	21	13	12	20	**17**
TIA	2	0	1	0	0	1	1	0	1	**1**
Stroke	0	0	2	0	0	0	0	0	1	**1**
PV stenosis	2	0	6	0	10	0	1	4	4	**3**
Pericarditis	0	0	3	3	10	1	1	4	3	**2**
Tamponade	0	0	2	0	0	0	0	0	2	**1**
Fistula	2	0	0	0	0	0	1	0	0	**0**
L at. tach/flutt.	2	31	12	8	20	21	5	27	15	**12**
R at. flutter	2	0	8	3	30	8	2	12	8	**6**
Minor revers.	5	0	3	7	10	1	6	4	3	**4**
Life-threaten.	0	0	1	0	0	0	0	0	1	**0**
Perm. damage	0	0	2	0	0	0	0	0	1	**1**
Ad. events, %	**26**	**44**	**59**	**34**	**90**	**55**	**30**	**62**	**57**	**47**

Over the period 1998-2006 hematoma in the groin and thigh area was the most common adverse effect at 17%.

Fortunately, this adverse event was short-lived and was completely resolved at the time the survey was submitted. The second most common adverse event was the development of post-procedural left atrial tachycardia/flutter. This complication arose in 44 of 358 procedures (12%). The left atrial tachycardia/flutter resolved on its own in about 40% of cases, but 6 (14%) ablatees underwent another ablation to deal with it. Post-procedure right atrial flutter was reported by 22 ablatees (6%) and 8 (36%) subsequently underwent an ablation to eliminate it.

In the remaining 64% the right atrial flutter was temporary and resolved itself prior to completion of the survey. NOTE: One hundred and fourteen (32%) of all ablation procedures included a right atrial flutter ablation as a precautionary measure. This approach prevented post-procedural right atrial flutter in 93% of cases.

Minor reversible events occurred during 4% of all procedures, pulmonary vein stenosis during 2.5%, and stroke and TIA accounted for 0.6% and 0.8% respectively. Tamponade (piercing of the heart wall) occurred during 3 procedures and thus accounted for 0.8% of events, pericarditis (inflammation of the heart wall) followed 8 procedures (2.1%), and one ablatee experienced a non-fatal fistula (0.3%). One respondent sustained permanent damage to the mitral valve, and another experienced a life-threatening event.

Afib Episodes after Procedure(s)

TABLE 15

	# in Group	Complete Success, %	Partial Success, %	Failure, %
Continuing afib episodes				
None	156	69	33	8
Less than 1 month	83	12	27	21
One month	21	7	3	3
Two months	30	6	7	7
Three months	21	3	3	5
More than 3 months	155	2	27	56
Total	466	100	100	100

Complete success was associated with only an 11% incidence of continuing afib episodes after the first, often unstable month. Failure, on the other hand, was associated with a 68% incidence of continuing episodes after the first month. This difference was extremely significant ($p=< 0.0001$). It is also evident that experiencing episodes beyond 3 months post-procedure is a strong indicator of ultimate failure. While only 2% of successfully ablated afibbers experienced episodes beyond 3 months, 56% of those ultimately unsuccessful did. These findings support the observation made by Italian researchers that patients who continue to have episodes beyond the first month post-procedure only have a 10% probability of eventual cure[1].

Right Atrial Flutter Ablation

A total of 386 respondents knew whether their procedure(s) had included a right atrial flutter ablation as a routine measure to prevent post-procedure right atrial flutter. Forty-one percent of respondents had undergone the procedure as part of their afib ablation, while the remaining 59% had not. There was no difference in procedural success rate between those who had undergone the flutter ablation and those who had not.

Recovery Time

A question about recovery time was not included in the 2007 ablation/maze survey, so the results from the 2006 survey are repeated below.

TABLE 16

	# in Group	Complete Success.%	Partial Success.%	Failure.%	Average.%
Time to full recovery					
Less than 1 month	96	28	29	33	31
1-2 months	84	26	25	28	27
2-3 months	54	24	8	14	17
More than 3 months	75	21	38	25	24
Total	309	100	100	100	100

About 58% of all ablatees recovered fully in less than 2 months, but 24% took longer than 3 months to return to their pre-ablation level of stamina.

Patient Outcome

Four hundred and nine patients knew the outcome of their procedures (NOTE: The first procedure for 43 of these patients was a flutter ablation) and had gone at least 6 months from the date of their most recent RF atrial fibrillation ablation procedure. The average (median) observation period after the most recent ablation was 17 months with a range of 6 months to 10 years.

Two hundred and twenty of the 409 respondents (54%) were no longer experiencing afib episodes and were no longer on antiarrhythmics (complete success). Forty-six (11%) were also afib-free, but only with the help of antiarrhythmics (partial success), while the remaining 143 (35%) were still experiencing episodes with or without the use of antiarrhythmics. Thus, the overall outcome after an average 1.3 procedures per patient was as follows:

	Objective Judgment	Subjective Judgment
Complete success	54%	65%
Partial success	11%	19%
Failure	35%	16%
TOTAL	100%	100%

The subjectively judged success rate is clearly higher than actually warranted by the actual outcome. It is likely that some afibbers considered their procedure a success even though they still experienced episodes, but generally of lesser frequency and/or shorter duration. Many also were less sensitive to former triggers adding to the feeling of success.

Continued Stroke Prevention

As shown in the table below 51% of afibbers continued a stroke prevention program after completion of their procedures.

TABLE 17

	# in Group	None,%	Warfarin,%	Aspirin,%	Natural Remedies,%
Stroke prevention					
Complete success	183	66	4	17	13
Partial success	30	37	30	23	10
Failure	110	25	36	18	20
Total	323	49	17	18	15

Not too surprisingly, most (96%) of afibbers whose final procedure had been completely successful did not continue with warfarin. Thirteen percent did, however, continue with a natural stroke prevention program, and 17% continued with a daily aspirin. Seventy-four percent of afibbers whose final procedure had failed continued with a stroke prevention program with most (36%) using warfarin, but a significant 20% used natural remedies. The most commonly used natural supplements used for stroke prevention were fish oil, nattokinase, vitamin E, and ginkgo biloba.

Trigger Avoidance

While 75% of successful ablatees no longer needed to avoid previous triggers, only 12% of those having undergone an unsuccessful procedure were so lucky. Nevertheless, it would seem that any ablation, whether successful or not, does help to reduce trigger sensitivity.

TABLE 18

	# in Group	Complete Success,%	Partial Success,%	Failure,%	Average,%
Trigger avoidance					
No longer necessary	163	75	43	12	51
Still necessary	63	7	23	39	20
Much less sensitive	55	11	20	25	17
Uncertain	41	6	13	24	13
Total	**323**	**100**	**100**	**100**	**100**

Post-Procedure Episodes

Seventy-two paroxysmal respondents whose ablation had not been successful had kept track of their episode frequency prior to and after their procedure(s). The median number of episodes in the 3 months prior to the first procedure was 26 compared to 5 after the last procedure. This is clearly a very noticeable improvement and is statistically extremely significant ($p < 0.0001$). The median duration of episodes decreased from 8 hours to 3 hours and this change was again statistically significant ($p= 0.002$).

The total afib burden (episode frequency times average duration over a 3-month period) decreased from a median of 156 hours to 12 hours, again, a highly significant decrease ($p < 0.0001$).

Although the average extent of improvement in afib episode frequency, duration, and burden was impressive, not all ablatees benefited to an equal degree. Thus, while 74% experienced a decrease in their episode frequency, 22% saw an increase, and 4% noticed no change. As far as episode duration is concerned, 75% experienced a decrease, 13% saw an increase, and 12% noticed no change. Finally, in regard to 3-month afib burden, 86% saw a decrease, while 14% experienced an increase in burden.

It is worth noting that 5 paroxysmal afibbers ended up in permanent afib post-procedure as ascertained 6 months after their most recent ablation. On the other hand, 5 out of 10 permanent afibbers became paroxysmal after their failed ablation. This, depending on the afibbers' psychological make-up, may be seen as an improvement, or a worsening of the condition. Overall, even a failed RF ablation is likely to lead to an improvement in afib status, but this outcome is, by no means, certain.

Late Recurrence

Several studies have concluded that the success of a RF ablation can be judged 6 months after the procedure. If one is afib-free at this time then one is likely to remain afib-free. Unfortunately, it now appears that recurrence after one or two years of afib-free bliss is not uncommon. Although not a specific question in the 2007 survey, 6 respondents (1.5%) reported that they had experienced symptomatic afib episodes 1 to 3 years after their initially successful procedure.

Use of Pill-in-the-Pocket Approach

Twenty-five percent of afibbers still experiencing episodes used the on-demand approach in an attempt to shorten their duration.

Changes in Heart Rate

Changes in resting heart rate after RF ablation were quite common among paroxysmal and persistent afibbers.

TABLE 19

	# in Group	Complete Success,%	Partial Success,%	Failure,%	Average,%
Heart rate change					
Increase	137	67	56	41	57
No change	67	23	36	33	28
Decrease	36	10	8	26	15
Total	**240**	**100**	**100**	**100**	**100**

The most frequent post-procedural change was an increase in heart rate (experienced by 57%). This increase was most common among afibbers who had undergone successful procedure(s) (67%) and least common among those whose procedures had failed to cure the afib (41%). This difference was statistically significant (p=0.04). A decrease in heart rate was fairly rare among successfully ablated afibbers (10%), but more common (26%) among those whose procedure had failed.

The reason for the increase in heart rate after an ablation is that a significant portion of vagal nerve endings is damaged during the RF ablation procedure. Because the vagal nerves imbedded in the myocardium serve as “speed controllers” counteracting the adrenergic influence, a reduction in the number of effective vagal nerves would be expected to lead to an increased heart rate. Thus, it is possible that a

more "aggressive" ablation, as indicated by a higher heart rate after the procedure, is more likely to be successful. However, this is speculation on my part and obviously assumes that the "aggression" is directed at the right spots on the atrium walls and pulmonary vein ostia.

It is generally assumed that the increase is temporary, however, this may not always be the case. A mini-survey (2006 survey) of 25 afibbers who had experienced a significant increase (average of 20 bpm) in post-procedure resting heart rate revealed that for 13 out of 25 respondents (52%) the heart rate was still significantly elevated a year or more after the last procedure. From personal experience I know that a substantial increase in heart rate (to 90 bpm or higher) can be very uncomfortable, so it is to be hoped that afib researchers will eventually address this problem.

Quality of Life

Although the main concern of the medical profession when it comes to lone atrial fibrillation is stroke risk, the overwhelming concern of the patient is quality of life. As all afibbers know, being in permanent afib or awaiting the next episode in a state of anxiety has a devastating effect on ones quality of life and radically changes the life of those nearest and dearest to us.

Considering quality of life improvement rather than strictly success or failure of RF ablation procedures, it becomes clear that even a failed ablation may improve life quality. The average complete success rate found in this survey (after an average 1.3 procedures) is 54%. Adding to this partial success (where afib is kept at bay with antiarrhythmics) brings the percentage of afibbers whose lives have been improved through RF ablation to 65%. Further considering that about 70% of ablatees whose procedure failed still reduced their afib burden by at least 50% brings one to the conclusion that RF ablation, whether successful or not, is likely to improve quality of life in close to 90% of those undergoing the procedure. A significant portion of the remaining 10% may however, see a worsening of their condition or may experience a serious adverse event.

Summary

- The overall objectively-rated complete success rate (no afib, no drugs) for 409 afibbers after an average of 1.3 RF

ablations was 54%; partial success was achieved in 11% of cases, and 35% of all afibbers who underwent one or more RF ablations continued to experience AF episodes.

- The subjective judgment of success by ablatees was somewhat more favourable with 66% feeling that the end result was total success, 19% claiming partial success, and 16% judging their procedures as a failure.

- The average objectively rated complete success rate for a single RF ablation procedure was 34%, that of partial success 7%, and that of failure 59%.

- Considering a 50% or greater reduction in afib burden (frequency x duration) as an indicator of improvement, it is estimated that close to 90% of RF ablations were ultimately successful in improving quality of life.

- Forty-one percent of 358 RF ablation procedures were accompanied by an adverse event, the most common (17%) being temporary hematoma in the thigh area. Left atrial tachycardia was also a fairly common adverse effect (12%), but resolved by itself in about 50% of cases. Stroke and TIA were rare at 0.6% and 0.8% respectively. About two-thirds of all adverse events were fully resolved at the time the survey was completed. Successful ablations were much less likely to be accompanied by an adverse event than were unsuccessful ones. NOTE: This data is from the 2006 ablation/maze survey.

- There were no significant differences in success and adverse event rates between a first and subsequent RF ablations, perhaps indicating that the technical difficulty in performing them is pretty much the same.

- The majority (79%) of respondents experienced AF episodes at least weekly prior to their ablation.

- There was no evidence that age at diagnosis and ablation, gender, years of afib, or type of paroxysmal afib affected the outcome to a significant degree. However, more frequent episodes were associated with a lower success rate.

- The most successful procedure for the period 2005-2007 was the pulmonary vein antrum isolation procedure (Natale

method) with a combined single procedure complete and partial success rate of 64%. The segmental PVI (Haissaguerre method) was the second-most successful procedure with a combined single procedure success rate of 47%.

- A significant majority (69%) of afibbers who had a completely successful ablation experienced no AF episodes at all after the procedure. Only 8% of those "doomed to failure" experienced no episodes at all after their procedure. Only 2% of completely successful ablatees experienced episodes for more than 3 months after the procedure, while 56% of unsuccessful ablatees did so. Thus, if AF episodes continue beyond 3 months the procedure is almost certainly a failure. On the other hand, if no AF episodes occur during the first month then the procedure is likely to be a success.

- Almost 60% of ablatees recovered fully in less than 2 months, but 24% took longer than 3 months to return to their pre-ablation level of stamina. NOTE: This data is from the 2006 ablation/maze survey.

- Most (96%) of afibbers who had a completely successful ablation did not continue with warfarin, but 13% of them continued to use natural stroke prevention remedies such as fish oil, nattokinase, vitamin E and ginkgo biloba. Seventeen percent took a daily aspirin for stroke prevention. In contrast, 36% of ablatees with a failed procedure continued on warfarin.

- While 75% of successful ablatees no longer needed to avoid previous triggers, only 12% of those having undergone an unsuccessful ablation were so lucky. Nevertheless, it would seem that any ablation, whether successful or not, does help to reduce trigger sensitivity.

- Even an unsuccessful ablation resulted in a significant reduction in episode frequency in 74% of cases and in 75% of cases was associated with a significant decrease in episode duration. Overall, 70% of unsuccessfully ablated patients experienced a 50% or better decrease in their afib burden.

- A post-ablation increase in heart rate was a common occurrence. This phenomenon was more prevalent among successful ablatees (67%) than among those whose ablation

had failed (41%). This may indicate that a more aggressive approach (increased destruction of vagal nerve endings) is associated with a better outcome.

Performance Rating

Previous ablation/maze surveys have all arrived at the same conclusion that the most important factor in determining the outcome of a RF ablation is the skill and experience of the EP performing it. In order to provide some guidance in regard to the chance of undergoing a successful and safe ablation at a particular institution, I have developed a Performance Rating scheme. This rating takes into account the success rates reported by afibbers treated at specific institutions and by specific EPs. The factors entering into the Performance Rating are as follows:

Success Score

- Completely successful ablation score = 10
- Partially successful ablation score = 5
- Failed ablation (continuing afib episodes) score = 0

Please note that in this evaluation of 549 single RF ablation procedures a procedure is not considered a failure unless followed by another RF ablation or continued afib episodes. The subsequent occurrence of left or right atrial flutter or tachycardia is treated here as an adverse event and not as an ablation failure.

It is clear that a performance rating is not very indicative in cases where just one or two procedures have been performed. Thus, performance ratings have only been established for institutions that had reports on 6 or more procedures. The results from 24 institutions with 6 or more procedures are presented in the table below.

TABLE 20

Rank	No. of Proc.	Rating	Institution
1	72	6.6	Cleveland Clinic, OH
2	30	6.3	Marin General, San Francisco
3	8	5	Freeman Hospital, Newcastle, UK
4	11	5	Medical University of South Carolina (MUSC)
5	13	5	University of Pennsylvania
6	50	4.7	Hop. Cardiol. du Haut Leveque, Bordeaux
7	9	4.4	Good Samaritan Hospital, Los Angeles
8	6	4.2	Johns Hopkins University Hospital
9	11	4.1	University of Michigan
10	10	4	Mayo Clinic, Rochester, MN
11	16	3.8	Royal Jubilee Hospital, Victoria, Canada
12	12	3.3	NYU Medical Center, NY
13	6	3.3	Loyola Medical Center, Maywood, IL
14	6	3.3	Sequoia Hospital, Redwood City, CA
15	15	2.7	St. Bartholomew's, London, UK*
16	7	2.1	University of Alabama, Birmingham
17	10	2	Centinela Hospital, Inglewood, CA
18	10	2	St. Paul's Hospital, Vancouver, Canada
19	10	2	University of California at San Diego
20	6	1.7	Hollywood Hospital, Perth, Australia
21	6	1.7	Scottsdale Healthcare, Osborn, AZ
22	7	1.4	Massachusetts General Hospital, Boston
23	13	1.2	Texas Heart Institute, Houston
24	10	1	Brigham and Women's Hospital, Boston, MA

* St. Bartholomew's includes procedures performed by Dr. Schilling at London Bridge Hospital

The first 14 institutions (performance rating of 3.0 or higher) in the above table account for almost 50% of all ablation procedures performed; their performance is evaluated in detail in Table 21 (ranked by complete success rate).

TABLE 21

Single Procedure Success – Top-Ranked Institutions

Rank	Institution	# of Procedures	Rating	Success Rate, % Complete	Partial	Failure
1	Cleveland Clinic, OH	72	6.6	63	7	31
2	Marin General, SF	30	6.3	60	7	33
3	Freeman Hospital, UK	8	5	50	0	50
4	Bordeaux	50	4.7	46	2	52
5	MUSC	11	5	45	9	45
6	Good Samaritan, LA	9	4.4	44	0	56
7	University of Penn.	13	5	38	23	38
8	Royal Jubilee, Canada	16	3.8	38	0	63
9	University of Michigan	11	4.1	36	9	55
10	Johns Hopkins	6	4.2	33	17	50
11	NYU Medical Center	12	3.3	33	0	67
12	Loyola, Maywood, IL	6	3.3	33	0	67
13	Sequoia, Redwood, CA	6	3.3	33	0	67
14	Mayo Clinic, MN	10	4	30	20	50
Grand Total – Top-ranked		**260**	**5.2**	**49**	**6**	**45**
Other Institutions		**289**	**2.5**	**21**	**7**	**72**
All Institutions		**549**	**3.8**	**34**	**7**	**59**

The electrophysiologists performing the procedures in the above 14 institutions are as follows:

Institution	Electrophysiologists
Cleveland Clinic, OH	Drs. Andrea Natale*, Robert Schweikert, Walid Saliba, Patrick Tchou, Oussama Wazni
Marin General, CA	Drs. Andrea Natale*, Steven Hao, Richard Hongo
Freeman, Newcastle, UK	Dr. Stephen Furniss
Bordeaux, France	Drs. Michel Haissaguerre, Pierre Jais
MUSC	Dr. Marcus Wharton
Good Samaritan, Los Angeles	Drs. Anil Bhandari, Neala Hunter, David Cannom
University of Pennsylvania	Drs. David Callans, Frank Marchlinski, David Lin
Royal Jubilee, Victoria, BC	Drs. Richard Leather, Larry Sterns
University of Michigan	Drs. Fred Morady, Hakan Oral, Frank Pelosi
Johns Hopkins	Drs. Hugh Calkins, Ronald Berger
NYU Medical Center	Dr. Larry Chinitz
Loyola Medical, Maywood, IL	Drs. David Wilber, Albert Lin
Sequoia, Redwood City, CA	Dr. Rob Patrawala

Mayo Clinic, Rochester, MN	Drs. David Packer, Thomas Munger, Paul Friedman

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The average performance rating for the top-ranked institutions is 5.2 as compared to 2.5 for the remaining 115 institutions (289 single procedures). In evaluating the results for the top-ranked institutions it should be kept in mind that some may have a greater load of "difficult cases" than do others. Thus, a significant proportion of procedures performed at the Cleveland Clinic, OH (22%), Hopital Cardiologique in Bordeaux (21%), Royal Jubilee in Victoria, BC (31%), and the Marin General Hospital (21%) involved patients with permanent or persistent afib. In contrast, the cases treated at Freeman Hospital in Newcastle, UK, Medical University of South Carolina, NYU Medical Center, and the Mayo Clinic did not include any permanent/persistent afibbers.

The statistics presented in Table 21 are indeed sobering. Undergoing a single RF ablation procedure at an institution not included in the top 14 is associated with an average complete success rate of 21%, a partial success rate of 7%, and a failure rate of 72%.

Despite this overall bleak picture for "other" institutions, there are some good performers in this group, bearing in mind that the number of procedures upon which this conclusion is based is extremely limited.

Electrophysiologist	# of Procedures	Complete Success
Dr. Sergio Pinski[1]	5	60%
Dr. Jasbir Sra[2]	5	40%
Dr. Jonathan Steinberg[3]	4	75%
Dr. Yaariv Khaykin[4]	3	100%
Dr. David Fitzgerald[5]	3	67%
Drs. Ian Melton and Ian Crozier[6]	3	67%
Dr. Dipen Shah[7]	2	100%

[1] Cleveland Clinic, Weston, FL
[2] Aurora/Sinai Medical Center, Milwaukee, WI
[3] St. Luke's Hospital, NYC
[4] Southlake Hospital, Newmarket, ON, Canada
[5] Wake Forest University Medical Center, Winston-Salem, NC
[6] Christchurch Hospital, NZ
[7] Hopital Cantonal Universitaire de Geneve, Switzerland

Final Success Rate

The ultimate measure of success for the individual patient is, of course, whether or not they are cured of afib irrespective of how many procedures it takes. This part of the evaluation includes 409 individual patients whose last reported procedures were RF ablations of the left atrium for the purpose of curing AF. All respondents included here reported their afib status 6 months after their last procedure. Results are presented in Table 22.

TABLE 22

Final performance rating

Ranking	Institution	Individual Patients	# of Procs.	Repeat Rate,%	Final Success Rate, % Complete Success	Partial Success	Failure
1	Cleveland Clinic, OH	65	72	11	74	9	17
2	Bordeaux, France	33	50	52	73	3	24
3	Marin General, SF	25	30	20	72	8	20
4	Freeman, Newcastle	6	8	33	67	0	33
5	Good Samaritan, LA	6	9	50	67	0	33
6	MUSC	8	11	38	63	13	25
7	NYU Medical Center	7	12	50	57	0	43
8	University of Michigan	8	11	38	50	13	38
9	Mayo Clinic, MN	8	10	25	50	13	38
10	Royal Jubilee, BC	13	16	23	46	0	54
11	Univ. of Pennsylvania	11	13	18	45	27	27
12	Johns Hopkins	5	6	20	40	20	40
13	Loyola, Maywood, IL	5	6	20	40	0	60
14	Sequoia, Redwood	5	6	20	40	0	60
Grand Total – Top-ranked		**205**	**260**	**26**	**64**	**8**	**28**
Other Institutions		**204**	**289**	**45**	**40**	**13**	**47**
All Institutions		**409**	**549**	**35**	**52**	**11**	**37**

NOTES:
Ranking is by highest % of patients achieving complete elimination of afib without use of antiarrhythmics.
Repeat rate is calculated as # of repeat ablations divided by # of initial procedures performed at the institutions.
First repeat procedure on patients who came to the institution from another one is not counted as a repeat.

The average complete success rate for the 14 top-ranked institutions is 64% with a failure rate of 28%. This compares to an average complete success rate of 40%, and a failure rate of 47% at other than top-ranked institutions.

Comparison with Other Surveys

At least 6 surveys of PVI procedure success rates have now been published. The most recent one done by J.D. Fisher and colleagues at the Montefiore Medical Center in New York compiled the results of ablations performed in major centers around the world and reported in 200 peer-reviewed medical articles and covered a total of 23,000 AF patients.[2] Another large study, the Cappato Study, published in 2005 involved 8745 patients treated at 90 different institutions world-wide.[3] The outcome experience at the Cleveland Clinic, Ohio was presented for 323 patients who underwent a PVI for drug-resistant AF.[4] The University of Michigan experience (755 patients) was presented in a 2006 paper by *Oral, et al*[5], while Johns Hopkins Hospital outlined their PVI outcomes for 200 PVI procedures in a 2006 study authored by *Cheema, et al*.[6] Finally, also in 2006, a group of Danish electrophysiologists outlined their results of a study involving 100 patients who underwent a PVI using either the Haissaguerre or Pappone method.[7]

A comparison of the results from these surveys and the 2007 ablation/maze survey is presented in Tables 23 and 24. Table 23 summarizes the results of initial procedures, while Table 24 summaries final outcome, that is, outcome after repeat ablations as required.

TABLE 23

Outcome after initial procedure						
		# of	Initial Success, %			Observ.,
Survey	Institutions	Proced.	Comp.	Part.	Fail.	mos.
TOP-RANKED INSTITUTIONS						
Bhargava[4]	Cleveland Clinic, OH	323	71	0	29	6
Afibbers.org	Cleveland Clinic, OH	72	63	7	31	6
Afibbers.org	14 top-ranked	260	49	6	45	6
OTHER INSTITUTIONS						
Nilsson[7]	Copenhagen Univ.	100	17	0	83	3
Afibbers.org	Other	289	21	7	72	6

There are, unfortunately, only two studies, other than the afibbers.org survey (2007 ablation/maze survey), that have provided data for initial procedure outcome. Complete success after one ablation varies from 17% to 71% with the afibbers.org survey finding a rate of 49% for top-ranked institutions and 21% for other institutions.

TABLE 24

		Outcome after final procedure					
		# of	Final Success, %			Repeat	Observ.
Survey	Institutions	Patients	Comp.	Part.	Fail.	Rate,%	mos.
TOP-RANKED INSTITUTIONS							
Bhargava[4]	Cleveland, OH	323	83	0	17	12	12
Afibbers.org	Cleveland, OH	65	74	9	17	11	6
Oral[5]	Univ. Michigan	755	73	?	?	?	12
Cappato[3]	Top-rank (world)	3244	64	16	20	27	12
Fisher[2]	Major (world)	23000	63	12	25	25	6
Afibbers.org	14 top-ranked	205	64	8	28	26	6
OTHER INSTITUTIONS							
Cheema[6]	Johns Hopkins	200	41	11	48	32	12
Nilsson[7]	Copenhagen	100	44	?	?	74	12
Afibbers.org	Other	204	40	13	47	45	6

The final outcome results are somewhat better documented with a recent world-wide survey of major institutions involving 23,000 patients finding an average complete success rate of 63%, a partial success rate of 12%, a failure rate of 25%, and a repeat rate of 25%. This compares well with our results for top-ranked institutions of a 64% complete success rate, a 8% partial success rate, a 28% failure rate, and a 26% repeat rate.

Conclusion

I have made every effort to ensure that the calculations and conclusions made in this survey are correct. I have observed good internal consistency in the data and am comforted by the fact that the success rates found in this 2007 LAF Ablation/Maze Survey agree reasonably well with those found in published studies. The LAF survey is based on a total of 549 procedures performed on 409 individual patients, not an overly large number, but enough to draw reasonably valid conclusions in general terms. Where the survey results become less “solid” are in the evaluation of the success rates of individual electrophysiologists and institutions. The ratings of the Cleveland Clinic and the Hopital Cardiologique, Bordeaux are probably reasonably indicative since they involve over 100 patients, but ratings based on just 5 or 6 patients are clearly much less reliable, and it is quite possible that larger samples would produce different results.

However, based on conversations with hundreds of afibbers, perusal of hundreds of articles relating to RF ablation, and my own instinctual feeling, I have no hesitation in recommending the electrophysiologists

specifically mentioned in this report, provided they, and not an assistant, perform the actual ablation procedure.

To summarize, the inescapable conclusion of this survey is that RF ablation for atrial fibrillation is still an emerging technology and that a half decent chance of success can only be expected in top-rated institutions. To go anywhere else, at this point in time, will no doubt lead to disappointment and perhaps serious adverse effects. That said, it is also clear that most, probably as many as 90%, RF ablations result in a significant improvement in quality of life whether they are completely successful or not. This also means that 10% of all afibbers embarking on the ablation path can expect no improvement and in a significant proportion, a worsening of afib or a major adverse event.

References

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Outcome of Other Procedures

Evaluation of Background Data

Ninety-eight afibbers had undergone a surgical procedure (maze or mini-maze) or a flutter, SVT, AV node, or cryoablation as their first procedure. Another 33 respondents had undergone one or more of the above procedures following one or more RF ablation procedures (PVI). All told, results were available for 152 procedures as detailed in Table 1.

TABLE 1
Distribution of Procedures

	Number of Procedures				
Procedure	1st	2nd	3rd	Further	Total
Cryoablation	6	3	1	0	10
Maze procedure	16	3	1	2	22
Mini-maze procedure	26	3	6	1	36
Right atrial flutter	37	12	4	1	54
Left atrial flutter	6	6	3	0	15
SVT ablation	0	2	1	0	3
AV node ablation + pacemaker	7	2	1	2	12
Total	**98**	**31**	**17**	**6**	**152**

General Background of Respondents

The general background data for the 98 respondents whose first procedure was a surgical one or a flutter, SVT, AV node, or cryoablation is given in Table 2.

TABLE 2

Demographics	
Male respondents	81%
Female respondents	19%
Average (median) age*, yrs.	59
Median age at diagnosis, yrs.	50
Age range at diagnosis, yrs.	10-73
Years since diagnosis (median)	8
Years since diagnosis (range)	1-45
AF confirmed by diagnosis	97%
Underlying heart disease	17%
Median age at last procedure, yrs.	57
Age range (last procedure), yrs.	34-73

* At time of completing questionnaire

There were no statistically significant differences between this group and the group whose first procedure was a RF ablation (PVI), although the incidence of underlying heart disease was considerably higher (17% vs. 6%) in the former group.

A total of 93 respondents had provided detailed information regarding their type of AF (adrenergic, mixed, vagal). The majority of respondents (78%) had paroxysmal afib. Mixed (random) AF was the most common type of paroxysmal AF at 70% followed by vagal at 24%, and adrenergic at 6%. These percentages are similar to those found in the RF ablation group covered in Part 1.

Most paroxysmal afibbers (83%) experienced episodes at least once a week and 36% had episodes every day. Only 8% of those seeking a cure through catheterization or surgical procedures had episodes less frequent than once a month. This indicates that most afibbers only opt for a procedure when the frequency becomes intolerable or permanent AF becomes a reality.

The median duration of paroxysmal episodes was 6 hours with a range from 1 to 36 hours.

Ninety percent of respondents were taking one or more drugs on a continuous basis to reduce their episode frequency and duration, or ameliorate the effects of their permanent afib. The most popular drug was flecainide used by 20% of respondents, sotalol used by 16%, and beta-blockers by 15%.

Catheterization Procedures

Right Atrial Flutter Ablation

Fifty-four respondents had undergone a right atrial flutter ablation either as an initial procedure (37 respondents) or as a follow-up procedure after a PVI, mini-maze or unsuccessful right atrial flutter ablation. In addition, 158 afibbers had undergone a right atrial flutter ablation as an integral part of their PVI isolation procedures.

Thirty of the 37 respondents who underwent a right atrial flutter ablation as their first procedure reported the outcome at least 6 months after their procedure. In 95% of the cases the right atrial flutter ablation was

unsuccessful in eliminating afib. Somewhat surprisingly, 22% of afibbers who underwent a first atrial flutter ablation underwent a second and even a third one in further attempts to cure their afib. In this regard, it should be mentioned that only 2 of the original 37 initial procedures were carried out at top-ranked RF ablation institutions and both were followed by standard PVI ablations. All told, 51% of initial right atrial flutter ablations were followed by standard RF pulmonary vein ablations.

Atrial flutter and AF are similar in that they both involve abnormal, sustained, rapid contractions of the heart's upper chambers (atria). In atrial flutter the atria contract 220 to 350 times a minute in an orderly rhythm. In AF the rate of contraction may be as high as 500 beats/minute and the rhythm is totally chaotic. The two arrhythmias can both occur as a result of an enlarged atrium or in the aftermath of open-heart surgery, but the mechanism underlying them is quite different. Nevertheless, they can coexist in the same patient and one may convert to the other.

There are two major types of atrial flutter – common or type 1 and atypical or type 2 flutter. Type 1 flutter is by far the most common (65-70% of all cases) and is characterized by a specific conduction abnormality in the lower right atrium. Type 2 or atypical flutter, on the other hand, has no easily discernible origin and is therefore harder to deal with.

Because the location of the origin of atrial flutter, at least in the common type, is so well known and consistent from patient to patient radio frequency catheter ablation can be used with considerable success to permanently eradicate atrial flutter. Unfortunately, this procedure is unlikely to cure AF, which may often coexist with atrial flutter. There is also some evidence that atrial flutter patients who have a successful ablation increase their risk of later developing AF by 10-22%. So undergoing RF ablation for atrial flutter may not remove the necessity of dealing with AF.

Because of the close connection between AF and atrial flutter, it was quite common, in the early days of ablation, to perform an atrial flutter ablation in the hope that it would cure the AF. The atrial flutter ablation involves only the right atrium so there is no need to pierce the septum to the left atrium as is done in a PVI.

After the 1998 discovery that 80-90% of paroxysmal episodes originate in the left atrium near the pulmonary veins, the use of the right atrial flutter ablation in an attempt to cure AF became less common, but the procedure is still used as a first attempt in patients with a combination of AF and flutter. It is, of course, also used in patients suffering from right atrial flutter only.

Conclusion – Right atrial flutter ablations, on their own, are generally not successful in eliminating atrial fibrillation, so if an ablation is contemplated for the purpose of dealing with AF, it would make sense to have it performed by an EP who is experienced in entering the left atrium and will perform a standard PVI at the same time.

Left Atrial Flutter Ablation

Six respondents had received a diagnosis of left atrial flutter as the primary problem responsible for their afib and underwent ablation for this condition. Only one of these procedures was partially successful, while the remaining were not. Three respondents went on to undergo another procedure (focal ablation, maze procedure, segmental pulmonary vein ablation). All were successful in eliminating both flutter and afib.

It is estimated that about 10% of afibbers undergoing PVI develop left atrial flutter or tachycardia as a results of the procedure. If the flutter or tachycardia develops within the first week following the procedure, it is usually transient and requires no treatment. However, it may develop as much as 2-3 months post-procedure and, in this case, treatment is required. Treatment may involve re-isolation of the pulmonary veins or the placement of long linear ablation lesions to interrupt the flutter circuit.

Nine respondents developed left atrial flutter after a PVI aimed at curing their afib. They underwent additional ablations of which 3 were fully successful, 3 were partially successful, and 3 were too early to tell.

Conclusion – Left atrial flutter is a fairly common complication of pulmonary vein ablation. Our 2006 ablation/maze survey showed an incidence of 12% of left atrial flutter/tachycardia post-procedure. The condition resolved on its own in about 40% of cases, but ablation was required in persistent cases.

Cryoablation

The cryoablation procedure is similar to the standard RF ablation procedure except that the ablation catheter is nitrogen-cooled rather than electrically heated. The advantage of cryoablation is that it reduces procedure stroke risk and does not create pulmonary vein stenosis even if the ablation is done inside the pulmonary veins.

Six paroxysmal afibbers (5 male, 1 female) had undergone cryoablation as their first procedure. Five knew the outcome of their procedure (the other respondent had not gone 6 months since the procedure). Only one

(20%) of these procedures was successful. Two of the respondents whose first procedure was unsuccessful went on to have another cryoablation, one of which was successful. One had two pulmonary vein ablations, which were both unsuccessful. Thus, 2 afibbers out of 5 (40%) achieved complete success after one or more cryoablations.

All told, 10 afibbers underwent a cryoablation as an initial or subsequent procedure. Nine of these had gone more than 6 months since the procedure. The complete procedural success rate was 22%, the partial success rate (still on antiarrhythmics) was 11%, and failure rate was 67%.

Conclusion – It is clearly not possible to conclude anything definitive about the effectiveness of cryoablation based on a sample of ten. However, the results do not appear to be significantly different from those obtained for RF ablation at another than top-ranked institution.

Ablation for SVT

Three respondents were ablated for supraventricular tachycardia occurring as an after effect of RF ablations. All the procedures were fully successful.

AV Node Ablation + Pacemaker Implantation

Palpitations, elevated heart rate, and other major symptoms of an atrial fibrillation episode are associated with rapid and irregular contractions of the left ventricle rather than with the actual "quivering" of the left atrium. So, although the root cause of AF is found in the left atrium, its symptomatic effects can, to a large extent, be eliminated by isolating the AV node (the ventricular beat controller) from impulses originating in the left atrium and feeding the ventricles their "marching orders" from an implanted pacemaker. AV node ablation + pacemaker installation is a relatively simple procedure and is therefore mostly successful. It does also provide substantial symptom relief allowing afibbers to live a fairly normal life. Nevertheless, the procedure is considered a last resort for the following reasons:

- It does nothing to stop the fibrillation in the atrium and may, in fact, hasten the progression to permanent AF.
- It does not reduce stroke risk as do PVIs and maze procedures. Thus, the patient must continue on warfarin for life.

- It makes the patient dependent on the pacemaker. If it or the leads malfunction, or the battery runs out the patient may die.
- It does little to prevent the fatigue and reduced exercise capacity felt by some afibbers during an episode.

Twelve respondents (25% female) had undergone the AV node ablation + pacemaker implantation. Seven underwent the procedure as their first and the remaining 5 underwent the procedure after failed PVIs (4) or maze (1) procedures. Four out of the 12 (25%) had underlying heart disease, a proportion substantially higher than the 8% in the entire group of survey respondents. Forty percent of the group was on amiodarone vs. only 9% in the overall group. There was one permanent and one persistent afibber in the group and the paroxysmal afibbers carried a median 3-month afib burden of 375 hours – substantially higher than the 180 hours experienced in the overall survey group. Thus, it is clear that the respondents who had opted for the AV node ablation were worse off than most.

Ten of the 12 respondents felt that the procedure had been a complete success even though it provided sympathetic relief only. One went on to have a PVI and one went on to undergo a maze procedure – both partially successful. It is worth noting that only one of the AV node ablations was performed at a top-rated AF ablation institution, perhaps indicating that less experienced EPs and cardiologists opt for this procedure more often than do experienced EPs.

Conclusion – Based on this small sample of 12 respondents, it is clear that AV node ablation + pacemaker installation is usually a successful procedure and provides significant symptomatic relief even though it does not cure AF. Nevertheless, it is still the procedure of last resort..

Surgical Procedures

Maze Procedure

Twenty-two respondents reported having undergone a full maze procedure – 16 as their initial procedure, 4 after failed PVIs, 1 after an unsatisfactory AV node ablation + pacemaker implantation, and 1 after a left atrial flutter ablation. As shown in Table 3 the maze group differed

significantly from the total survey group of 516 afibbers in several respects.

TABLE 3

Variable	Total Group	Maze Group
No. in group	516	22
Age at diagnosis, yrs.	48	47
Underlying heart disease, %	8	32
Permanent AF, %	16	33
Paroxysmal with daily episodes, %	24	50
Amiodarone usage, %	9	17

It is clear from the above comparison that respondents undergoing the maze procedure had a higher incidence of underlying heart disease and permanent afib than did the total group.

Three out of the 22 procedures were cryo-maze. In other words, the maze lesions were applied with a nitrogen-cooled catheter rather than with RF energy or the cut-and-sew approach. Only one of these procedures was successful. It is, of course, problematical, perhaps even unwise, to pronounce on success rates with only 22 procedures in the sample. Nevertheless, as with other procedures, there would appear to be a definite trend for procedures performed by top-ranked cardiac surgeons to be more successful than those performed by less prominent ones.

TABLE 4

	# of	Success Rate,%		
Surgeon	Procedures	Complete	Partial	Failure
Top-ranked	8	75	12	13
Other	14	36	7	57
Total	22	59	9	32

It is, of course, open to argument who is and who is not “top-ranked”, but I do believe that the surgeons in the above group (Drs. Damiano, Geiss, Gillinov and McCarthy) would all fall in this category.

The relatively low complete success rate for even top-ranked surgeons is unexpected. The success rate for the full maze procedure is often quoted at 90% or better. However, a recent report issued by the Washington School of Medicine, Barnes-Jewish Hospital (Dr. Damiano’s “home base”) arrived at a complete success rate of 67% and a partial success rate of 24% for an overall success rate of 91%.[1]

It would thus seem that success rates for the maze procedure include patients who are afib-free, but only with the help of antiarrhythmics (at the 12-month check-up). Using this measure the success rate of top-ranked surgeons in our survey was 87%. An overall average success rate of 84%

was observed in a study of 3832 patients who had undergone a Cox-Maze III procedure.[2] Thus, while lower than expected, the success rate for top-ranked surgeons found in our survey is not out of line with published studies.

Our results, albeit based on a very small sample, lead to the conclusion that, just as in the case of conventional PVIs, the choice of surgeon or EP is the all-important variable with the type of procedure playing a lesser role in the final outcome.

As reported in the 2006 Ablation/Maze Survey, 7 out of 12 (58%) of patients undergoing the maze procedure experienced one or more adverse events, some of them quite serious. Two suffered a transient ischemic attack (TIA, mini-stroke), one reported excessive fluid retention, and one pericarditis. This rate of serious adverse events is higher than experienced in any other procedure.

A comparison of objective and subjective success rates show that the respondents' subjective impression of outcome is pretty close to the actual (objective) outcome, except that respondents were more likely to feel that even a failed procedure was at least partially successful.

	Objective	Subjective
Complete success	59%	52%
Partial success	9%	29%
Failure	32%	19%
Total	**100%**	**100%**

Only one (9%) of the fully successful maze respondents continued on warfarin, while 78% of unsuccessful ones did continue anticoagulation. Five (23%) continued on a natural stroke prevention program with fish oil being the most popular supplement. Most (73%) of successful patients no longer needed to avoid triggers, but 80% of those whose procedure had failed still needed to do so. There was no indication that resting heart rate increased after a maze procedure whether successful or not.

Conclusion – The full maze procedure performed by a top-ranked cardiac surgeon provides the best chance of being cured of afib with one single procedure. However, full maze procedures performed by less skilled surgeons tend to be considerably less successful. This, combined with the potential for significant adverse effects (especially associated with the use of the heart/lung machine), would lead one to the conclusion that it may be "overkill" for a paroxysmal afibber, with no underlying heart disease, to select the full maze over a conventional radiofrequency PVI or mini-maze procedure.

Mini-Maze Procedure

Thirty-six respondents reported undergoing a mini-maze procedure, 26 as their initial procedure and 10 after one or two failed radiofrequency PVIs. As shown in Table 5 there were no significant differences in 5 key variables between the total group of survey respondents and the mini-maze group, except for a somewhat greater incidence of underlying heart disease, and a somewhat higher incidence of daily afib episodes in the mini-maze group.

TABLE 5

Variable	Total Group	Mini-Maze Group
No. in group	335	36
Age at diagnosis, yrs.	48	49
Underlying heart disease, %	10	19
Permanent AF, %	19	19
Paroxysmal with daily episodes, %	22	32
Amiodarone usage, %	11	11

The final outcome 6 months after procedure was known for 31 procedures. Of these, 13 were carried out by 4 top-ranked cardiac surgeons.

- Dr. Randall Wolf University of Cincinnati Hospital – 9 procedures
- Dr. Adam Saltman University of Massachusetts – 2 procedures
- Dr. Michael Mack Medical City, Dallas, TX – 2 procedures
- Dr. James Cox Ohio State University Hospital – 1 procedure

RF-powered catheters or clamps were used for lesion creation in all but one of the procedures (microwave). The outcome results are presented in Table 6.

TABLE 6

	# of	Success Rate,%		
Surgeon	Procedures	Complete	Partial	Failure
Top-ranked	13	69	15	16
Other	18	47	0	53
Total	31	57	7	36

NOTE: Two of the successful procedures involved the full maze set of lesions

The incidence of adverse events (as per 2006 Survey) tended to be slightly higher than for the conventional PVI and were generally more serious as shown in Table 7.

TABLE 7

Adverse Event	Patients Involved,%
Left atrial tachycardia/flutter	17
Right atrial flutter	13
Pneumonia	9
Tamponade	4
Serious hemorrhage	4
Subcutaneous nerve pain	4

The chance of a successful outcome with one single procedure is clearly better for the mini-maze than for the standard RF ablation (57% vs. 34%). Even when the single procedure success rates for such top-ranked institutions as the Cleveland Clinic, Bordeaux, and Marin General is compared to the complete success rate for the top mini-maze surgeons, the mini-maze still comes out ahead (69% vs. 57%).

The standard RF ablation can, of course, be repeated, whereas I have not seen any example of full maze and mini-maze patients being given the option of undergoing a second procedure if the initial one fails. The complete success rate after repeat ablations is 64% in the 14 top-ranked RF ablation institutions (73% when results for the Cleveland Clinic, Bordeaux, and Marin General are combined). This compares to 69% obtained by top surgeons after one mini-maze procedure – not a statistically significant difference. The overall mini-maze success rate of 57% is also comparable to the 52% obtained by all RF institutions combined.

None of the patients whose outcome had been completely successful continued on warfarin after their procedure, but 28% continued on a daily aspirin. None of the successful mini-maze patients still had to avoid previous afib triggers.

Four of the patients whose mini-maze procedures had failed went on to undergo RF pulmonary vein isolations. None of these were immediately successful, but one patient regained normal sinus rhythm after a repeat procedure.

There was, based on this very small sample, no indication that success was associated with an increased resting heart rate post-procedure and there was no statistically significant difference in resting heart rate overall when comparing patients pre- and post-procedure.

Conclusion – A mini-maze procedure performed by a top-ranked cardiac surgeon provides the second-best chance of being cured of afib with one single procedure. It is also likely that even a mini-maze performed by a less than top-ranked surgeon will have a substantially better outcome

than a standard RF ablation performed by a less than top-ranked EP. However, the risk of adverse events accompanying the mini-maze procedure is somewhat higher than for RF ablation procedures.

Summary

A total of 152 procedures, other than the conventional RF PVI, was performed in order to eliminate AF or flutter. The following observations were made:

- Right atrial flutter ablations are generally successful in eliminating right atrial flutter, but only very rarely (5% of cases) do they cure AF as well.

- Left atrial flutter or tachycardia occurs fairly frequently as a sequel to a RF PVI or mini-maze. In most cases it resolves on its own, but in some cases a repeat ablation is necessary to correct it.

- There were only 10 responses from afibbers who had undergone cryoablation, so it is not possible to draw conclusions as to the effectiveness and safety of this procedure. However, it does appear that post-procedural heart rate elevation is not a problem with cryoablation.

- Based on a small sample of 12 respondents it would appear that AV node ablation + pacemaker installation is usually a successful procedure and provides significant symptomatic relief even though it does not eliminate the fibrillation of the atria.

- The full maze procedure performed by a top-ranked cardiac surgeon provides the best chance of being cured of afib with one single procedure. However, full maze procedures performed by less skilled surgeons tend to be considerably less successful. This, combined with the potential for significant adverse events (especially associated with the use of the heart/lung machine), would lead one to the conclusion that it may be “overkill” for a paroxysmal afibbers, with no underlying heart disease, to select the full maze over a conventional RF ablation or mini-maze procedure.

- A mini-maze procedure performed by a top-ranked cardiac surgeon provides the second-best chance of being cured of afib with one single procedure. It is also likely that even a mini-maze performed by a less than top-ranked surgeon will have a substantially better outcome than a standard RF ablation performed by a less than top-ranked EP. However, the risk of adverse effects accompanying the mini-maze procedure is somewhat higher than for RF ablations.

This concludes the evaluation of the 2007 Ablation/Maze Survey.

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Acknowledgement

This survey obviously would not have been possible without the wholehearted (pun intended) cooperation of over 500 afibbers who have undergone an ablation or maze procedure. On behalf of our fellow afibbers and myself, I would like to extend a sincere thank you to all respondents.

Appendix A

Glossary of Medical Terms

Ablation
A procedure for destroying heart tissue that is creating abnormal electrical impulses.

Accessory pathway
A collection of muscle fibres that bypass the normal pathway for electrical impulses going from the atria to the ventricles through the atrioventricular (AV) node.

ACE inhibitor
A pharmaceutical drug that inhibits the enzyme which converts angiotensin I to angiotensin II.

Acetylcholine
The neurotransmitter released at parasympathetic (vagus) nerve endings.

Acidosis
A condition in which the blood is excessively acidic (pH below 7.38). It is caused by an imbalance in the bicarbonate-carbonic acid buffer system that keeps the pH of blood within a very narrow range.

Acute
Of rapid onset, severe symptoms and short duration.

Adenoma
A benign tumour of epithelial origin.

Adrenaline
See Epinephrine.

Adrenergic
Pertaining to the sympathetic branch of the autonomic nervous system.

Adrenergic LAF
Lone atrial fibrillation triggered by excessive sympathetic stimulation.

Adrenergic tone
The strength or vigour of the sympathetic branch of the autonomic nervous system.

ADP (adenosine diphosphate)
A compound involved in energy transfer within cells. It consists of adenine, ribose and two phosphate groups.

Afferent
Pertaining to nerves or neurons that carry impulses (information) from an organ to the brain or spinal cord (See also efferent).

Alkalosis
A condition in which the blood is excessively alkaline (pH above 7.44). It is caused by an imbalance in the bicarbonate-carbonic acid buffer system that keeps the pH of blood within a very narrow range.

Aneurysm
A bulge formed by dilation of the wall of the heart or blood vessel.

Angina pectoris
Pain in the center of the chest, which is induced by exercise and relieved by rest. Angina occurs when the demand for blood exceeds the supply and is usually caused by atherosclerosis of the coronary arteries.

Antiarrhythmic
Pharmaceutical drug designed to prevent abnormal heart rhythms or to convert abnormal rhythms to normal sinus rhythm.

Anticoagulant
Pharmaceutical drug designed to prevent blood clotting.

APC [activated protein-C resistance]
A condition caused by the presence of a mutation of blood coagulation factor V (factor V Leiden). APC is associated with an increased risk of venous thromboembolism.

Apoptosis
Self-destruction (suicide) of individual cells to avoid a threat to the survival of the organism as a whole.

Arrhythmia
An abnormal heart rhythm.

Atherosclerosis
The development of fatty plaque and scar tissue on the inner wall of the arteries – eventually leading to obstruction of blood flow and an increased risk of thrombosis.

Artery
A blood vessel that carries blood away from the heart.

Atria
The two upper chambers of the heart. The right atrium receives returning blood from the body and the left atrium receives oxygenated blood from the lungs.

Atrial appendages
Small pouches connected to the right and left atria. The left atrial appendage (LAA) is associated with the generation of blood clots during atrial fibrillation.

Atrial fibrillation
A chaotic movement of electrical impulses across the atria leading to a loss of synchrony between the atria and the ventricles.

Atrial flutter
An abnormal, sustained, rapid contraction of the atria. The rhythm is rapid, but regular as opposed to atrial fibrillation where it is rapid and irregular.

Atrial natriuretic peptide [ANP]
A hormone formed in the atria. ANP is involved in regulating blood pressure and salt and water balance in body fluids.

Atrial refractory period [ARP]
See Refractory period

Atrioventricular (AV) node
A set of specialized heart cells that conducts the normal electrical impulses from the atria to the ventricles.

Auscultation
The act of listening for sounds in the body to ascertain the functioning of the heart, lungs, abdomen and other organs (usually done with a stethoscope).

Autonomic nervous system [ANS]
The part of the central nervous system that is not under conscious control (involuntary). It controls the body's internal organs including the heart and digestive system and is responsible for regulating blood pressure.

AV node ablation
Full or partial destruction (by ablation) of the AV node's ability to conduct signals between the atria and ventricles. A permanent pacemaker is required after AV node ablation.

Baroreceptors
Specialized muscle cells located in the walls of the heart and major arteries. They "measure" blood pressure by stretching or relaxing as blood flows past them.

Beta-blocker
A pharmaceutical drug which blocks the receptor sites for the neurotransmitters (catecholamines) used by the sympathetic (adrenergic) branch of the autonomous nervous system.

Bigeminy
An abnormal heart rhythm in which a normal heartbeat (originating from the SA node) is followed by an ectopic beat (originating outside the SA node) in rapid succession.

Biopsy
The removal of a small piece of living tissue from the body for microscopic examination. Biopsy is often carried out with a special hollow needle (needle biopsy) to minimize invasiveness and discomfort.

BMI [body mass index]
Equals a person's weight (in kilograms) divided by height in meters squared (BMI= kg/m^2). A BMI between 18.5 and 24.9 is ideal; above 25 is overweight and above 30 is obese.

Bradycardia
An abnormally slow heart beat.

Brain natriuretic peptide [BNP]
A hormone released almost exclusively from the ventricular myocardium. Elevated levels may indicate heart failure.

Bundle of His
A small bundle of specialized cardiac muscle fibres connecting the AV node with the upper part of the ventricles.

Calcium-channel blocker
A pharmaceutical drug that inhibits the flow of calcium ions through or across cell membranes. It is used in the treatment of stroke and certain heart conditions.

Carcinoma
A malignant tumour of epithelial origin.

Cardiogenic
Originating in the heart

Cardiogenic emboli
Blood clots originating in the heart

Cardioversion
The conversion of an irregular heart rhythm to normal sinus rhythm. Cardioversion can be done with drugs or through an electric shock administered to the chest area.

Carotid artery
The artery that carries blood from the heart to the brain. It is situated in the front of the neck.

Catecholamines
A group of chemical compounds (amines) derived from tyramine and tyrosine. The group includes epinephrine (adrenaline), norepinephrine (noradrenaline) and dopamine.

Catheter
A tube designed to be inserted into a narrow opening or hollow organ such as the urinary bladder or a vein. The catheter is used to drain fluids or to allow the insertion of special instruments used for imaging or ablation.

Catheter ablation
Destruction of tissue by the application of electrical current, usually at radio frequencies, via a catheter threaded through a vein to reach the area to be ablated (AV node, pulmonary veins, “hot spots” in the atria).

Cerebrovascular event
See Stroke.

Chronic
Persisting over a long period of time.

Circumferential pulmonary vein isolation [CPVI]
An ablation procedure involving the creation of two rings of lesions in the left atrium; one completely enclosing the left pulmonary veins and another completely enclosing the right pulmonary veins; the two rings are usually joined by a linear lesion. Also known as the Pappone method.

Coagulation (of blood)
Process whereby blood is converted from a liquid to a solid state.

Comorbidity
A disease condition accompanied by one or more unrelated disease conditions.

Congestive heart failure [CHF]
Failure of the heart to pump sufficiently strongly to prevent the accumulation of fluid in the lungs.

Coronary arteries
The arteries that supply the heart itself with oxygenated blood.

Cortex
The outer part of the adrenal gland. Aldosterone, cortisol and DHEA (dehydroepiandrosterone) are synthesized here.

Couplet
An abnormal heart rhythm involving two ectopic beats in a row.

Deep vein thrombosis [DVT]
A condition where a blood clot is formed in a deep vein, usually in the legs.

Depolarization
The sudden surge of ions across heart cell membranes that initiates the contraction of the heart.

Diastolic
Pertaining to the time period between fillings of the ventricles. The diastolic pressure is the lower of the two readings reported when measuring blood pressure.

Diuretic
An agent that increases the excretion of urine.

Docosahexaenoic acid [DHA]
A main component of fish oils.

Echocardiogram
An ultrasound picture of the heart as it beats.

Ectopic beat
A heart beat that is initiated at a location other than the sinoatrial node. The junction between the left atrium and the pulmonary veins is a primary spawning ground for ectopic beats.

Edema
Swelling caused by an abnormal accumulation of fluid in body tissues.

Efferent
Pertaining to nerves or neurons that carry impulses (instructions for action) from the brain or spinal cord to a target organ or muscle.

Ejection fraction
The proportion of the blood volume in the left ventricle that is actually pumped out in each heartbeat. The proportion for a healthy heart is 50-60 per cent. A value of 40 per cent or below indicates ventricular dysfunction.

Electrocardiogram [ECG]
A recording of the electrical activity of the heart during contraction.

Electrolytes
Chemical substances that dissociate into two or more ions when dissolved in water.

Embolism
A condition in which a blood clot becomes lodged in an artery and obstructs the flow of blood [embolic].

Endarterectomy
Surgical removal of the inner lining of an artery that is clogged with atherosclerotic build-up.

Endogenous
Originating from within an organism, cell or tissue.

Endothelium
The single layer of cells that line the heart, blood vessels and lymphatic vessels [endothelial].

Enzyme
A protein-based substance (catalyst) that speeds up the rate of a biological reaction without being consumed in the process.

Epidemiology
Dealing with the study of the causes, distribution and control of diseases in populations [epidemiologic].

Eicosapentaenoic acid [EPA]
A main component of fish oils

Epithelium
Membranous tissue that covers most internal and external surfaces of the body and its organs [epithelial].

Exogenous
Derived or developed from outside the body, originating externally.

Epinephrine
A hormone secreted by the medulla of the adrenal gland. Also known as adrenaline.

Factor V Leiden
A mutation in blood coagulation factor V that results in an increased tendency to blood clotting – especially deep vein thrombosis.

Fibrillation
Rapid and chaotic beating of the heart.

Fibrinolysis
The process by which blood clots are removed from the circulation. It involves digestion of insoluble fibrin by the endogenous enzyme plasmin [fibrinolytic].

Focal Ablation
The original radio frequency ablation procedure in which specific active foci of aberrant impulses are located and ablated.

Framingham Heart Study
A large epidemiologic study begun in 1948 with the purpose of discovering the causes of heart disease and stroke. The study now involves thousands of men and women and their offspring from the town of Framingham in Massachusetts.

Gastrointestinal
Relating to the stomach and intestines [gastrointestinal tract].

Glucose tolerance test
A test used in the diagnosis of diabetes and impaired glucose tolerance. It measures how well the body deals with sugar (glucose).

Glycemic index
A measure of how much and how quickly glucose is released and absorbed from a carbohydrate food. Pure glucose has a value of 100.

Heart failure
See Congestive heart failure.

Heart rate variability [HRV]
A measure of the beat- to-beat variability in heart rate.

Hematoma
A localized swelling of blood resulting from a break in a blood vessel.

Hemorrhagic stroke
See Stroke

Holter monitor
A portable device for measuring heart rhythm over a 24-hour period.

Homocysteine
A sulphur-containing amino acid used by the body in cellular metabolism and the manufacture of proteins.

Hyperhomocysteinemia
An elevated blood level of homocysteine.

Hyperlipidemia
An excess of fats or lipids in the blood.

Hypertension
A blood pressure that is persistently above the upper limit of the reference range (140/90).

Hyperthyroidism
An overactive thyroid gland. The condition is characterized by increased metabolic rate, high blood pressure and a rapid heartbeat.

Hypocalcemia
An abnormally low blood level of calcium.

Hypoglycemia
A lack of glucose in the blood stream. The condition can cause sweating, mental confusion, atrial fibrillation and muscle weakness.

Hypokalemia
An abnormally low blood level of potassium.

Hypomagnesemia
An abnormally low blood level of magnesium.

Hyponatremia
An abnormally low blood level of sodium

Hypotension
An abnormally low blood pressure.

Hypothyroidism
An underactive thyroid gland. The condition is characterized by fatigue, hair loss, feeling cold, constipation and skin pallor.

ICD
Implantable cardioverter-defibrillator.

Idiopathic
Of no known cause.

Incidence
The extent or frequency of occurrence.

Infarction
Localized cell death (necrosis) resulting from obstruction of the blood supply.

INR
International Normalized Ratio. A measure of the blood's tendency to coagulate (form clots) when on warfarin (Coumadin). A normal INR is 1.0. Warfarin dose is usually adjusted to give an INR between 2.0 and 3.0.

Intermittent claudication
Muscle pain, usually in the calf muscles, that is brought on by exercise and relieved by rest. It is usually caused by atherosclerosis of the arteries feeding the affected limb.

Intracardiac Echocardiography [ICE]
An ultrasound technique for visualizing the inside of heart chambers.

Intracellular
Situated or occurring inside a cell.

Intracranial
Within the head.

Ion
An electrically charged atom or molecule.

Ion channel
A pore in a cell's membrane that provides a channel for ions to cross the membrane.

Ischemia
Inadequate blood flow to the heart or other body parts [ischemic].

Ischemic stroke
See Stroke

Left atrial appendage
See Atrial appendages.

Left ventricular dysfunction
Inadequate pumping capacity of the left ventricle. Characterized by a left ventricular ejection fraction below 40 per cent.

Macrophages
Large scavenger cells found in connective tissue and in many major organs and tissues including the liver, lymph nodes, spleen, bone marrow and central nervous system.

Mast cells
Large cells in connective tissue that release heparin, histamine and serotonin in response to inflammation or allergens.

Maze procedure
A surgical procedure that involves the creation of a pattern of scar tissue to contain and channel the heart's electrical impulses and thereby prevent atrial fibrillation.

Medulla
The inner part of the adrenal gland. Epinephrine and norepinephrine are synthesized here.

Mitral stenosis
A narrowing of the opening of the mitral valve.

Mitral valve
A valve that allows blood to flow between the left atrium and the left ventricle while preventing back flow.

Mitral valve prolapse [MVP]
A usually benign abnormality of the mitral valve resulting in regurgitation (back flow) of blood from the left ventricle to the left atrium.

Monocyte
A variety of white blood cells whose purpose is to ingest foreign particles such as bacteria and tissue debris.

Mortality
Incidence of death in a given period.

Myocardial infarction [heart attack]
Destruction of heart tissue resulting from obstruction of the blood supply to the heart muscle.

Myocarditis
An acute or chronic inflammation of the heart muscle.

Myocardium
The middle of the three layers that form the wall of the heart. It is composed of muscle fibres.

Myocyte
A muscle cell.

Myxoma
Benign gelatinous tumour of connective tissue. Atrial myxoma most commonly involves a tumour in the left atrium.

Necrosis
Death of cells through injury, disease or obstruction of blood supply.

Neutropenia
Decrease in the number of neutrophils (a type of white blood cell) resulting in an increased susceptibility to infection.

Nitric oxide [NO]
A colourless gas produced in cellular metabolism. It is involved in oxygen transport to tissues, the transmission of nerve impulses and the relaxation of blood vessel walls.

Non-valvular atrial fibrillation
Atrial fibrillation that is not caused by malfunctioning or damaged heart valves.

Norepinephrine
The neurotransmitter released at sympathetic (adrenergic) nerve endings. Also known as noradrenaline.

Normal sinus rhythm [NSR]
The normal rhythm of the heart when beats are initiated only at the sinoatrial node.

Ostial PVI
A pulmonary vein isolation procedure where the ablation lesions are placed in the left atrium around the openings of the pulmonary veins rather than inside the pulmonary veins. The ostial procedure eliminates or sharply reduces the risk of pulmonary vein stenosis.

On-demand-approach
A method of self-terminating atrial fibrillation episodes. It involves taking propafenone or flecainide immediately following the start of the episode. Also known as the pill-in-the-pocket approach.

Oxidative stress
A condition that occurs when the body's natural antioxidant defences are overwhelmed by reactive oxygen species and other free radicals.

Pacemaker
An implanted device meant to provide small electric shocks to the heart to initiate heartbeats (contractions) at a predetermined rate.

Palpitation
A sensation of a rapid, irregular heart beat.

Parasympathetic
Pertaining to the parasympathetic branch of the autonomic nervous system.

Paroxysmal
Occurring at intervals (intermittent).

Peripheral arterial disease [PAD]
Atherosclerosis in arteries other than the coronary arteries. Intermittent claudication may occur if the atherosclerotic deposits are blocking the arteries feeding the legs.

Permanent LAF
Continuous lone atrial fibrillation that does not respond to cardioversion.

Persistent LAF
Lone atrial fibrillation episodes lasting more than seven days, but amenable to cardioversion.

Pheochromocytoma
A tumour of the adrenal gland that produces epinephrine and norepinephrine.

Platelet
Blood cell involved in the initiation of blood clotting [thrombocyte].

Platelet inhibitor
A drug that prevents the aggregation of platelets.

Plaque
A build-up of cholesterol and fatty substances on the inner lining of arteries.

Postprandial
Occurring after a meal, especially dinner.

Premature atrial complex [PAC]
A premature heart beat originating in the atrium other than at the sinoatrial node.

Premature ventricular complex [PVC]
A premature heart beat originating below the atrioventricular node, often in the ventricular muscle itself.

Prevalence
The total number of cases of a disease in a given population at a specific time.

Proarrhythmic
Capable of inducing arrhythmia.

Prophylaxis
Action taken to prevent disease [prophylactic].

Prostaglandin
A hormonelike compound synthesized in the body from 20-carbon unsaturated fatty acids, notably arachidonic acid. Prostaglandins are involved in a wide range of physiological functions including control of blood pressure, contraction of smooth muscle and modulation of inflammation.

Prothrombin time
A measure of the blood's tendency to clot when medicated with warfarin. See INR.

PUFA
Polyunsaturated fatty acid.

Pulmonary embolism
A blood clot lodged in the pulmonary artery.

Pulmonary vein ablation [PVA]
Ablation of sources of ectopic heartbeats located at the junction of the left atrium and the pulmonary veins.

Pulmonary vein isolation [PVI]
Isolation of the pulmonary veins from the left atrium by ablating (generating lesions) a ring around each pulmonary vein.

Pulmonary veins
The veins draining oxygenated blood from the lungs to the left atrium.

Pulse pressure
Difference between systolic and diastolic blood pressure

Purkinje fibres
A group of specialized heart cells that conduct electrical impulses in the ventricles.

QT Interval
The duration of the activation and recovery of the ventricular myocardium. A prolonged QT

interval is associated with ventricular arrhythmias.

Refractory period
The rest period following a contraction of the heart muscle. The cell does not respond to stimulation during this period.

Reperfusion
The restoration of blood flow to an organ or tissue that has had its blood supply cut off due to a stroke or heart attack. Reperfusion is associated with increased free radical activity.

Rheumatic heart disease
Heart disease caused by rheumatic fever.

Run
An abnormal heart rhythm characterized by four or more ectopic beats in a row.

Sinoatrial (sinus) node
The specialized (pacemaker) tissue that initiates a heart beat. It is located near the top of the right atrium.

Sinus rhythm
See Normal sinus rhythm.

Stasis
Stagnation or cessation of flow; for example, of blood or lymph fluid.

Stenosis
A constriction or narrowing of a duct or passage; for example, pulmonary vein stenosis.

Stroke
An event that damages nerve cells in the brain. It is caused by an interruption of the oxygen supply to the brain due to a blood clot (ischemic stroke) or a burst blood vessel (hemorrhagic stroke).

Subcutaneous
Beneath the skin.

Supraventricular
Located above the ventricles, that is in the atria or atrioventricular node.

Supraventricular tachycardia [SVT]
A rapid, but regular heart rate caused by a fault in the conduction system around the atrioventricular node.

Suture
The closure of a wound or incision with material such as silk or catgut. The term is also used to describe the material used in closing the wound or incision.

Sympathetic
Pertaining to the sympathetic branch of the autonomic nervous system.

Systemic
Relating to or affecting the body as a whole.

Systolic
Pertaining to the time at which the ventricles contract. The systolic pressure is the higher of

the two readings reported when measuring blood pressure.

T-cells
A specialized kind of white blood cells (lymphocytes) that help identify foreign cells and antigens so that killer cells can dispose of them.

Tachycardia
A rapid, but regular heart beat usually in excess of 100 bpm.

Tamponade
Compression of the heart caused by the build-up of fluid or blood in the space between the sac (pericardium) surrounding the heart and the heart muscle (myocardium) itself.

Thallium stress test
A test used to assess the blood flow through the coronary arteries before and after exercise.

Thrombosis
A condition in which blood changes from a liquid to a solid state, i.e. forms a clot [thrombotic].

Thrombus
A blood clot.

Thrombolysis
The dissolution of a blood clot by the infusion of an enzyme, such as streptokinase, into the blood [thrombolytic].

Thyrotoxicosis
A serious condition resulting from an excess of thyroid hormones.

Transesophageal
Through or across the esophagus. The term is often applied to a special form of echocardiography used to check for blood clots in the left atrial appendage.

Torsade de Pointes
A distinctive form of ventricular tachycardia associated with a prolonged QT interval.

Transient ischemic attacks (TIAs)
A sudden, temporary loss of neurological function caused by blockage of small arteries supplying blood to the brain (mini-stroke).

Transthoracic
Through or across the chest. The term applies to the standard form of echocardiography.

Tricuspid valve
A valve that allows blood to pass between the right atrium and the right ventricle.

Trigeminy
An abnormal heart rhythm in which every third beat is ectopic (originating outside the SA node).

Triplet
An abnormal heart rhythm involving three ectopic beats in a row.

Vagal
Pertaining to the parasympathetic branch of the autonomic nervous system.

Vagal LAF
Lone atrial fibrillation triggered by excessive parasympathetic stimulation.

Vagal tone
The strength or vigour of the parasympathetic branch of the autonomic nervous system.

Vasodilatation
An increase in the diameter of blood vessels, especially arteries. It is brought about by a relaxation of vessel walls mediated, for example, by nitric oxide.

Vagus nerve
The tenth cranial nerve originating in the brain stem. It enervates the heart, gastrointestinal tract and larynx (voice box).

Valsalva manoeuvre
A manoeuvre that increases vagal tone. It is performed by attempting to forcibly exhale while keeping the mouth and nose closed for about 15-30 seconds. It may sometimes help to abort an episode of supraventricular tachycardia or adrenergic LAF.

Vein
A blood vessel that carries blood towards the heart.

Vena cava
The large vein(s) that returns blood from the body to the heart (right atrium).

Ventricles
The two lower chambers of the heart.

Ventricular fibrillation
An often-fatal cardiac arrhythmia characterized by rapid, irregular fibrillation of the ventricles. Ventricular fibrillation is the main cause of sudden cardiac death (cardiac arrest).

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