Lone Atrial Fibrillation

Toward a Cure – Volume III

By

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WITH CONTRIBUTIONS 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 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 2005 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 III***, hopefully, solves this problem. Its 220 pages contain all the information published in the 2005 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 III* makes it an ideal and essential companion to *Lone Atrial Fibrillation: Towards a Cure* and *Lone Atrial Fibrillation: Towards A Cure – Volume II*.

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. Peggy Merrill, George Newman, Alistair Thomson, Chuck Miller, and David Weisenthal deserve my special thanks for taking the time to put their own personal afib experience into words for others to share. Also my heartfelt thanks to Patrick Chambers for his excellent article on P cells and potassium and to the many afibbers who participated in the LAF-9 survey and 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
June 2006

AFIB Journeys

My Success with the Paleo Diet and Potassium

Peggy Merrill

My first brush with afib was in late '99 while working a grim, low-wage cashier job involving a lot of overtime and too few days off to recuperate. I was 57 years old, seriously overweight, had that year gone through a lot of stressful life changes, was eating poorly [whatever I could pick up in the convenience store I worked in], it was hot weather and I had no air conditioning, and I was surviving on coffee. I had a couple of short episodes that went away before I could get to a doctor, and of course when I did get to the doctor he found nothing wrong. Then I had one that did not go away, and ended up in the hospital for 3 days. I changed jobs after that, and worked more normal hours, dropped the coffee and ate better [more vegetables, less junk], and had no more afib until August 2000, when I was hospitalized again with another "just-won't-go-away" episode. This again was associated with caffeine [green tea this time, dozens of cups of it, trying to stay awake at work] and hot weather, compounded by lack of sleep. After that I dropped caffeine altogether, and got an air conditioner.

For the next several years I had short episodes occasionally, but they always went away by themselves, and in any case, I was getting turned off by hospital emergency rooms. I had learned a little about using computers by that time, and was researching better nutrition. I retired and moved back to Maine, and eventually got my own computer, and found Hans' site. Here I found there were a lot of people taking various drugs, and none of these drugs seemed to be curing their afib. They were still getting afib attacks, trading drug advice, going on different drugs, and still getting afib. Some of them were talking about, and some even resorting to, heart surgery. I couldn't blame them for doing this, because their afib had started small and gradually increased until it ruled their lives. I was afraid mine would do that too.

Worse yet, by no means all of those ablation patients had gotten rid of their afib either. Two of them had had near-death experiences, and I was pretty sure that the reason there were not more stories like that was because most ablations that went bad had resulted in death, and of course, we are not very likely to hear from those people. And then there were 2 people posting who claimed to have gotten rid of their afib by diet and supplements. These were Fran and Erling.

Well, I thought, if these 2 people so different from one another can do that, maybe I can too. Food choices are something I can control. So I changed to a mostly paleo diet, and sent away for some Carlson's magnesium glycinate. At first I still did get some short, mild afib episodes, but then I began seeing posts about low sodium V8 juice, 850 mg potassium per 8 oz. glass. I was having trouble consuming enough vegetables and fruits to get in 3-5 grams K a day, and this seemed like just what I needed, and sure enough it was. I haven't had any more afib from that day forth, and that was December 2003.

The Paleo Diet

The paleo diet is based on the premise that the human body thrives best on the diet of our hunter/gatherer forebears of 10,000 years ago, ie. before the introduction of agriculture. The proponents of the diet point out that the human genomic make-up is very slow to change and has not had a chance to adjust to the very major changes in diet that have occurred since the Stone Age.

The Stone Age hunter/gatherers consumed a diet based on fish and meat from wild animals, vegetables, berries, fruits and nuts. Grains and dairy products were not available. The paleo diet thus emphasizes the above food sources and excludes dairy products, grains, starchy vegetables, sugar and legumes, and of course, chemical food additives.

The paleo diet is described in detail in the book "The Paleo Diet" by Loren Cordain, PhD or at www.paleodiet.com

Concerning those few short, mild episodes, I think a lot of what paleo did for me was eliminate postprandial hypoglycemia. A paleo diet pretty much prohibits high glycemic load foods. Jackie and others had called my attention to the fact that a lot of my afib symptoms were the same symptoms as those of reactive hypoglycemia - shaky, lightheaded, cold sweat, panic - and sure enough, the minor episodes I got soon after converting to paleo lacked just those features. I wasn't sorry to see them go.

Also, I need to mention that those last episodes, mild though they were, appeared right after use of a seasoning containing MSG. I had never had an afib episode that I could tie to MSG before, but then I had never been without it for any period of time before either. For all I really know, they could have all had to do with MSG, in combination with stress, hypoglycemia, dehydration, electrolyte deficiency, caffeine, and any of the other myriad stressors of modern life.

Any paleo diet purist will point out that I ingest a lot of stuff that isn't paleo. The V8 certainly isn't, and neither are the supplements I take. I do

eat a little cheese, too, though not the plasticized processed cheese. I cannot afford organic food, so I make do with what I can find in the local supermarket, cheapest first. I go out to eat sometimes, and on those occasions I commit excesses like baked potato and gravy, or bread on sandwiches. I cheat outrageously sometimes, too, particularly with chocolate baked goods.

Speaking of bread, gravy, and bakery goodies, if I hadn't gone to paleo I would also never have realized that I have a bad reaction to wheat. Since taking up the paleo diet my antacid consumption has gone way down, except when I eat anything with wheat in it. That will have me eating antacids for a good 12 hours and sometimes more.

Another good thing about the paleo diet is that I fit the classic profile for insulin resistance - fat, high blood pressure, relatively inactive, cholesterol a bit on the high side - and the paleo diet is good for insulin resistance. I hope to avoid type 2 diabetes this way, or at least to slow it down.

For those concerned about whether my afib is "really cured", I do not think I can expect to be cured of needing proper nutrition, any more than cars are cured of needing gasoline. I don't think I am going to ever again be just like I was in my 20's either. To use the same metaphor, old cars are never again just like they were when new.

I think afib is one of the long latency deficiency diseases, and that is why, in most people, it does not appear until a relatively 'older' age, and why it appears in the context of stress so often. I am still old, fat, and lame in the knees, but I don't have afib any more. If I can do this, you can too.

Postscript – January 2006

I am thrilled to report that I still remain afib-free.

My Analytical Road to Success?

George E. Newman

Hans kindly asked me to contribute my story this month. First I'd like to say that I'm a bit new at this afib business and I'm not sure my success is long-lived enough to qualify as an example (and it is still a work in progress), however, I'm happy to contribute so that others can possibly learn from my experience. I can say that I'm sure I would not have the success I've had without the work of Hans, PC, Jackie, PeggyM, Fran and the many others who've come before me and generously shared their expertise and experience. For this I'm very grateful.

I'm a 49-year-old male vagal afibber. Like many on this site, I've been a life-long exerciser. I played American Football in college and then continued running until about 10 years ago, when I took up 4 miles of daily walking at a pace of about 11-12 minutes/mile. I found this kept me in sufficiently good condition to compete annually in a 13 1/3 mile race up Pikes Peak (a 14,000 ft peak, the race gains 7,850 ft in elevation). I could finish within 20 minutes of the 4 hr 20 min median time. I've also had a mostly vegan diet for 15 years and my blood chemistry has been excellent since then. In my early 20's, I was diagnosed with "white-coat hypertension." So, I've routinely taken my own blood pressure with a stethoscope and cuff since.

This last summer, I was again training for the Pikes Peak race. I was climbing 14,000 ft peaks on the weekends here in my home state of Colorado. One Thursday morning, in early July, I woke up and decided to take my blood pressure. It was fine, however, my pulse "sounded" weird. I took my pulse rate. It was about 80. This was unusual for me as my resting pulse is normally in the low 50's (and I had done no activity). I put on an old heart rate monitor and started walking around. Going up the stairs, my pulse soared to 150. Normally it would be 80 or 90 doing this. I really wondered what was happening to me. Was I having a heart attack? So I drove myself to the ER. They put me on a monitor, but my pulse converted to NSR before they could get a printout. The doctor did a variety of tests, chest x-rays, asked me if I drank (no), etc. The doctor sent me home with a Holter and said he thought it might be atrial flutter. The one significant item out of these tests was a low serum potassium (K) value of 3.2 mmol/l (normal range is 3.5-5.2 mmol/l). They did give me a potassium pill at the ER.

The following Tuesday, I went to my GP. He said my Holter was normal, one nonspecific run of 10 seconds and an average of 24 PVC's and 2 PAC's per hour. He wasn't too concerned, started me on a baby aspirin/day and told me to schedule a treadmill test, and a 30-day event monitor test.

The event monitor/treadmill tests were scheduled for a month hence. In the meantime, nobody was too concerned about my condition. I also learned that for me, it wasn't an ER event. This was important as I've been self-employed for 18 years and carry only very high deductible medical insurance. My ER bill was $2,500 and it would be very costly to keep paying for those visits. About two weeks after the 1st event, I had another one. It came on at 3 AM. This time, I put on my HR monitor and decided to watch it. I went ahead and went to the office and around noon I decided to see what would happen if I did a little exercise (I knew very little about my condition and did not even know that it was afib at this point). I found I could walk at a 15 min/mile pace and my HR would go to 140. When I slowed down, my HR would drop, so I wasn't too concerned. At one point, I had to sprint across a street to avoid traffic. My HR monitor shot up to 233 (I'm still not sure if this was real, as readings like this can also happen if one of the leads looses contact). I was a little concerned, however, after a couple of minutes, I had converted to NSR. I called my GP and told him what I had done. He said that I had acted properly.

I had two additional episodes before my treadmill test. They both came on about 3 AM and I converted them with exercise. When I took my treadmill test, it showed no underlying disease, and it did not put me into afib. I went quite a bit longer than my expected time. During the test, I told the cardiologist that my events came on at around 3 AM and I had been able to convert them to NSR with exercise. I asked, "How common is this?" He told me that I was the first patient he'd seen who could do this. Wow, I thought, I'm unique. I went home wearing an event monitor. Sure enough, I had another event. I even took a reading while in afib and exercising, then converted it and took another reading. These readings showed that I did have atrial fibrillation. Of course the HR that was reported was the one while I was exercising, not resting. My GP suggested a consultation with the cardiologist, but I hadn't scheduled one yet.

I went ahead and did my Pikes Peak race, with no problems. In the meantime, I'd done some Internet searching and found a couple of papers that reference vagal afib. The early morning initiation of afib and return to NSR with activity described in those papers fit my situation. I now knew I wasn't a solitary case. I also knew I wasn't going back to the cardio who had done my treadmill test! Three days after the race, I had

another event. The only thing that was different is that I didn't convert on this one.

I asked around and got referrals to a cardiologist and an electrophysiologist. It turns out they were partners. I didn't know any different, so I went to see the cardio. By the time I had an appointment, I'd found www.afibbers.org and read Hans' book. Feeling well armed, I went to my first meeting and talked to the cardio about my 3 AM events and (up until now) conversion with exercise. I said I thought I was vagal. He said, "I don't believe in that." I was a bit shocked. I offered to bring in some papers to discuss with him. He said, "don't bother, I won't read them." He also said, "I'm sure I could find some papers in your field that you wouldn't agree with." Then he told me that digoxin was his favorite drug. I was really worried then. He ordered an echocardiogram and scheduled another appointment. He started me on Coumadin. My echo came back fine, but after 6 weeks in persistent afib my ejection fraction had dropped some. I could tell this in daily activities, as I got winded more easily. I was such a pain that he referred me to his partner the EP. I told the EP my story (3 AM and exercise conversion). He said, "you're obviously vagal, and there are a whole category of drugs that are contraindicated for you. We will not prescribe them." "Wonderful, finally somebody who has a clue!" I thought to myself. This guy sent me home with a Holter, so he could see what my average HR was, out of rhythm.

During the weeks this was happening, I read more and also had a few tests ordered by my GP and my integrative MD. These included an EXATEST for cellular levels of Mg (and other minerals), a Comprehensive Digestive Stool Analysis (CDSA) test, and a C-Reactive Protein (CRP) test. The EXATEST showed that I had low-normal magnesium levels, the CDSA, a very small amount of Candida and everything else looked good; and the CRP was very low. So, there was nothing obvious to treat. I did add some magnesium to my supplement plan.

The results of my Holter were that my average rate was ~80 when out of rhythm. The EP suggested that the best course of action was not to convert me, because of the risks of treating me with rhythm drugs if I converted and the fact that I was doing OK out of rhythm. We had already talked about this, so I had done my research. I'd read Hans' book and looked at all the reports of those who had managed to stay in rhythm with supplements. I also learned about flecainide on demand. So, I proposed my plan "B." It was 1) to convert me, 2) I would try to stay in rhythm with supplements and trigger avoidance, and 3) I would take flecainide on demand if 1 and 2 didn't work. He accepted my plan. He gave me a prescription for flecainide and at first thought he'd give me a 300 mg dose to see if I converted. Then he came back and said that the studies showed that this was only effective if given right after going out of rhythm.

I'd been out of rhythm for 2 ½ months at this time. He told me to schedule a cardioversion in a couple of weeks. I got the prescription and went home. I looked at the pills and thought, "Well, I've already been cleared to take these, what do I have to lose?" I took a 300 mg dose and converted in about 18 hours. Needless to say, I was ecstatic after being out of rhythm for so long. I faxed a note to the EP who asked me to come in for an EKG to make sure I was doing OK on the flecainide. This turned out fine.

I went on my supplement program big time, determined to stay in rhythm (the conversion took me by surprise). This has worked well for 5 months. I did have one event at exactly 4 weeks. I determined that eating a bunch of junk, late was a trigger. I then thought back to my other events in the summer and could also remember similar triggers. At this point I decided to not eat after 7 PM. I wasn't sure if the trigger was GERD, hypoglycemia or a vagal response to eating, but early eating will help all of these.

I also wanted a finer gauge of how I was doing than "either I'm in afib", or "I'm not". To this end, I purchased a Polar S810 HR monitor, and the FreezeFramer HR monitor. They both accomplish the same thing, namely a beat to beat recording of your heart rate. The Polar records, and then the data is downloaded to your computer. The FreezeFramer has a finger cuff (now an ear cuff, too), which you wear while hooked up to your computer. You can watch the display in real time. Both devices suffer from artifacts and noise if you move around too much. I've taken to monitoring myself while meditating, as I am most still then. In recent testing with an EKG device[1], I've determined that I can differentiate PAC's from PVC ectopic beats. The PAC's have an anomalously fast beat or fast immediately followed by an anomalously slow beat. The PVC's have an anomalously slow beat[2]. Both the Polar and the FreezeFramer have the same PAC/PVC response. In testing the Polar with my EKG, I found that several anomalies that I thought were ½ period artifacts turned out to be real PVC's per the EKG. If you use a FreezeFramer, you need to make sure that the Enable Artifact Detection box is unchecked (this defeats the purpose), as well as uncheck the Enable HRT Filter box. In counting ectopics in a 20-minute period (the length of most meditations), I can see if I'm doing well with my program. My initial July Holter showed 24 PVC's and 2 PAC's per hour. Generally, I'm way below that now. My readings have ranged from 0 to 20 per hour, but most range in the 3 to 10 range. There is data to show that ectopics increase to 5 or 6 per minute right before the initiation of afib. I actually feel very few of my ectopics; in fact, I feel them only rarely and then only when I'm sitting quietly with a monitor on and my attention on my throat. The monitors pick up several orders of magnitude more ectopics than I feel.

I also wanted to address the possibility that my trigger was a hypoglycemia event. In addition, I had added about 10 pounds during my 2½-month afib event, and my blood pressure had crept up to 130/85. I wanted to address these issues also. I purchased a Bayer Ascencia home blood glucose monitor. It was the most accurate I could find. Many home models are very inaccurate (according to their own specs – OK for a diabetic, but not for my purposes). What I found was that hypoglycemia wasn't my problem, but hyperglycemia was. Hans' first book had also referenced that vagal afibbers might have a "flat" blood glucose response. This was not my case. I found that high glycemic index (GI) carbs could spike my blood sugar. Also the addition of fat, even "good" fat would keep my blood glucose high on a fasting test and so would a high GI meal. In a literature search, I found that this is because circulating lipids impair insulin's ability to work[4-7]. For me, I could get a 112 mg/d (6.2 mmol/l) reading on a fasting test by eating solely two helpings of ice cream for dinner, however, this would drop to the mid 80's (~4.7 mmol/l) the next day on a fasting test following a day of eating my no added fat, whole food vegan diet. I also found that drinking 1 liter of a whole fruit drink, that I make by grinding up whole apples, oranges and other fruits hardly moves my blood sugar at all.

After two weeks of paying attention to keeping my blood sugar even, I'd dropped the 10 pounds I'd added, and my fasting glucose and my blood pressure normalized. One detriment to this approach is the lack of essential fatty acids (EFA's) in the diet. There has been discussion of the fact that people don't convert fat from flax seeds to EFA's; however, there are some interesting abstracts on one of Hans' other sites. One reports the non-conversion of the flax-type fatty acid (percent of dietary fat not stated). However the other shows that people do convert, if their dietary fat intake is limited to 20% of calories (see the first two abstracts listed at http://www.oilofpisces.com/weightcontrol.html).

Now some people may think "this guy goes nuts buying stuff to measure himself." You would probably be correct. However, you must remember that I have very high deductible insurance and if I can save one ER visit, I've paid out my monitoring investment many times.

Here is my supplement program:

Morning supplements, normally around 7 AM, with breakfast
2 mg Copper
1000 mg Taurine
800 mg NOW brand Trace minerals
200 mcg Selenium
B-50 B-complex
500 mg Vitamin C

400 IU Vitamin E
1000 mg Acetyl L-Carnitine
500 mg L-Tyrosine
500 mg L-Lysine

Mg & K
400 mg Magnesium Glycinate
400 mg Magnesium Maleate (will switch to only Glycinate when done with this bottle)
1.5 grams Now Brand KCl powder

Evening, normally around 6 PM, with dinner
Repeat the Mg & K

I also take CANDEX per directions to rid myself of any Candida, as per Jackie's suggestion.

My best estimate is that the Mg, K, Taurine and Acetyl L-Carnitine are the most active with respect to afib. Also the B6 helps the absorption of magnesium. If you decide to go this route, start slowly and increase your dosages. Also, make sure your kidneys are OK, so have your BUN and creatinine levels checked. PeggyM says that when your stores of Mg are full, your bowel tolerance for Mg will decrease. At this point, just reduce your dosage till you don't have a problem maintaining your Mg levels.

I don't know that I've optimized this. At some point, I plan to repeat the EXATEST and see how I'm doing bringing the Mg levels up in my cells, or as PeggyM suggests, I can wait till I have a bowel tolerance problem and cut back my dosage then. All of these supplements have not helped my digestion, however, the addition of Betaine HCl and dietary enzymes seems to help this. I may add a pre-bedtime dose of K, as my morning ectopic samples are much lower if I do. However, I think that the chlorine in the KCl negatively affects my blood pressure. I may substitute the potassium gluconate and see if this will still lower my ectopics while not affecting my blood pressure.

My digestive system doesn't really like all those fillers and capsules. However, if I can back off at all, my ectopic rate is right back up again. At some point, I'd like to see if I can accomplish the addition of these nutrients mostly within the confines of my vegan diet. However, since what I'm doing has kept me in NSR for 4 months, I'm loath to change it too much. One reason I chose the supplement route to begin with is that a dietary approach takes a lot more analysis and organization (perhaps not for the paleo or blood-type diet folks, but it does with my vegan plan and, otherwise, I do very well as a vegan with a lot more energy than my peers). Also, I'm very active, leading a youth group of 14- to 20-year-olds

camping on a regular basis. It is much easier just to pack a few supplements.

As an aside, several months ago a friend also had his first two afib episodes. I suggested that he up his intake of Mg and K. He did this and now makes his own version of the PAC-Tamer. He has had no more afib episodes since he started the Mg and K.

Thanks to all for suffering through this long-winded story and I hope some of you find it useful.

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Postscript

I sent my story to Hans before going on a snow cave outing with my youth group. I snow shoed into our camp for 3 ½ hours carrying a 70-pound (32 kg) pack, breaking trail much of the time in >3 feet (1 meter) of snow. I then worked for another 4 ½ hours constructing a snow cave. Although I wasn't wearing a heart rate monitor, I can tell you that I was working at maximum exertion for those 8 hours. Also, the elevation was 10,500 ft (3,200 meters).

I crawled into my sleeping bag around 8 PM. At about midnight, I went into afib. I brought my flecainide along, so I decided to take a 300 mg dose (my conversion prescription). The instructions given on this board are to take it crushed in warm water as soon as possible after the start of the afib. Well, my water bottle had ice in it, as the cave temperature was below freezing (better than the –5 deg. F (-21 deg. C) outside). So, I chewed the three tablets and washed them down with ice water. Happily, I converted in less than 30 minutes. This was much better than my first two conversions on flecainide, 18 and 22 hours, and even exercise conversions I'd had. These ranged from 7 to 10 hours.

So, I've broken my four-month spell of not having to use my flecainide on demand as backup. However, I'm not unhappy – the plan I presented to my EP is still working. On this trip, I certainly stressed my system and probably messed up my electrolytes as well as being dehydrated from the exertion and altitude. The flecainide worked much more quickly than before. I would attribute this to all of the supplements I've taken. As I mentioned, this is a "work-in-progress", and I obviously need to fine tune my program if I want to continue exerting myself like this (some would observe that this would not be a bright move).

In addition, my blood glucose observation program has yielded an 18-pound weight loss in 8 weeks (usually with much more modest exercise than this latest outing). All in all, I'm very pleased with my progress. NSR to all readers!

Postscript – January 2006

I am very pleased to report that my last episode was on April 22, 2005, so it is nearly nine months of being afib-free.

My Bordeaux Experience

Alistair Thomson

The following is an account of my ablation for atrial fibrillation carried out at the Hospital of Haut-Leveque, Bordeaux, France, in the week of March 14th-18th 2005.

I was admitted to the hospital at 8:30 am on March 14th. The cardiology building is a rather ugly concrete edifice of about 7 or 8 floors situated on a sort of campus of other unprepossessing hospital buildings in Pessac, a suburb of Bordeaux. I was shown to a very clean but spartan room with two beds and a bathroom and TV where my wife and I were to spend the next four nights.

After changing into hospital garb, usual affair, I was wheeled to a lower floor to have an echocardiogram and a TEE (trans oesophagal examination). The result was good in that I didn't have a clot. The TEE, which others have described as 'uncomfortable', was for me the worst experience of the week.

At about 12:30 I was again taken downstairs to the operating theatre and placed on a table surrounded by a mass of monitors, etc. I was prepped for surgery (having already been shaved); getting me ready took about half an hour. I was to be sedated but to remain conscious during some of the operation. The drugs were commenced and the sedation was such that I did not really notice the catheters being introduced into the main vein in my right groin. They start by inducing fibrillation. The procedure after that took about four hours. I must have dozed quite a bit, occasionally felt a little pain (which was quite bearable) at which point they would ask if they could continue a bit more. After a while I became quite interested in the screens, one of which showed a scene rather like a fairground where you look in a box and work levers trying to lift something out. There were three little loops being dangled about. Another screen showed what I assumed was my pulse beating at around 90-130. I then heard an exclamation, 'finally!' and saw my pulse rate drop to 65-66 and hold and realised that fibrillation had stopped.

After that I became quite confused, as my pulse rate alternated quickly between 50, 100, 130 and so on. I was then told that the procedure was over and my main doctor who carried out the procedure, Dr Pierre Jais, told me that it had gone well. Later Dr Jais who possibly does the

procedure at least twice daily or maybe 400 to 500 times a year, told me my case was 'very difficult'.

A nurse put a bag of sand on my groin wound and held it in place by wrapping a cloth around my leg several times. I was then wheeled upstairs at about 6:30 pm. I was still on a drip. I had had nothing to eat since 8:00 pm the night before and with the relief that the procedure was over felt quite hungry. However I was not allowed anything until 11:30 pm and then was only allowed a yogurt and a fruit compote. I felt quite beaten up, but it was tempered with pleasure that the worst was over.

At about 8:30 pm Dr Jais came to see me in my room and explained how the procedure had been much more complex than he had anticipated. Having initiated fibrillation, he isolated the pulmonary veins. In many cases at this point fibrillation ends spontaneously but not in my case. He then made two linear lesions in the left atrium. Fibrillation still continued and he then had to tackle other areas of activity. 'Finally' was when the fibrillation stopped. At this point he attempted to induce fibrillation – that was the explanation for me seeing my pulse jump about – but could not do so. He found this inability to induce fibrillation to be very positive. At this stage his optimism about the outcome for me seemed quite guarded. [He did say that the most likely time for fibrillation to restart was in the first 24 hours after the operation].

That night there were many nocturnal visits by pleasant nurses taking blood and re-adjusting my drips. I was on two drips, one of heparin, an anti-coagulant, and the other the usual glucose drip. I was also rigged up with a monitor for my heart-beat which transmitted to the office at the other end of the corridor.

The nurses were most concerned about my lack of desire to pee, as I had absorbed four litres of fluid during the procedure. The following morning they gave me a diuretic and admonished me to pee as much as I could. The quantity of my urine was then monitored for a couple of days.

That same morning I had another echocardiogram and was also taken to have a chest x-ray. Thereafter it was a day in bed, still feeling beat up and having to keep my right leg straight to promote healing of the groin entry which was still under pressure from the bag of sand. I did not have time to be lonely as I had continual visits from well-dressed and cheerful nurses to take blood, etc. Moving around or even sitting in a chair at this stage was not easy with my drips and bag of sand. These were both removed at 8.00 pm that night. Being off the drips meant that I was mobile at last but the heparin drip was replaced by injections of heparin (Calciperin). These took place every eight hours, including one at 2:00 am, followed by

extraction of a blood sample at 6:00 am. This routine was to continue until Friday.

On Day 3 I was feeling much better. The main activity of the day was to go on an exercise bike and have what seemed like a full physical workout, pulse up to 135. After 15 minutes on the bike I had worked up a big sweat and was quite tired afterwards, but was able to have a bath and a shave. In the early afternoon Dr Jais came to visit again. He appeared much more confident of my eventual outcome and told me that all the tests had been quite satisfactory. He explained that one risk was that during the healing process one of the scars might heal itself. If that happened, I would have to come back for a 'touch-up'. He was surprised that I was not in more discomfort, as my heart was quite inflamed due to the amount of burning. He prescribed some anti-inflammatory drugs and recommended that I stayed in the hospital until the Friday as scheduled. He was off to Vienna for a conference for a few days.

Day 4, and after a good sleep – one gets used to the nightly visits – I was feeling fully recovered. No activities were planned. I was going to learn how to inject myself with the anti-coagulant so that I could continue the injections on the journey home, [but decided not to. My wife was also not willing to learn how to do the injections].

In general, though the first sight of the hospital was a bit depressing, I was astonished at the level of care I received. The staff, doctors, nurses, and nurses' aides were all immaculately turned out and very nice to me. (Doctors in white coats, nurses in blue and white striped coats, and assistants and orderlies in green and white stripes). The nurses work in a team, and there was no feeling that they were understaffed. The wards have two beds, and one can have one's spouse occupy the second bed at a little extra charge. Everywhere was spotlessly clean; with the linoleum floors washed and polished each day until they glistened.

The food is plentiful except at breakfast. Both lunch and dinner are three or four courses, once you are well enough to eat them all.

The advantages of Bordeaux for AF ablation are:

1. It is certainly in the top one or two institutions in the world for treatment of afib.
2. The unit has the best of equipment; they perform as a large team; and do one to three ablations each weekday.
3. The institution provides wonderful aftercare. The ward has a large nursing team which specialises in ablation aftercare.
4. If necessary, they proceed beyond the initial stage of PV ablation and attempt to eliminate all tissue which is conductive of AF. This

is certainly what happened in my case. Had I gone to a hospital in Canada or somewhere else where the doctors are less experienced, the procedure would likely have ended after PV isolation. I would almost certainly have continued with afib in this case. Now, according to the hospital's statistics, I have an 80 per cent chance of being afib free.

The disadvantages are:

1. The cost is not covered by private insurance. It costs 7.500 euros for those covered by EU medical cover or 10,600 if paying personally. There are no extra charges and all medications and tests are included in the hospital fee of about 650 euros a day.
2. We found ourselves speaking French to everyone except Dr Jais. Some of the nurses may speak some English, but they were not letting on to us. This was not a problem for us, but might be of others.

Postscript – March 2006

I am still afib-free after a year and am off all meds and hoping for the best. It took me a month to get my strength back, but I am now back to all my usual golf and hiking, etc.

My Battle With and Success Over Afib

Charles L. Miller (av8or@eos.net)

I am a 66-year-old male, retired US Air Force Heavy Jet Tanker/Transport pilot, with a long history of afib, and currently living in Cincinnati, Ohio. My afib doesn't make me unique; there are over 2 million afib sufferers today, in the US alone. Though many don't suffer any discomforting symptoms and have a relatively low frequency of episodes, there are a substantial number of us that are "symptomatic" and very aware of our afib. This is my story.

After several years of acid reflux (a possible warning sign), I had my first afib episode 14 years ago (June, 1991) under conditions of extreme psychological work stress as a mid-level executive, program manager in the aerospace industry. An Emergency Room visit was able to convert me back to sinus rhythm with intravenous (IV) drugs over a period of about 8 hours. This episode was followed a few weeks later by what appeared to be a flu-like viral infection resembling the worst case of flu one could imagine (aching joints, fever, cough, night sweats, continuous headache, back aches, etc.). This illness lasted unabated for 9 weeks. My family doctor tried numerous medications and treatments without success and ultimately diagnosed the problem as possible viral pericarditis (heart lining inflammation).

I went for another year without any heart medications until I had my second isolated episode. This was triggered by an improper drug prescription (Hytrin), which was prescribed by an urologist to treat BPH (prostate enlargement), at an initial dosage level contrary to the manufacturer's warning/recommendation. The first application of this drug (designed for hypertension) caused me to pass out and I awoke in afib. Again I was converted at the ER with IV medications, this time taking over 15 hours.

I remained arrhythmia free, without medication, after that for 5 years (until 1997) when the arrhythmia episodes began again in very short duration (less than an hour) and in frequencies many days apart; they converted spontaneously and were of a mostly vagal nature. Gradually the episodes got longer and the interval between them became shorter. I was aware from the www.afibbers.org website

that atrial fibrillation was not a heart condition, but was a neurological problem in the electrical system that controlled the heart pulses, so I opted to make initial contact with an electrophysiologist (EP). He took my history, made no tests (except an EKG which showed a normal sinus rhythm, at that point in time), and prescribed several drugs, including antiarrhythmics, beta-blockers, and digoxin. These had no positive effect, as the episodes got progressively worse. By March of 1999, my afib had worsened to the point that it had become permanent (chronic). Meanwhile, I had changed to a different EP who merely changed the variety and dosage of medications as he unsuccessfully tried to treat the symptoms without determining any possible cause(s). Neither EP suggested or attempted to use electro-cardioversion.

By this time, the ongoing afib had caused my first episode of congestive heart failure (CHF) symptoms (shortness of breath, cough, and swelling ankles), with my EP seemingly remaining uninterested and unconcerned. My family doctor diagnosed a fluid build up in my lungs with an X-ray and started me on a temporary regimen of Lasix (a diuretic) to purge the fluid build-up. After this experience, at the suggestion of my family practitioner, I changed cardiologists again, and the new doctor was quite upset that no one had attempted to electro-cardiovert my afib early on. He scheduled me for the procedure after stopping all medications in May '99. This attempt proved unsuccessful.

I remained in continuous afib, and was referred to another EP, 120 miles away in Indianapolis, Indiana, who assured me that he could successfully cardiovert me. The second attempt was scheduled for July 1999. This new EP hospitalized me for 3 days while he loaded my system up on Tambocor (flecainide), digoxin and beta-blockers. The attempted electro-cardioversion was again unsuccessful and I had to remain in hospital for two additional days while they attempted to bring my heart rate and blood pressure under control. I left the hospital on medications substantially elevated from those used prior to the attempt, but still in continuous afib. Up to this point I had been prescribed virtually every one of the popular anti-arrhythmic and/or heart drugs currently in use and all without any apparent affect other than a variety of undesirable side affects. These included Quinaglute, Toprol-XL, digoxin, sotalol (BetaPace), flecainide (Tambocor), propafenone (Rythmol), Cardizem-CD, Lopressor, and Altace, all in individual and in multiple combinations and various dosage levels incurring a variety of combinations of the side-affects known for each.

After being in continuous afib for over 15 months, and suffering a worsening quality of life including occasional CHF symptoms, in desperation I made contact via email and finally went to the Cleveland Clinic some 250 miles away. They recommended immediate attempt at cardioversion, again by hospitalization and loading up my system with appropriate drugs prior to the cardioversion. After

three days of high-level loading again with Tambocor (to a level nearly 50% higher than the previous cardio-version attempt) and other drugs, I spontaneously converted just mere hours before the electro-shock was to take place – having been in continuous afib for exactly 17 months (since Aug. 2000). When I was discharged, I was on a very elevated Tambocor dosage along with BetaPace, digoxin and beta-blockers, but was suffering from headaches and BP in the 160/100 range. The Tambocor at the high levels (525 mg/day) completely scrambled my brain, affecting hand-eye coordination, balance and cognitive functions.

After five days the afib returned, slowly at first and then once again increasing. At this point I self-discontinued the digoxin and the afib stopped within 27 hours of my last dose. When I told the Cleveland Clinic EP that I had quit the digoxin, he just agreed that, "this was probably a good idea and was an old drug and essentially not indicated for afib". (I wondered why was I paying a doctor for care and advice?). Eventually I reduced my daily level of Tambocor from 525 mg/day to 300 mg/day. This largely alleviated the severe side affects, that I had been experiencing, to a tolerable level. However, the afib once again started up on an intermittent basis.

In Feb 2002, I began to suffer from angina induced by walking my dog outside in the frigid sub-zero wind chill. After 5 increasing attacks over four weeks, I went to the ER. An angiogram was performed and I was scheduled for an immediate dual bypass graft. My afib abated somewhat after the bypass surgery, but again began to increase. I remained on the Tambocor at 300 mg/day. By mid summer 2002 I was again in near-continuous afib.

By Nov 2002, I was suffering from over 30 health issues that were all traceable directly to published Tambocor side affects. At this point I had been on this drug since 1999 and it was no longer controlling the afib. Upon presentation of this list to my family doctor he agreed to phase me off of the Tambocor and substitute amiodarone, a highly toxic and dangerous anti-arrhythmic drug; a "medication of last resort".

I related the shortness of breath to the Tambocor toxicity and tried to offset this as a temporary initiative by taking hyperbaric treatments, making hyperbaric chamber "dives" to 2 atmospheres for an hour every other day. This helped somewhat, but had no lasting benefit. On Dec 26, 2002, I went to the ER to obtain a supplemental oxygen prescription. They diagnosed CHF and admitted me for IV treatments to purge the retained fluids and reduce heart rate and blood pressure. While still heavily under the effects of Tambocor toxicity, which I had just fully eliminated in the previous 24 hours, and while still full of fluids, the "holiday assigned" resident junior cardiologist ordered an echocardiogram. With

the retained fluid, high heart rate and residual effects of the Tambocor, my ejection fraction was reported as 15% (norm is 50 to 60%) and the resident wanted me to take an immediate angiogram with a preliminary diagnosis of stenosis of my bypass graphs, or possibly the need for additional bypass grafts. I refused on the basis that according to my family doctor, if this had been my typical ejection fraction, I would have needed a pacemaker long before now. Also I had taken a cardiolite stress test (treadmill plus nuclear trace dye) a mere two months previously, which had shown normal circulation in the heart. I insisted on obtaining a second opinion before undergoing what I believed to be an unwarranted angiogram. Changing cardiologists, once more, I was again diagnosed with elevated heart rate and B/P, and he focused on bringing these numbers into the normal range by medication. Once this was achieved, a follow-up echocardiogram was taken in April 2002 which showed a "remarkable" recovery of ejection fraction to 40% (confirming my earlier suspicion that the first echo was not representative due to the circumstances). Though the rate control technique reduced my symptoms, I was still plagued with significant quality of life issues (depression, fatigue, malaise, anxiety, insomnia, lost libido, a feeling of being much older, etc.) and increasing episodes of congestive heart failure.

In the meantime, the University of Cincinnati, and Dr. Randall Wolf were making breakthrough technology on a capability to perform the "maze procedure" using micro-surgery and an endo-scopic device, rather than as an open-chest procedure. Called the **"mini-maze",** this procedure is performed by making a 3 to 4 inch incision on the side between the ribs, high in the rib cage, with a smaller incision several ribs below for the endo-scope, which is used to observe the surgical field.

Through my current cardiologist, I received a referral to see Dr. Wolf for an evaluation to see if I might be a candidate for this newly developed procedure. Initially he was reluctant to consider me as a candidate due to the prior bypass surgery (which could cause potential difficulties due to related scar tissue), and the length of history I had with afib (recognizing that this was still a new and developing technique). However, I was able to prevail on him to take on my case with some added latitude that would permit him to abort the procedure, with my advance agreement, if it proved questionable.

The procedure was performed and the results were better than anticipated. During accomplishment of the mini-maze procedure, Dr. Wolf discovered that an adhesion had taken place during my Feb. 2002 dual bypass surgery, which had fused the top of my right lung to my heart. This adhesion had caused unexplained substantial muscle pain and spasms on a near 24/7 basis for nearly three years following the bypass surgery and had triggered and aggravated my arrhythmia. He was able to separate and cauterize this adhesion. He also removed the left

atrium appendage (cause of 90+% of heart related blood clots that trigger strokes). He found that one of the bypass grafts had formed an adhesion to the appendage and he had to separate that adhesion very carefully before the appendage could be removed. He also conducted NPT (neurological path testing) on the nerve bundles in the heart and found several nerves that were hyperactive (a probable source of the afib extra pulses). He surgically desensitized or neutralized these.

I awoke from the surgery in wonderful sinus rhythm and have remained continuously in sinus rhythm, ever since. The recuperation period lasted about ten weeks with gradual reduction of the soreness and restrictions from the surgery. Recovery to a nearly pain-free state took approximately 5 months (unique in my case due to the added scope of surgery to clear scar tissue from the prior surgery).

A follow-up exam was done two weeks after the surgery, and again at six weeks. Dr. Wolf kept me on my pre-surgery medications so that any changes that occurred were attributable only to the surgery. At the six-week follow-up, Dr. Wolf terminated my amiodarone antiarrhythmic medication with no negative affects. At nine weeks after the surgery, a follow-up echocardiogram was performed to see what the impact was on my ejection fraction and mitral regurgitation. The results were very positive showing a noticeable reduction in the size of the left atrium, a substantial reduction in the mitral regurgitation to "trace" levels, and an improvement in the ejection fraction (up from the pre-surgery reading of 40% to near normal range of 46%). At twelve weeks (dictated by being off amiodarone for six weeks), I was monitored on a 24/7 basis by a portable CardioNet device for a period of two weeks to assess if there are any remaining episodes of arrhythmia. This verified a stable sinus rhythm with absolutely zero abnormal beats. At this point my Coumadin medication was next eliminated. Subsequently, my energy levels and routine have returned to normal levels. The symptoms of CHF have disappeared. And I am no longer on the Lasix medication.

I must add a personal observation. At the outset of my atrial fibrillation in 1997, I was acutely aware anytime my heart went into or came out of afib. It even would wake me up from a sound sleep; it was so conspicuous. During one pre-bypass period of 17 months, I was in continuous afib. After the bypass, I was again in persistent and near-continuous afib for more than a year, but I had either become acclimatized to it, or there was less of a transition since I didn't perceive the afib initiation as much. For the past 10 to 14 months, I had once again been in continuous afib. My post mini-maze surgery with its total return to sinus rhythm gave rise to a surprising and delightful psychological effect. The long-term continuous afib had subconsciously created a sense of anxiety, depression, and malaise — things weren't right in my physical condition, and there was little

motivation to pursue new long-term goals, adventures, or even any desire to travel far from home. After the surgery, I awoke in strong sinus rhythm and euphoria that "all was well with the world" and I now have motivation, energy, and a bright outlook on life (even though I just turned 66 two days before the surgery). My health continues to improve as the various bodily organs resume to full oxygen circulation that was deprived by the chronic afib. I now walk two plus miles every day when the weather is not wet, and can do so without becoming winded or strained. I have begun a course of physical exercise to limber and strengthen muscles left weak from the fatigue caused by the afib.

Dr. Wolf is now traveling all over the US and a half dozen international sites (including Canada) teaching his new mini-maze procedure. In the US, Medicare and most major medical insurance policies have certified this procedure for coverage. I highly recommend this advanced surgical procedure to anyone afflicted by major, uncontrolled afib problems. Not only will it successfully improve your quality of life, it may also save you from congestive heart failure.

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Postscript – January 2006

I am happy to report that I remain afib-free for the entire period approaching 15 months since my Wolf mini-maze procedure.

My Journey to Bordeaux

Hans R. Larsen

As some of you already know, I have been a lone afibber since December 1989 and in the intervening 15 years have tried pretty well everything (trigger avoidance, dietary changes, supplementation and antiarrhythmics) to vanquish the beast – all to no avail. My situation was complicated by the fact that it was discovered a couple of years ago that I had hyperaldosteronism, which makes it very difficult to maintain a normal potassium level. My episodes increased in frequency and duration until I began using the on-demand approach (450 mg of propafenone (Rythmol) at the onset of an episode). Using this approach I was able to keep episode duration to about 3 hours. However, the fatigue and depression accompanying my frequent episodes were wearing me down, so during the summer of 2004 I decided to have a pulmonary vein isolation (PVI) procedure here in Victoria, BC with Dr. Richard Leather. It was eventually scheduled for December 22. Just as well, during the first 3 weeks of December I had 10 episodes.

The procedure went well and the next two weeks were pure bliss with no afib at all. Unfortunately, the bliss did not last. On January 6 I experienced a pretty debilitating episode with accompanying enormous disappointment and depression. From then on things got steadily worse. In January I had 7 afib episodes and a 50-hour episode of bradycardia (very slow heart beat) that was later attributed to the propafenone. I found the bradycardia more frightening than the afib, so I reluctantly gave up the on-demand approach. This meant that my episodes now lasted considerably longer. I had 9 episodes lasting a total of 98 hours in February and 12 episodes in March totaling 129 hours. Things were definitely going from bad to worse. A touch-up was scheduled with Dr. Leather, but the earliest I would be able to have it would be the end of June and even that was not guaranteed – waiting times are very long in Canada.

Now a bit of a miracle happened. A good friend of mine is scheduled for an ablation in Bordeaux on July 11th. On Friday, April 1 (no fooling :~)) he received an e-mail from Mlle. Deixonne (Professor Haissaguerre's secretary) informing him that there had been a cancellation for April 11 and enquiring if he would be able to come. He had to decline since he had not been on warfarin for the requisite two months prior to the procedure. Fortunately, he immediately thought of me (I had been on

warfarin ever since my December 22 PVI) and over the weekend contacted me with the news. Judi and I did not need a great deal of discussion before deciding that this was one opportunity we could not miss – no matter what the cost. So on Sunday I e-mailed Laurence (Mlle. Deixonne) and said that I would like to come for the procedure. Monday morning I received an e-mail with confirmation that I was "on" for April 11 along with detailed information about the whole procedure including cost, preparation, and even a list of recommended hotels close to the hospital – a very impressive start to my relationship with Hopital Cardiologique du Haut-Leveque.

The week starting Monday, April 4th turned out to be rather hectic. The hospital requires you to have a TEE (transesophageal echocardiogram) prior to the procedure in order to ensure that there are no clots in the left atrium or left atrial appendage. They could do this procedure in Bordeaux, but if they did find a clot they would not proceed so the trip would have been in vain. Monday morning I called Dr. Leather's office to see if he could arrange for a TEE (normal waiting time for this procedure would probably be about 2 months) and also to obtain copies of my medical records so I could fax them to Bordeaux. Dr. Leather was most cooperative and pulled the necessary strings to let me have the TEE done on Wednesday morning. I faxed my medical records to Laurence later on the Monday. Tuesday was spent arranging flight and hotel reservations. The TEE turned out to be OK so Wednesday afternoon we picked up our tickets for a KLM flight from Vancouver to Amsterdam followed by an Air France flight to Paris.

We left Victoria Friday, April 8th and caught the early morning flight from Vancouver on the Saturday. Sunday, April 10th we arrived at the Charles de Gaulle airport in Paris and walked to the train station located right in the airport. Here we obtained tickets for the TGV to Bordeaux leaving at 1:44 pm and arriving at Gare St. Jean in Bordeaux at 6 pm. Going by TGV is a bit like low-level flying with speeds of almost 200 miles/hr (300 km/hr). From Bordeaux we took a rather expensive cab ride to the hotel Chantafred in Pessac, a suburb of Bordeaux where the hospital is located. At this point, we were somewhat tired to say the least! Just prior to arriving in Bordeaux I had gone into afib – an episode that was to last 40 hours.

As scheduled, we checked into the hospital at 2 pm and handed over the bank draft for 11,731 Euros ($14,400 US) which covered the cost of the 5-day hospital stay, the procedure done by Pr. Haissaguerre and Dr. Jais (chief EP) and all tests, catheters etc. as well as room and board for Judi. NOTE: Full payment is normally required one month prior to admission. We were shown to a very pleasant, spotlessly clean room with two beds, and a large wardrobe, which also housed a very solid looking safe for

storing our valuables. Shortly after settling in two nurses arrived to take blood samples, blood pressure and ECG. Then Pr. Haissaguerre arrived for a chat. He is a very personable physician, extremely intelligent and with a complete grasp of the intricacies of afib. To say that I was impressed would be an understatement. He said that my procedure was scheduled for Tuesday afternoon and that Dr. Jais would be doing the actual ablation. Later another doctor arrived and asked a lot of questions. Then a nurse's aide came in with a special surgical scrub solution that I was supposed to use when having a shower before bed and in the morning. At 6 pm I was taken for an x-ray and at 7 pm we had a nice supper served in the room. Later on a nurse came in and gave me a heparin injection as my INR had proven to be a bit low (I had stopped warfarin 48 hours earlier as instructed). I also received a potassium supplement as the initial blood test had shown that I was low on that as well. Just before bed I was hooked up to a wireless Holter monitor, which transmitted my vital signs to the nurses' station. At 2 am I was woken up for another heparin injection.

Tuesday morning was taken up with more blood samples, ECGs, blood pressure measurements, heparin injections, groin and chest area shaving and in general, procedure preparations. At 9:15 am I finally reverted to sinus rhythm after 40 hours of afib. Around noon Dr. Jais arrived for a chat. Again I was mightily impressed. One of the questions he asked me was whether I had ever had episodes lasting over 24 hours. I said that I certainly had and he then remarked that, in their experience, this probably meant that there were one or more ectopic sources outside the pulmonary vein area – so after having isolated the pulmonary veins he would go looking for other sources on the atrium wall and ablate them as well. As I understand it, the procedure is done while the atrium is fibrillating; thus when the fibrillation stops, it is likely that the ablation is complete. Nevertheless, several attempts are made to induce fibrillation before the catheters are withdrawn.

At 12:30 pm I was given a sedative and had a painkiller patch put on my groin area to reduce the risk of pain when the catheters were inserted. I was then wheeled down to the operating room and prepared for the procedure. After administering a local anesthetic Dr. Jais inserted the catheters and started the procedure – at about 2 pm I believe. I was given more sedative (intravenously) and really did not feel a lot until I woke up about 2 hours later. Occasionally it hurt a bit, but not intolerably so. At 3:30 pm Pr. Haissaguerre told Judi that the procedure was over and all had gone well. I don't remember too much of what went on during the rest of the day, but I know I had more tests and heparin injections. I was also hooked up to the wireless Holter monitor again and would be continually monitored for the next three days.

Wednesday started out with more tests. While I had the ECG Pr. Haissaguerre came in and immediately noticed that I had a lot of PVCs (I was feeling them as well). He took one look at the ECG as it rolled off the machine and said: "You must be very low in potassium". A blood test immediately confirmed that my level was low at 3.2 mmol/L and within ½ hour I was hooked up to an intravenous feed of potassium chloride and within another ½ hour the PVCs were gone – a clear demonstration of the importance of potassium in preventing PVCs. Otherwise the day was pretty routine with more tests and heparin injections as well as a nice lunch and dinner. I pretty well spent the whole day resting while Judi went for a long walk around the hospital grounds.

Thursday morning Dr. Jais came in for a long chat. He explained in detail how the procedure had gone. They had found no signs of stenosis after the first ablation in Victoria, but had discovered that three of the four veins isolated during that procedure had become conductive again. So he had re-isolated them and had then attempted to put me into afib again. I did go into afib so he went hunting for the offending cluster of rogue cells and found it on the atrial wall. After ablating it he was no longer able to induce afib. On the way out from the left atrium he had done a standard flutter ablation in the right atrium. Apparently, from 10 to 20% of afib ablations result in the development of atrial flutter, so in order to prevent that, they routinely do the flutter ablation on their patients from overseas. His overall conclusion was that everything had gone well and he would not expect me to have anymore afib episodes. However, just to make sure he would send me for a bicycle stress test to make certain that did not put me into afib. I passed this test with flying colors. I was certainly apprehensive before I went into it, since the last time I had a stress test, I went straight into afib after finishing. Later on I had a standard echocardiogram, which proved normal.

Friday morning I had more blood tests and an ECG and we were shown how to self-inject heparin. This had to be done every 8 hours over the weekend. I also had to continue with an oral potassium supplement and spironolactone in order to keep my potassium level up. After lunch we packed our things and went back to the Chantafred where we were to spend the next two nights since the special ward we were on closes for the weekend. In retrospect, we would have been better off staying in Bordeaux because there is not much to do in Pessac, especially on a Sunday. We did take the train from Pessac to Bordeaux on the Saturday and explored the city a little. It is a wonderful city with lots to see and do. While there we arranged to stay at a delightful small hotel (the Hotel Acanthe) in the old part of town from Monday until our return to Canada via Paris on Thursday April 21.

Monday morning (April 18) we returned to the hospital for final tests and consultation. If I had experienced any signs of afib, or shown any abnormalities in the tests, Dr. Jais would have gone back in and fixed the problem on Monday afternoon and I would then have had to stay a couple more days in the hospital before being discharged. As it turned out, everything was fine, so after lunch I was finally discharged with prescriptions for Coumadin (to be taken for one to three months), the beta-blocker bisoprolol (to be taken for one month) and time-release potassium chloride (to be taken as needed to keep potassium level above 4.0 mmol/L). After saying our goodbyes we headed for Hotel Acanthe where we spent a most delightful 3 days exploring Bordeaux and nearby St. Emilion – but that, as Hans Christian Andersen would have said, is another story!

Postscript

After returning home I continued supplementing with potassium in order to ensure my potassium level remained above 4.0 mmol/L. I have found that taking about 800 mg/day of elemental potassium (in the form of potassium gluconate) spread throughout the day keeps the level at about 4.4 mmol/L – not taking any potassium supplements drops it to 4.0 mmol/L. In any case, PVCs are a thing of the past and I have now gone 12 weeks without the slightest hint of an afib episode. Life is great – and I am eternally grateful to Dr. Jais and Prof. Haissaguerre for giving it back to me!

The Bordeaux clinic can be contacted at laurence.deixonne@chu-bordeaux.fr

Postscript – May 2006

Life can't get much better – I have been afib-free since my ablation in Bordeaux in April 2005!!

Cleveland Rocks! One Patient's Experience with PVA

David Weisenthal

The initial step

I am a 55-year-old male in good physical condition except for my Afib. Over the past 25 years I have competed in 35 marathons, dozens of triathlons and many ocean swimming races, including a swim from Alcatraz. In 1997, I finished the Hawaiian Ironman triathlon. In addition, I have observed a heart-healthy, very low fat diet for 25 years. My Afib symptoms began over five years ago. My principal trigger was strenuous, anaerobic exercise (as opposed to, say, easy jogging or swimming). However an Afib episode also would pop up occasionally for no apparent reason. In March of 2004 I was alerted by Hans Larsen's Afib Newsletter that a paper had been published by investigators at the Cleveland Clinic reporting a pulmonary vein ablation (PVA) success rate of approximately 80% with an incidence of stenosis (a principal concern for me and the reason I elected not to have the procedure sooner) in the 2 – 5% range. I phoned the Cleveland Clinic immediately, hoping to obtain an appointment with Dr. Patrick Tchou. I chose Dr. Tchou largely because, in checking on his publications in MedLine, I found him to be widely-published in the field of electrophysiology and PVA. The earliest appointment with Dr. Tchou that I could obtain was not until November 2004, almost seven months away at that point.

In September 2004, the Cleveland Clinic phoned to inform me that they would have to reschedule – pushing my appointment back to January 2005. By this time, I already had booked my airline reservation from Laguna Beach, California to Cleveland. A bit of whining on my part elicited a compromise date of December 2, 2004. At that appointment, I was examined briefly by a nurse. Then, I met with Dr. Tchou, who patiently and thoroughly counseled me as to my options, apart from PVA. Dr. Tchou is a warm and sincere person who, despite his extremely busy schedule, took ample time to ascertain my goals and expectations and to thoroughly educate me as to all of the treatment options that were available to me. Clearly, it was not his goal simply to "sell" me an ablation procedure. However, I was determined to go forward and, since I was found by Dr. Tchou to be an appropriate candidate for PVA, I was scheduled to have the procedure upon the soonest available date – April 19, 2005! This

was to be 13 months after the date upon which I originally had contacted the Cleveland Clinic. In fairness, I could have been seen by other physicians at the clinic much sooner but I am a firm believer in entrusting substantial body parts such as my heart only to those physicians in whom I have the greatest confidence. In this case, going first class cost me no more as Dr. Tchou and the Cleveland Clinic are participants in my relatively no-frills Blue Cross PPO plan. Therefore, I was able to self-refer with no out-of-plan surcharge by my insurance carrier.

The procedure

On April 17, 2005, I checked into the Cleveland Clinic Guesthouse, a hotel located immediately adjacent to the hospital. Patients can also elect to stay at the affiliated and considerably more upscale Intercontinental Hotel, which is connected to the hospital by an enclosed walkway. On April 18th, from 10 A.M. until 1 P.M., I underwent a series of tests, including a CAT scan, electrocardiogram, EKG, and various blood tests. I had been instructed to discontinue Coumadin three days prior to my procedure. Dr. Tchou had started me on Coumadin two months in advance of my scheduled procedure date. Previously, I had been taking only a daily aspirin, prophylatically. I spent the night before the procedure in my hotel room with orders to eat or drink nothing after midnight.

The next morning, at 6 A.M., I reported as directed to the check-in desk at the Cleveland Clinic's Electrophysiology Lab. I was relieved of my "civilian" clothing, issued a gaily-patterned and generously-vented hospital gown, shaved, and I'V.'d – one I.V. in each forearm. A saline drip was started. I was then invited to use the restroom (I declined and, of course, immediately began imagining that I had to "go" but it was too late for regrets). I was allowed to walk to the procedure room under my own power, wheeling my metal I.V. stand along beside me and, caught up in the solemnity and magnitude of the moment, feeling a lot like Charlton Heston wielding his wooden staff in the Ten Commandments.

The procedure room resembled a small O.R., which it was, except that there were a lot more monitors and electronic gizmo's than usual festooning the walls and ceiling. The O.R. nurses were affable and attentive and we joked amiably as they arranged me on the table and introduced the magic, twilight sleeping potion into one of the I.V. ports. I was told, and also had read, that I would be awake, though sedated, throughout the procedure. I was also told that I might feel pressure or an occasional twinge of "discomfort". In fact, felt nothing, saw nothing, and remember nothing. My last recollection is of myself nervously regaling the O.R. staff with an "amusing" anecdote (for which the staff graciously accorded me a courtesy laugh). The next thing I knew I was being awakened by a smiling nurse who informed me, "Okay, it's all over – everything went just fine." The procedure had taken about four hours.

The recovery

I was wheeled to a recovery area which contained about ten beds arrayed around a central nurse's station. Privacy was afforded by standard hospital curtains surrounding each bed. There was just enough room in each patient cubicle for a heart and blood pressure monitor, a visitor chair or two, and a TV. Within thirty minutes of returning from the procedure room, I was offered a hot and hearty lunch and, later, I ate an excellent dinner, which I was able to order from a multi-choice menu. I was subjected to minimal handling, while receiving wonderful, seeing-to-my-every-need care from the congenial and capable nurses. No blood was drawn from me and only two EKG's were taken at bedside. I was attached to a heart monitor and, overnight, to a Holter monitor. I was required to keep my legs straight - no bending – for six hours after returning from the O.R. Sterile wadding had been placed in my groin and bound tightly to prevent bleeding and excessive bruising (I had been heparinized during the procedure to prevent clotting and potential embolism).

After six hours, my thighs were unbound and I was allowed to stand and even walk to the bathroom. Unlike another patient, who reported in the Afib Newsletter that he did not urinate for some time following his procedure, I was up every couple of hours with an urgent need rid myself of copious amounts of fluid. Perhaps this was a function of the volume of our respective I.V. drips or perhaps my need to urinate was caused by the diuretic effect of the prednisone tablets I began taking (and continued for a week thereafter) immediately upon returning from the O.R. That first night passed without much discomfort – a little soreness in my groin and a bit of a dull ache in my chest but nothing worth complaining about.

The next morning at 9 A.M. sharp, less than 24 hours following my procedure, I was released. I eagerly dressed, received my instructions (no heavy lifting for three days – okay to resume normal activities in seven days), was issued a week's supply of prednisone tablets, and bolted from the hospital. I was able to walk unaided the hundred yards or so back to the hotel, albeit still a bit sore in the groin and swaggering with a cowboy's bowlegged gait as a consequence. I had planned originally to spend that night in the hotel and fly back to California the next day but, since I was feeling so good, I hurriedly packed my bags, checked out of the Cleveland Clinic Guest House, and took myself off the to the airport where I traveled unaided from Cleveland to Orange County's John Wayne Airport by way of a stopover (complete with long walk between terminals) in Dallas-Ft. Worth.

Return to normal

In the days that followed, I felt a bit of transient soreness in my chest and had some very minor bruising in my groin but, seven days after the

procedure, I went for (an easy) five mile run. For the most part (and on Hans' suggestion) I took it fairly easy for the first month. One week following my procedure the tiny incisions in my groin had healed nicely and so, with Dr. Tchou's blessing, I resumed surfing. I have since resumed full athletic activities at normal intensity. How about the Afib? Well, I was warned that I would continue to experience transient Afib episodes for up to eight weeks as the scar tissue that would eventually interfere with the errant electrical signals was forming at the site of the lesions that were created in my pulmonary veins. I was told that these Afib episodes might even be more frequent and more severe than before the procedure. They weren't kidding. Early on I experienced a minor Afib episode in association with almost every physical exertion that raised my heart rate. However, the episodes I experienced were all of very brief duration, resolving within minutes of cessation of activity, and these became increasingly less frequent as the weeks passed.

Upon my discharge from the Cleveland Clinic, I was loaned a nifty device consisting of a polyurethane case about ten inches long by eight inches wide and three inches thick. It contains two wristbands, each attached to a wire leading into the case. There is a molded cradle that accepts a standard telephone receiver. The device is powered by a small battery. When I experienced symptoms, I was supposed to phone into the Clinic, day or night, don the wristbands, and thereby transmit my pulse rate through the phone lines to a technician at the Clinic. I was to be monitored in this fashion for three months, at which time I was to return to the Cleveland Clinic for a follow-up examination.

As I write this, it is three months after my procedure. My Afib episodes decreased in number for about four or five weeks, at which point they ceased entirely. I now run every day, often hard, pushing my heart rate into the anaerobic zone – something I haven't been able to do in years. I am also surfing and swimming several times a week. Despite this level of activity, I have not experienced an Afib episode in weeks. The quality of my life has improved immeasurably and, most importantly, I feel like myself again for the first time in five years.

Journal Summaries

Incidence & Management

Quality of life in persistent atrial fibrillation
BALTIMORE, MARYLAND. Cardiologists have long debated whether it is best for **persistent** afibbers to stay in fibrillation and just take beta or calcium channel blockers to keep their heart rate down (rate control) or whether it is best to attempt to convert them to sinus rhythm and maintain them in sinus rhythm through the use of antiarrhythmic drugs (rhythm control). The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial concluded that rate control is at least as effective as rhythm control. The trial involved 4060 AF patients with a mean age of 70 years. Seventy-one per cent had a history of hypertension, 38% had coronary artery disease, and 26% had impaired left ventricular function. Only 12% had lone AF. Half the patients were randomized to rate control plus anticoagulation while the other half were randomized to rhythm control plus anticoagulation. After 5 years of follow-up 21.3% of the patients in the rate control group had died as compared to 23.8% in the rhythm control group[26].

To quote the authors of the study, "the results probably cannot be generalized to younger patients without risk factors for stroke (i.e. patients with primary, or "lone" atrial fibrillation), particularly those with paroxysmal atrial fibrillation."

Quite apart from the fact that the study is not particularly applicable to lone afibbers especially paroxysmal ones, I believe it had several serious flaws:

- The most "popular" drug used in the trial was digoxin. Over 70% of the people in the rate control group had used this drug at one time or another. Digoxin had been used by 54% of the participants in the rhythm control group as well. So as far as digoxin use is concerned, there was little difference between the two groups.
- Beta-blockers were used liberally in both groups as well – 68% in the rate control group and 50% in the rhythm control group.
- The main antiarrhythmic used was amiodarone (Cordarone). This drug was used by 63% of the patients in the rhythm control group and by 10% in the rate control group.
- The second most popular "antiarrhythmic" used in the rhythm control group was sotalol (Betapace) – this drug was used by 41%

of patients despite the fact that it is well known that it does little, if anything, to maintain sinus rhythm, although it may help control the heart rate during an afib episode.

- Propafenone, flecainide and disopyramide had been used by only 4-15% of patients in the rhythm control group. It is impossible to say whether any of these drugs were beneficial or detrimental because of the way the data is reported.

The AFFIRM trial investigators have now compiled and reported the results of a sub-study aimed at determining whether quality of life (QoL) is significantly different between rate control and rhythm control patients. After a 4-year follow-up they conclude that QoL scores were similar in the rate- and rhythm-control groups at baseline as well as after 2 months, 12 months, and annually. They also conclude that QoL scores were similar irrespective of whether the participants were in sinus rhythm or in afib at the time the QoL scores were determined. They also suggest that attempts to improve QoL by restoring sinus rhythm will usually be unsuccessful.

Dr. David Newman from the University of Toronto, in an accompanying editorial, points out that participants in the AFFIRM trial were old and already suffering from other heart-related conditions; they were also significantly less symptomatic than the average afib population. Both these factors could well have affected their QoL scores. He also points out that a similar, but somewhat smaller trial (RACE) concluded that sinus rhythm at follow-up was strongly correlated with an improved QoL score.

Quality of life in atrial fibrillation: the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study. American Heart Journal, Vol. 149, January 2005, pp. 112-20

Newman, D. Atrial fibrillation and quality of life: clarity or evidence-based confusion? American Heart Journal, Vol. 149, January 2005, pp. 4-6 (editorial)

Editor's comment: It would be unfortunate indeed if these latest conclusions by the AFFIRM investigators concerning quality of life for afibbers were to be accepted unquestionably by EPs and cardiologists. For most of us being in sinus rhythm is associated with an immeasurably better quality of life than being in afib and again most of us will go to considerable lengths (like having an ablation or maze procedure) to achieve NSR. It is probably safe to assume that none of the AFFIRM investigators were suffering from symptomatic afib themselves or were living with someone who did.

Cost effectiveness of ablation

There are basically three management approaches to atrial fibrillation:

- left atrial catheter ablation (LACA)
- rhythm control
- rate control with thrombotic therapy.

Researchers at the University of Michigan have compared the cost effectiveness of these approaches. They conclude that LACA is cost effective in patients with paroxysmal or permanent AF and moderate risk for stroke. LACA is highly cost effective for younger paroxysmal afibbers (55 years of age) with a low stroke risk, but somewhat less so for 65-year-olds with paroxysmal or permanent AF. All three management options were superior when combined with aspirin therapy as opposed to warfarin therapy among 65-year-olds with low stroke risk (1.4%/year).

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1164-270, p. 125A

Treatment options for atrial fibrillation

CENTO, ITALY. Dr. Paolo Alboni and colleagues at the Civic Hospital present an excellent overview of the treatment options for patients with atrial fibrillation. The following groups of afibbers, in their opinion, are better off with no treatment at all:

- Patients who have only experienced one episode.
- Patients with infrequent, short and well-tolerated episodes.
- Patients whose first afib episode occurred after surgery or during or after a heart attack.
- Patients whose episodes are due to binge drinking (they should be counselled to avoid excessive alcohol consumption).

Afibbers who have longer episodes less than once a month should preferably use the on-demand (pill-in-the-pocket) approach to convert to normal sinus rhythm and thus avoid a visit to the emergency room for conversion. The on-demand approach involves taking propafenone (Rythmol) or flecainide (Tambocor) as soon as possible after the onset of the episode. The recommend dose is 200 mg of flecainide or 450 mg of propafenone for persons weighing less than 70 kg (154 lbs) and 300 mg of flecainide or 600 mg of propafenone for people weighing 70 kg or more. The on-demand approach is effective in achieving conversion within 2 hours in 94% of episodes. However, it is not appropriate for all afibbers and should be tried in the hospital or the doctor's office for the

first time. The researchers conclude that the use of the on-demand approach can reduce the number of emergency visits and hospitalizations by 90%.

Continuous treatment with antiarrhythmics should be reserved for those afibbers who have frequent, debilitating episodes. Amiodarone is the most effective drug for afibbers with underlying heart problems, but for lone afibbers beta-blockers (for those with the adrenergic variety) and disopyramide (Norpace) or flecainide (for those with vagal afib) are the drugs of choice.

Patients with frequent and/or badly tolerated episodes that markedly reduce their quality of life and are resistant to drug therapy should consider ablation or maze surgery, either on its own or in combination with antiarrhythmic drugs.

Alboni, P, et al. Antiarrhythmic drugs in patients with recurrent atrial fibrillation: where are we? Italian Heart Journal, Vol. 6, March 2005, pp. 169-74

Men more susceptible to AF

Researchers at the Mayo Clinic report that men tend to develop lone AF at an earlier age (average age of 45.2 years) than women (average age of 52.4 years). They also confirm at least 15% of lone afibbers may have a genetic (familial) disposition toward the disorder.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1050-268, p. 97A

Antiarrhythmics versus ablation – A comparison

CLEVELAND, OHIO. Ablation (pulmonary vein isolation or PVI) is usually only considered appropriate for afibbers with highly symptomatic episodes who have failed to obtain relief through the use of antiarrhythmic drugs. A group of American, German and Italian researchers now suggests that perhaps PVI should be considered the first-line approach for treating patients with symptomatic AF. They base their conclusion on a study of 70 patients (mean age of 54 years, range of 18-75 years) who had experienced highly symptomatic episodes for at least 3 months. The average time the participants had been suffering from AF was 5 months and 95% of them had the paroxysmal variety. About 25% of them had structural heart disease or hypertension, and about 60% of them were on beta-blockers.

The patients were randomized into receiving standard treatment with antiarrhythmic drugs (mainly flecainide – 100-150 mg twice daily, or sotalol – 120-160 mg twice daily) or a PVI procedure using the segmental procedure with the added feature of intracardiac echocardiographic (ICE) monitoring to ensure proper mapping catheter position and to guide energy delivery so as to avoid microbubble formation. All patients were treated in one German and two Italian centers specializing in AF treatment. Follow-ups were scheduled for 1, 3, 6 and 12 months after entering the study and all patients were given 24-hour Holter recordings prior to discharge from hospital and at 3, 6 and 12 months after enrollment. Event recorders were also used during the first and third months.

During the initial 2 months of follow-up, 20 patients (54%) of those in the medication group had at least one afib episode as compared to 9 patients (27%) in the PVI group. During the next 10 months, 63% of the afibbers on antiarrhythmics had recurrent, symptomatic AF episodes as compared to 13% in the PVI group. Asymptomatic AF was documented in 16% of the medication group as compared to 2% in the PVI group. Overall, the average (mean) number of episodes per 24-hour period decreased from 13 to 1 in the PVI group and from 12 to 6 in the medication group. The average duration of episodes prior to treatment was about 8-9 minutes in both groups. This decreased to 15 seconds in the PVI group and 45 seconds in the medication group after treatment. There were no transient ischemic attacks (TIAs), strokes, deep vein thrombosis or pulmonary embolism in either group during the follow-up period, but one patient (3%) in the PVI group developed moderate pulmonary vein stenosis, while 3 patients (9%) in the medication group developed bradycardia. Hospitalization during follow-up occurred in 54% of patients in the medication group versus 9% in the PVI group.

The researchers conclude that PVI is a feasible first-line approach for the treatment of selected patients with symptomatic AF. They caution that larger scale studies with longer follow-up are required before PVI can be considered standard care as first-line therapy for atrial fibrillation. NOTE: This study was partially funded by an unrestricted grant from Siemens, the manufacturer of the ICE system.

Wazni, OM, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation. Journal of the American Medical Association, Vol. 293, June 1, 2005, pp. 2634-40

Editor's comment: The main conclusion from this study is that PVI successfully prevents recurrence of afib during the first year following the procedure in 87% of patients undergoing a first procedure. This compares to the 37% of afibbers on antiarrhythmic therapy who remained afib-free during the first year. Clearly the EPs at the three participating

centers were highly skilled as they were able to achieve a first pass success rate of 87%. My surveys and published reports put the average success rate closer to 50% in "the real world". Perhaps my biggest problem with the study is that the participants were not typical of the real afib population. Having experienced afib for only 5 months with one or more monthly episodes lasting 8 minutes each would, in my opinion, not qualify for either aggressive drug treatment or a PVI. Furthermore, it should be kept in mind that about 60% of participants were taking beta-blockers on a continuous basis. This may well have impacted negatively on the medication group, which is bound to have contained at least some vagal afibbers. Finally, it is indeed unfortunate that the study did not include a placebo group – it may have fared just as well as the medication group.

Atrial fibrillation rings alarm bells in Japan

MORIOKA, JAPAN. Atrial fibrillation (AF) is a common arrhythmia in Japan although the prevalence is lower than in Western countries. Japanese scientists have just completed a study to determine the actual level of AF found in Japan and to estimate the future burden of the condition on the health care system. The study involved 10,042 men and 13,671 women who were examined (12-lead electrocardiograms) in 1980, 1990, or 2000.

The prevalence of AF among men and women over the age of 30 years increased from 0.7% in 1980 and 1990 to 0.9% in 2000; an increase of 29%. The prevalence among men (1.0%) was higher than that among women (0.6%). The prevalence of AF increased markedly with age; among men aged 70 years and older it was 3.5% in 2000 as compared to 2.1% for women. The researchers estimate that the number of Japanese citizens suffering from AF will exceed 1 million within another 10 years. NOTE: The survey did not distinguish between lone atrial fibrillation and AF associated with heart disease.

Ohsawa, M, et al. Rapid increase in estimated number of persons with atrial fibrillation in Japan. Journal of Epidemiology (Japan), Vol. 15, No. 5, September 2005, p. 194-96

Editor's comment: AF is clearly a significant health concern in Japan; however, it is likely that its prevalence was underestimated in this study. Whether or not a participant had afib was based on just one 12-lead electrocardiogram; it is thus likely that many cases of paroxysmal afib were missed.

Survey of AF management in Europe

MAASTRICHT, THE NETHERLANDS. A large team of European cardiologists has just released the results of a study aimed at determining just how well European cardiologists are following the official

European/North American guidelines for the management of atrial fibrillation (AF). The guidelines can be found at http://circ.ahajournals.org/cgi/content/full/104/17/2118

The study included 5333 AF patients enrolled in 182 centers in 35 countries. About 18% of the participants were enrolled after experiencing just one initial episode, 28% had paroxysmal afib when enrolled, 22% had the persistent variety, and 29% were in permanent afib. The status of the remaining 3% is unknown. About 10% of all participants had the lone (idiopathic) type of AF with the prevalence of lone afib being highest in the paroxysmal group (15%). About 65% of participants were hypertensive and 28% of paroxysmal and 52% of permanent afibbers had heart failure or a left ventricular ejection fraction below 35%. Thirteen per cent of patients with permanent AF had mitral valve stenosis as compared to only 3% among paroxysmal afibbers. The average left atrial diameter was 43 mm for paroxysmal, 48 mm for persistent, and 51 mm for permanent afibbers.

Highlights of the study are as follows:

- About 33% of patients who should have been on anticoagulation (warfarin) therapy according to the guidelines were not. Perhaps more disturbing is the finding that 49% of patients who did not need anticoagulation were receiving it. This despite the fact stated in the report, "In patients with low risk for stroke, the bleeding risk of anticoagulation therapy outweighs the benefit of stroke prevention, but aspirin is recommended in these patients." The report draws the following conclusion in regard to anticoagulation, "Altogether it seems that in daily practice selection of stroke prevention therapy is not strongly determined by the clinical indications as recommended by the guidelines."

- Only half of the patients had their thyroid hormone levels checked. This despite the fact that thyroid problems are a well established underlying cause of afib. Even more disturbing, 40% of all patients on amiodarone never had their thyroid function determined even though amiodarone is known to damage the thyroid gland.

- The majority (69%) of participants had symptomatic afib with the most common symptoms being palpitations and fainting.

- About 40% of all patients received rhythm control medication (primarily amiodarone and sotalol) even though almost half (44%) of them had no symptoms warranting the use of

dangerous antiarrhythmics. This is in direct conflict with the guidelines, which state that rhythm control should only be prescribed for symptomatic patients. For most patients, taking antiarrhythmics did not eliminate their symptoms indicating that, "available rhythm control strategies are inadequate and that there is at present an unmet need for safe and efficacious antiarrhythmic drugs for control of AF." I think most of us can probably agree with this statement. The report, unfortunately, did not distinguish between medication schemes for lone afibbers and those for afibbers with underlying heart conditions.

The researchers point out that most of the centers involved in the study specialized in AF. Thus clinical practices in less specialized centers and private practices are likely to deviate even more from the guidelines.

Nieuwlaat, R, et al. Atrial fibrillation management: a prospective survey in ESC member countries – The Euro Heart Survey on Atrial Fibrillation. European Heart Journal, Vol. 26, November 2005, pp. 2422-34

Wyse, DG. The Euro Heart Survey on atrial fibrillation: a picture and a thousand words. European Heart Journal, Vol. 26, November 2005, pp. 2356-57 (editorial)

Editor's comment: The finding that inappropriate prescription of warfarin and antiarrhythmics is fairly common is fully in line with the results of our surveys, so there is no reason to believe that adherence to the guidelines is more pronounced in the US and Canada than it is in Europe.

Survival of lone afibbers

Mayo Clinic researchers have reviewed the clinical records of 4618 residents of Olmsted County, Minnesota who were diagnosed with a first episode of atrial fibrillation during the period 1980-2000. About 9% (413 subjects) were classified as having lone AF. While lone afibbers below the age of 70 years at diagnosis had a mortality rate similar to that of the general population, those over 70 years of age had a 25% higher mortality rate over the 8.3-year follow-up period. The incidence of transient ischemic attacks (TIAs) was 1.5% over the follow-up period. Stroke was experienced by 5 lone afibbers (1.2%), while 2.4% developed angina (ischemic heart disease), 6.5% congestive heart failure, and 3.9% died from cardiovascular disease. The researchers conclude that lone afibbers have a low incidence of cardiovascular events and a survival rate similar to that of the general population.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1050-272, p. 98A

Mechanistic Insights

LAF and brain natriuretic peptide

BOSTON, MASSACHUSETTS. Brain natriuretic peptide (BNP), a cousin to atrial natriuretic peptide (ANP), is a hormone released from the walls of the ventricles during unusually strenuous activity. It is stored as a prohormone within secretory granules in the ventricles and is secreted as a N-terminal fragment, N-terminal pro-brain natriuretic peptide (nt-pro-BNP), and the smaller active hormone BNP. BNP has effects similar to those of ANP, that is, it decreases sodium reabsorption rate, renin release, and aldosterone release; it also increases vagal (parasympathetic) tone and decreases adrenergic (sympathetic) tone. Because nt-pro-BNP is easier to measure than BNP it is often used as a marker for BNP.

It is well established that BNP and nt-pro-BNP levels are elevated in heart failure and that the degree of elevation is directly proportional to the seriousness of the failure. Researchers at the Massachusetts General Hospital now report that lone afibbers also have elevated nt-pro-BNP values even when in sinus rhythm. Their study involved 150 participants with lone atrial fibrillation (LAF) and 75 afib-free controls matched according to age, gender, race, and ethnicity. The majority of participants (81%) were men, the average age at enrolment was 54 years, and the average age at first diagnosis was 45 years. The demographics of the study group thus closely mirrors that of the much larger groups involved in our own LAF surveys and, once again, puts “paid” to the still widely held notion that afib is a disease of old age, which it clearly is not. At the time of enrolment 130 afibbers had the paroxysmal variety, while 20 were in permanent AF.

Blood samples were obtained from all participants at enrolment. The researchers found that the median level of nt-pro-BNP was significantly higher among lone afibbers (even when in sinus rhythm) than among controls (166 versus 133 fmol/mL); they also observed that nt-pro-BNP levels were higher in afibbers with permanent LAF than in those with paroxysmal LAF (189 versus 157 fmol/mL), and that afibbers with high nt-pro-BNP levels at study entry were more likely to progress to the permanent version than were those with lower levels (197 versus 163 fmol/mL). There were no significant differences in ANP levels between afibbers and healthy controls, but levels in afibbers who later developed hypertension were significantly higher than in those who did not (3764 versus 1622 fmol/mL). The researchers speculate that BNP may be

involved in sustaining fibrillatory rotors through its potentiating effect on vagal nerve impulses transmitted from the brain.

Ellinor, PT, et al. Discordant atrial natriuretic peptide and brain natriuretic peptide levels in lone atrial fibrillation. Journal of the American College of Cardiology, *Vol. 45, January 4, 2005, pp. 82-86*

Editor's comment: It is known that medication with ACE inhibitors produces an almost immediate, dose-dependent reduction in natriuretic peptide levels. Could this be another possible pathway by which ACE inhibitors may help prevent afib and, in particular, prevent it from becoming permanent?

Heart rate during atrial fibrillation

WASHINGTON, DC. The maximum heart rate (resting ventricular rate) experienced during an atrial fibrillation episode varies from person to person. Some afibbers barrel along at 200 bpm or more, while others experience afib at rates as low as 40 bpm. The LAF Survey V found that maximum rates varied between 55 and 280 bpm among 132 respondents.

A team of American researchers has just completed a study in which they investigated the relationship between the maximum heart rate experienced during afib (at rest) and other afib variables. The study included 4059 participants in the AFFIRM trial. This trial involved persistent afibbers with one or more risk factors for stroke who were randomized to a rate control group (no attempt made to convert to sinus rhythm) or a rhythm control group (attempts made to regain and maintain sinus rhythm through the use of electrical cardioversion and antiarrhythmic drugs).

The researchers found that the maximum rate during afib varied between 37 and 300 bpm. The rate tended to be higher among women and smokers and was also higher during the first afib episode than during subsequent ones. Afibbers with a normal left ventricular ejection fraction also tended to have higher heart rates during afib. Afibbers with a history of coronary artery disease, hypertension or myocardial infarction (heart attack), and patients with an enlarged left atrium and long episodes (greater than 48 hours), on the other hand, tended to have a lower maximum heart rate during episodes. This would tend to indicate that afibbers with healthier hearts have higher maximum heart rates during afib. The results of the study also showed that afibbers with a high maximum rate had a higher probability of achieving and maintaining normal sinus rhythm than did those with lower maximum rates.

The researchers conclude that the maximum heart rate during AF may be a useful indicator in deciding whether a persistent afibber should be steered toward rhythm control (those with high maximum heart rates) or rate control (those with low maximum heart rates).

Cooper, HA, et al. Relation of initial resting ventricular rate to the ability to achieve and maintain normal sinus rhythm in patients with atrial fibrillation. American Journal of Cardiology, *Vol. 95, March 1, 2005, pp. 597-602*

Progression to permanent AF

VANCOUVER, CANADA. A nagging concern among paroxysmal afibbers is whether or not their AF will eventually become permanent (chronic). Researchers participating in the Canadian Registry of Atrial Fibrillation survey now report that about 25% of patients originally diagnosed with paroxysmal (intermittent) AF progress to permanent within 5 years of initial diagnosis. Their study included 757 patients diagnosed with a first episode of AF. The average age of the patients was 64 years (range of 14-91 years) and 38.3% were female. Eight-six per cent of participants reported symptoms (palpitations, chest pain, breathlessness, dizziness, fatigue or nausea), while 14% were asymptomatic (their AF discovered through an ECG). The majority of participants had a comorbid condition including heart disease (45%), hypertension (37%), respiratory disease (15%), thyroid disorder (10%) or diabetes (9%). Antiarrhythmic drugs were used by 41% and 12% used beta-blockers.

During the first year of follow-up, 8.6% of patients progressed to permanent status and by year five 24.7% had done so. The risk of becoming permanent increased by 40% for every 10 years of aging, by a factor of 3 if aortic stenosis was present, by a factor of 2.7 in the case of an enlarged left atrium (left atrial dimension greater than 45 mm), by 70% with moderate to severe mitral regurgitation, and by a factor of 2.4 in the presence of cardiomyopathy. Hypertension was not associated with an increased risk of progressing to permanent AF. A more rapid heart rate during fibrillation was associated with a slightly lower risk of progression to permanent with an increase of 5 beats per minute corresponding to a 6% decrease in risk.

Kerr, CR, et al. Progression to chronic atrial fibrillation after the initial diagnosis of paroxysmal atrial fibrillation. American Heart Journal, *Vol. 149, March 2005, pp. 489-96*

Editor's comment: As is unfortunately common in studies of atrial fibrillation, no attempt was made to treat lone afibbers as a separate group in the evaluation of the data. Thus, it is not known whether the findings would apply to lone afibbers. However, since the most important variables associated with progression involve heart disease, I would guess that the progression among lone afibbers would be considerably slower. Nevertheless, a significant increase in left atrial diameter, degree of mitral

regurgitation, or a drop of 30-50 bpm in heart rate during fibrillation may be a good time to consider an ablation or maze procedure.

AF precipitated from left atrial appendage

BORDEAUX, FRANCE. Most AF episodes have their origin in and around the pulmonary veins. However, AF foci have also been found on the back wall of the left atrium, the coronary sinus, the ligament of Marshall, and in the superior and inferior vena cava. Now electrophysiologists at the Hopital Cardiologique du Haut-Leveque report a case where the ectopic beats precipitating the AF originated in the left atrial appendage (LAA).

A 35-year-old woman with drug-resistant paroxysmal AF underwent a standard PVI whilst in AF. Successful isolation of all four pulmonary veins did not terminate the AF, so the EPs went looking for other sources of AF-precipitating ectopic beats. They located the source in the LAA. After successfully creating a continuous lesion around the opening of the LAA the AF ceased and the patient has now been in sinus rhythm for 5 months.

The French EPs point out that isolation of the LAA is a very tricky procedure and should be considered a last option as perforation of the heart wall and damage to the phrenic nerve are very real risks.

Takahashi, Y, et al. Disconnection of the left atrial appendage for elimination of foci maintaining atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 16, August 2005, pp. 917-19*

Survey of lone afibbers

BOSTON, MASSACHUSETTS. Researchers at the Massachusetts General Hospital have carried out a survey of 188 lone AF patients to determine their symptoms, triggers, medication use, and family history of LAF. Among the highlights of their findings are:

- The majority (94%) had the paroxysmal from of LAF when first diagnosed. Almost 8% of these afibbers progressed to permanent AF within a mean of 6 years of initial diagnosis.

- Average age at study enrolment was 54 years and age at first diagnosis was 45 years (range of 15-67 years). The majority of study participants (82%) were male.

- Afibbers who had hypertension were excluded at enrolment, but 8.3% did develop hypertension during the study (2-28 years after diagnosis).

- The majority (54.5%) had experienced more than 100 episodes of AF, while 70.7% had experienced more than 20 episodes. About a third (35%) had undergone one or more cardioversions.

- Thirty-four per cent of all study participants reported having a first degree relative with AF. Only 5% of participants smoked, but 76% reported alcohol consumption. High cholesterol levels were reported by 20% and diabetes by 3.9% of participants.

- The average systolic blood pressure within the group was 124 mm Hg and the diastolic pressure average was 76 mm Hg. Average pulse rate when in sinus rhythm was 68 beats/minute.

- Echocardiograms revealed structurally normal hearts with a mean left ventricular ejection fraction of 62% and a left atrial size of 39 mm. Permanent afibbers tended to have a larger left atrium (42 mm).

- The most common triggers were sleeping (44%), exercise (36%), eating (34%), chocolate (16%), soda (11%), and coffee (9%).

- The most common symptoms experienced during an AF episode were palpitations (88%), fatigue (77%), dizziness (67%), breathing difficulties (51%), and fainting (9%). Women were more likely to experience palpitations and breathlessness than were men and were also more likely to experience frequent episodes. It is also interesting that nausea was listed as a trigger by 7% of women, but 0% of men.

- The risk of progression to permanent AF was associated with a family history of AF, having undergone one or more cardioversions, having developed hypertension after diagnosis, and having an enlarged left atrium.

- Three participants (0.6%/year) sustained a stroke during the two and a half year study period, while 2 (0.4%/year) had a documented transient ischemic attack (TIA).

- Medication usage among the participants was as follows:

- Beta-blockers – 56.1%
- Calcium channel blockers – 16.7%
- Digoxin – 20.0%
- Flecainide – 16.9%
- Amiodarone – 13.5%
- Sotalol – 10.7%
- Propafenone – 7.9%

- Twenty-eight per cent of women, but only 3% of men reported having an inflammatory disease such as systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis, ulcerative colitis, ankylosing spondylitis or sarcoidosis. This suggests that chronic inflammation, in women at least, may be an underlying cause of LAF.

Patton, KK, et al. Clinical subtypes of lone atrial fibrillation. PACE, *Vol. 28, July 2005, pp. 630-38*

Editor's comment: This study parallels the findings made in our own LAF surveys. It is particularly interesting to see the genetic connection confirmed. Our LAF Survey V found that 40% of all afibbers had a first degree relative with AF. The Massachusetts survey found that 34% of respondents had such a connection. It is also interesting to note the close correlation between age at first diagnosis in the Massachusetts survey of 188 afibbers (45 years) and our LAFS-8 survey of 619 afibbers (48 years). Similarly, the percentage of men and women having AF was also very close in the two surveys (82% and 79%).

Afib and the gene connection

SYRACUSE, NEW YORK. Atrial fibrillation now affects over 3 million Americans and its prevalence among people over the age of 65 years is about 6%. AF is usually associated with underlying heart disease including hypertensive heart disease, cardiomyopathy, valvular disease, or atherosclerosis. About 2-16% of all afib patients have no underlying heart abnormalities and are classified as having "lone" atrial fibrillation. In the absence of risk factors like hypertension, diabetes or previous stroke these patients have a low risk of embolism (stroke and heart attack).

Dr. Ramon Brugada of the New York Heart Center, an expert on inherited AF, estimates that up to 15% of lone afibbers may have a familial (inherited) from of the disorder. He describes his pioneering study done in 1996 of 6 Spanish families with 132 members 50 of whom were diagnosed with lone AF. The age of diagnosis varied between 0 and 45 years with 2 patients diagnosed in utero. All but two of the AF patients

now have the permanent form, but in the majority of cases are asymptomatic.

Chinese researchers have also studied the genetic connection and have found two genes on chromosome II, which appear to have mutated in families with familial AF. These genes are involved in the control of potassium currents in the heart and thus the findings of the Chinese researchers confirm the role of channels responsible for potassium currents in the development of AF.

Other researchers have found a connection between genetic abnormalities in the renin-angiotensin system and the presence of non-familial AF with underlying heart disease.

Dr. Brugada concludes that efforts to control or cure AF will undoubtedly benefit from the discovery of the genes that cause the familial forms of the disease and from the knowledge of the alterations in gene expression caused by AF.

Brugada, R. Is atrial fibrillation a genetic disease? Journal of Cardiovascular Electrophysiology, *Vol. 16, May 2005, pp. 553-56*

AF originating outside the pulmonary veins

TAIPEI, TAIWAN. It is known that most afib episodes are initiated by ectopic beats originating in the pulmonary veins (PV) and that isolation of these veins can eliminate afib in 65-85% of paroxysmal afibbers. Clearly it is important to identify those patients whose main initiating areas lie outside the pulmonary veins so that an ablation can be properly directed.

Chinese researchers now report the results of an electrophysiologic study aimed at determining the prevalence and location of non-PV sources of ectopic beats. The study included 215 men and 78 women with clinically documented paroxysmal AF. The average age of the participants was 60 years and none had been able to control their afib with antiarrhythmic drugs. During the study the researchers used drugs or intermittent atrial pacing to put the patients into afib while observing where the AF-initiating ectopic beats originated. They found that the initiating beats originated in the PV in 68% of cases. In 12% of cases, the initiating beats originated in an area other than the PV, and in the remaining 20% of cases the initiating beats occurred both in and outside the PV. Of the non-PV originated episodes, 40% started out at the superior vena cava (right atrium), 34% on the left atrial posterior free wall (LAPFW), and 15% at the crista terminalis (right atrium). The researchers found that female gender was a strong predictor of initiating beats originating at the superior vena cava, while left atrial enlargement (greater than 40 mm in diameter) was

a strong predictor of initiating beats originating on the back wall of the left atrium (LAPFW).

The researchers conclude that it is important to provoke ectopic beats from the superior vena cava (SVC) in women during the electrophysiologic study so that the SVC can be isolated if necessary during the ablation process. Similarly, it is important to ensure encirclement of initiating areas on the LAPFW in patients with left atrial enlargement. The patients underwent radiofrequency ablation. After a follow-up of 52 months, 67% of those with ectopic beats originating solely in the PV remained afib-free (without the use of antiarrhythmics), 76% of patients with the initiating beats located outside the PV also remained afib-free, as did 60% of those with the initiating beats originating both inside and outside the pulmonary veins.

Shih-Huang Lee, et al. Predictors of non-pulmonary vein ectopic beats initiating paroxysmal atrial fibrillation. Journal of the American College of Cardiology, *Vol. 46, September 20, 2005, pp. 1054-59*

Editor's comment: There is also evidence that episodes lasting longer than 24 hours may predict the presence of originating sources outside the pulmonary veins, most likely on the back wall of the left atrium.

Chronic AF affects DNA

South Korean researchers have analyzed the gene expression in atrial tissue taken from patients with permanent atrial fibrillation of more than 6 months duration and compared it to tissue from patients without AF. They found consistent, significant differences in 66 genes with 31 being down-regulated and 35 being up-regulated more than 2-fold. The overall result of the changes in gene expression was an increase in apoptosis (self-destruction [suicide] of individual cells to avoid a threat to the survival of the organism as a whole) in the cardiac myocytes (heart muscle cells) of patients with permanent AF. The researchers speculate that drugs, which help prevent the unfavourable changes in gene expression, may be helpful in the treatment of permanent afib.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1163-256, p. 122A

Risk Factors & Triggers

Pulmonary vein diameter and afib risk

NEW YORK, NY. Researchers at the Columbia University College of Physicians and Surgeons report that an enlarged pulmonary vein diameter is associated with an increased risk of atrial fibrillation. Their study involved 100 AF patients (42% with lone AF) who were scheduled to undergo a PVI and 24 age- and sex-matched controls with no AF. All participants underwent spiral-computed tomography prior to the PVI procedure. The researchers drew the following conclusions from their data:

- The average ostial pulmonary vein (PV) diameter was significantly larger in AF patients than in controls (150 mm versus 120 mm) and all four veins were similarly affected.
- An enlarged left atrium was associated with increased PV diameters.
- PV diameters in patients and controls with hypertension were larger than in patients and controls without hypertension.
- Patients with persistent AF had larger PV diameters than did patients with paroxysmal (intermittent) AF.

The researchers speculate that impaired left ventricular diastolic function is associated with a stretch-induced PV arrhythmia mechanism. They also suggest that the finding that persistent afibbers have larger vein diameters than paroxysmal afibbers would tend to support a progressive nature of PV enlargement and associated afib severity. They do acknowledge though that AF is a multifactorial disease and not solely associated with enlarged veins.

Dr. John McAnulty of the Legacy Heart Institute in Portland, Oregon speculates that the measurement of PV diameters may ultimately prove useful in deciding whether a specific AF patient is more likely to benefit from medication, an ablation or implantation of an ICD.

Herweg, B, et al. Hypertension and hypertensive heart disease are associated with increased ostial pulmonary vein diameter. Journal of Cardiovascular Electrophysiology, *Vol. 16, January 2005, pp. 2-5*

McAnulty, J. Probing for mechanism of atrial fibrillation: pulmonary vein ostia. Journal of Cardiovascular Electrophysiology, *Vol. 16, January 2005, p. 6*

LAF linked to left atrial enlargement

STANFORD, CALIFORNIA. Several studies have concluded that an enlarged left atrium (as determined by conventional Doppler echocardiography) is associated with an increased risk of developing atrial fibrillation (AF). Most of these studies, however, included older patients, patients who were in afib during the examination, and patients who had experienced afib for a long time. It is also known that afib itself tends to lead to atrial enlargement.

Researchers at Stanford University have now investigated left atrium size in 15 young lone afibbers (mean age of 39 years, range of 22-50 years) with no history of diabetes, hypertension, hyperthyroidism, previous heart attack or structural heart disease. All had a left atrial diameter less than 40 mm when measured in the conventional anteroposterior dimension. The 15 study participants and 15 age-matched controls all had two-dimensional and Doppler echocardiographic studies done while in sinus rhythm. There was no difference in left atrial size when considering only the anteroposterior dimension (average of 35 mm in both groups). However, when measurements were carried out in the inferosuperior dimension (vertical dimension between tricuspid/mitral valve openings and the top of the atrium – excluding pulmonary veins) a significant difference was found between lone afibbers and controls (average of 52.9 versus 46.7 mm). Significant differences were also found in the mediolateral dimension (width) of the left atrium (45.2 versus 39.7 mm) and area (19 versus 15.2 square centimeters). No significant differences were seen in right atrial dimensions, but the volume of the left atrium in afibbers was significantly greater than in controls (average 79.7 mL versus 68.2 mL).

The researchers conclude that left atrium volume is significantly greater in young lone afibbers than in age-matched controls and suggest that this, along with pulmonary vein foci, may be important in the initiation and maintenance of lone paroxysmal AF.

Phang, RS, et al. Echocardiographic evidence of left atrial abnormality in young patients with lone paroxysmal atrial fibrillation. American Journal of Cardiology, *Vol. 94, August 15, 2004, pp. 511-13*

Obesity linked to AF epidemic

FRAMINGHAM, MASSACHUSETTS. Both obesity and atrial fibrillation are reaching epidemic proportions in the US. Nearly 65% of the population is overweight (BMI greater than 25) and 31% are obese (BMI greater than or equal to 30). About 2.5 million Americans have AF – a number expected to double over the next 4 decades.

Researchers involved with the Framingham Heart Study now suggest a strong link between obesity and the risk of developing AF. Their study involved 2384 men (mean age of 56 years) and 2898 women (mean age of 58 years). Seventeen per cent of the men and 16% of the women were obese at the beginning of the study.

During a mean follow-up period of 13.7 years, 10% (292 men and 234 women) developed atrial fibrillation. Compared to normal weight individuals (BMI less than 25) obese study participants had an average 50% greater risk of developing AF. This increased risk remained after adjusting for gender, age, and the presence of hypertension. Every one-unit increment in BMI (over 25) was associated with a 4% increase in risk. Detailed examination of study results revealed that the increased AF risk associated with obesity was almost entirely attributable to the fact that overweight and obese individuals tend to have larger than normal left atrial diameters (3.8 cm for normal weight men, 4.1 cm for overweight men, and 4.4 cm for obese men). The corresponding numbers for women were 3.5, 3.8 and 4.0 respectively. Obese persons also have a higher incidence of sleep apnea, a condition that has also been linked to an increased risk of AF. The authors note that weight reduction has been linked to a decrease in left atrial diameter and suggest that efforts to contain the obesity epidemic may also reduce the incidence of AF.

Wang, TJ, et al. Obesity and the risk of new-onset atrial fibrillation. Journal of the American Medical Association, *Vol. 292, November 24, 2004, pp. 2471-77*
Coromilas, J. Obesity and atrial fibrillation: is one epidemic feeding the other? Journal of the American Medical Association, *Vol. 292, November 24, 2004, pp. 2519-20*

Editor's comment: Our initial LAF survey did not find any indication that lone afibbers tended to be more overweight or obese than the general population.

Caffeine and atrial fibrillation

AARHUS, DENMARK. Although there is some evidence that very high intakes of caffeine can produce cardiac arrhythmias, it is not known whether normal consumption increases the risk of developing AF or flutter. The Danish Diet, Cancer, and Health Study is designed to investigate the association between diet and cancer, but the data generated in the study are also being used to determine possible links between diet and other disorders.

Researchers at Aarhus University Hospital recently released the results of their investigation of a possible link between the consumption of caffeine, mainly in the form of coffee, and the risk of developing atrial fibrillation or flutter. A total of 22,533 men and 25,416 women between the ages of 50 and 64 years were followed for an average 5.7 years. During this time 373 of the men (1.7%) and 182 of the women (0.7%) developed AF or

flutter. The researchers found no correlation between caffeine intake and the risk of developing AF or flutter. Participants with the lowest intake of caffeine (average 248 mg/day or about 2-3 cups of coffee a day) were no more likely to develop AF or flutter than were participants who consumed an average of 997 mg/day corresponding to about 10 cups of coffee a day. The researchers do point out that coffee intake in Denmark is generally high and that it is possible that someone with no caffeine intake would have a lower risk of developing AF or flutter.

Frost, L and Vestergaard, P. Caffeine and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. American Journal of Clinical Nutrition, *Vol. 81, 2005, pp. 578-82*

Katan, M and Schouten, E. Caffeine and arrhythmia. American Journal of Clinical Nutrition, *Vol. 81, 2005, pp. 539-40 (editorial)*

Editor's comment: Several of our surveys have shown caffeine to be a strong trigger for afib episodes. Almost a third of adrenergic afibbers listed caffeine as a trigger as did 22% of vagal, and 20% of mixed afibbers. So, while caffeine may not be responsible for the development of afib, it certainly can be involved in triggering subsequent episodes.

Helicobacter pylori and atrial fibrillation

MILAN, ITALY. Both myocarditis (inflammation of the heart lining) and atherosclerosis have been linked to a bacterial infection involving *Chlamydia pneumonaie*. There is also some evidence that the *Helicobacter pylori* bacterium may play a role in the formation of atherosclerotic lesions. Italian researchers now report that *H. pylori* may play a role in atrial fibrillation as well. The researchers had noted that many of their afib patients appeared to have gastric problems also. Based on this finding they instituted, as standard practice, that all newly admitted afib patients be tested for *H. pylori*. This, in turn, spawned a pilot study in which 59 consecutive patients with paroxysmal or persistent afib and no structural heart disease were tested for blood levels of C-reactive protein (CRP), a marker of inflammation and IgG antibodies to *H. pylori*. Their results were compared to those obtained by testing 45 healthy volunteers without heart disease, diabetes, or acute or chronic infections.

The researchers found that the average IgG level in the afib group was 97.2 IU/mL as compared to 5.3 IU/mL in the control group. A value higher than 20 IU/mL is usually considered indicative of a *H. pylori* infection (seropostive). The CRP levels among afibbers were also significantly higher with an average value for afibbers of 8 mg/L as compared to 1 mg/L in the control group. Within the group of afibbers persistent afibbers had higher IgG levels than paroxysmal afibbers (100 IU/mL versus 60.2 IU/mL) and higher CRP levels as well (9 mg/L versus 7 mg/L) indicating a more serious *H. pylori* infection.

The researchers speculate that the H. pylori bacterium may adversely affect the Na^+/K^+-ATPase pump responsible for maintaining homeostatic balance in individual heart cells. A disturbance of this balance may trigger afib by creating abnormal automaticity or triggered activity that causes a depolarization delay, which can result in very rapid premature atrial contractions (PACs) – a forerunner for a full-blown afib episode.
Montenero, AS, et al. Helicobacter pylori and atrial fibrillation: a possible pathogenic link. Heart *Vol. 91, July 2005, pp. 960-61*

Editor's comment: The finding that a *H. pylori* infection could be associated with atrial fibrillation is indeed an exciting one and should be confirmed in larger trials. What is, unfortunately, less clear is what can be done about eradicating the bacterium if indeed it does reside in the heart lining. *H.pylori* can be eradicated successfully in the stomach through a 2- or 3-week course of an antibiotic, a proton pump inhibitor (omeprazole), and bismuth subsalicylate. The *H. pylori* bacterium "hides" in the folds of the stomach lining and it is believed that the bismuth subsalicylate is essential for "opening up" the access to the bacteria so that the antibiotic can do its work. Presumably, the mechanism for eradicating *H. pylori* in the heart lining would be quite different and it is not at all clear that the present drug regimen for *H. pylori* eradication would work for this.

Psychological factors in LAF

MODENA, ITALY. Major disasters have been associated with a 5-fold increase in sudden cardiac deaths caused by ventricular arrhythmias. There is also evidence that everyday stress, such as driving and public speaking, can produce ventricular ectopy (PVCs) and runs of ventricular tachycardia. Researchers at the University of Modena now report that stress also affects the spontaneous conversion and recurrence of lone atrial fibrillation.

Their study included 116 patients who had experienced a first afib episode. The average age of the patients was 54 years and 30% of them were female. The afib group was compared with an age- and gender-matched group of volunteers who did not have afib. None of the patients were on beta-blockers, calcium channel blockers or antiarrhythmics.

The researchers found a significantly higher proportion of type A individuals among the afibbers than among the controls (20% versus 9%). High scorers on the type A scale were classified as hard-driving, fast-moving, and work-oriented individuals who frequently became impatient, irritable and annoyed. Recent exposure to acute life stress (death of a spouse, divorce, jail term, retirement, Christmas, etc) was found to be

significantly more common among afibbers than among controls. Afibbers were also more likely to be high consumers of espresso coffee than were controls. A body mass index (BMI) greater than 27 was also more prevalent among afibbers than among controls. No differences in alcohol consumption, income, education, and smoking were observed between the two groups.

Spontaneous conversion of afib to normal sinus rhythm within 48 hours was observed in 72 patients (63%). Afibbers with a high BMI were less likely to convert spontaneously (they also tended to have enlarged atria) as were afibbers who had a high coffee consumption. On the other hand, afibbers who had a high score on the acute life stress scale, or exhibited distinct type A personality traits were more likely to convert spontaneously than were afibbers without these characteristics.

Recurrence of afib within 3 months of conversion was significantly less common in patients whose initial episode was related to stress than in those who had scored low on the acute life stress scale. None of the other variables affected the risk of recurrence.

The researchers speculate that the positive association between high scores on the acute life stress and type A personality scales and the likelihood of spontaneous conversion is probably due to the fact that in these types of afibbers the episode was induced by an exaggerated cardiovascular reactivity (likely over-stimulation of the sympathetic nervous system) of relatively short duration.

Mattioli, AV, et al. The relationship between personality, socio-economic factors, acute life stress and the development, spontaneous conversion and recurrences of acute lone atrial fibrillation. **Europace**, *Vol. 7, May 2005, pp. 211-20*

Editor's comment: These findings are most interesting, but it would have been helpful and perhaps more illuminating if the investigators had distinguished between adrenergic, vagal and mixed afibbers in their study.

AF and alcohol consumption

COPENHAGEN, DENMARK. There is ample evidence that periodic heavy alcohol consumption (binge drinking) can trigger afib episodes. However, it is not clear whether regular alcohol consumption increases the risk of initiating AF as well. Danish researchers now report that heavy, regular alcohol consumption is indeed associated with an increased risk of initiating afib, while moderate or no alcohol consumption is not. Their study involved 7588 men (average age of 56 years) and 8827 women (average age of 57 years) enrolled in the Copenhagen City Heart Study begun in 1976. At enrolment all participants were free of coronary heart

disease and previous stroke, and none used heart or antihypertensive medications.

The participants were examined in 1976-78, 1981-83, 1991-94 and at that time completed questionnaires regarding their alcohol intake. During the follow-up period (until January 1, 2001) 891 participants were hospitalized with a first episode of AF, 68 were diagnosed during one of the follow-up investigations, and 112 were both diagnosed and hospitalized. The overall incidence of new AF was 1.16% per year. This compares to an incidence rate of 1.92% observed in an older population in the USA.

The researchers found no association between moderate drinking or no drinking and the risk of initiating afib. However, men who consumed 35 or more drinks per week had a 45% greater risk of developing AF than did men who consumed less than 34 drinks a week. No excess risk was seen for women who consumed up to 21 drinks a week, which was the highest intake observed in this group. A drink was defined as one bottle of beer, one glass of wine, or one unit of spirits.

The researchers estimate that 5% of all new cases of afib among men are attributable to heavy drinking (more than 35 drinks a week). Other observed major risk factors for AF development were the development of hypertension, coronary heart disease, or congestive heart failure during follow-up. They point out that studies investigating the association between alcohol consumption and recurrent afib severity are still needed.
Mukamal, KJ, et al. Alcohol consumption and risk of atrial fibrillation in men and women. Circulation*, Vol. 112, September 20, 2005, pp. 1736-42*

Diabetes and risk of AF

A very large study involving almost 850,000 American veterans has shown that patients with diabetes have a substantially increased risk of developing atrial fibrillation. The researchers found that the incidence of AF among diabetics was 14.9% as compared to 10.3% among a control group of veterans with hypertension but no diabetes. The incidence of atrial flutter was 4% and 2.5% respectively. Veterans with diabetes also had a 3 times higher risk of congestive heart failure and twice the risk of coronary artery disease.
ACC, 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1050-267, p. 97A

Prevention & Treatment with Antiarrhythmics

Safety of "on-demand" approach

CENTO, ITALY. The on-demand or "pill-in-the-pocket" approach is now used by many paroxysmal afibbers to quickly and effectively terminate afib episodes and return to normal sinus rhythm. This approach involves swallowing 450 mg of propafenone (Rythmol) or 200 mg of flecainide (Tambocor) with water within 5 minutes of the onset on an episode. The dosages are increased to 600 mg and 300 mg respectively for patients weighing more than 70 kg (154 lbs). It is recommended that patients rest (in a supine or sitting position) until palpitations have stopped or at least 4 hours have passed. The on-demand approach was originally tested in patients with supraventricular tachycardia (SVT) and its use among afibbers was first reported in 2002 in *Lone Atrial Fibrillation: Towards A Cure*.

A group of researchers from 8 Italian hospitals now report that the on-demand approach is safe and effective and that its use is associated with a very significant decrease in hospitalizations and visits to the ER. Their study involved 268 AF patients who had undergone chemical cardioversion in the hospital using either propafenone or flecainide. Two hundred and ten of these patients (average age of 59 years, 118 lone afibbers) were selected to participate in the study involving the on-demand approach at home. During a mean follow-up of 15 months, 165 patients experienced a total of 618 episodes. The majority (92%) was self-treated within about half an hour after the onset of symptoms and the treatment was successful in 94% of cases. The average time to conversion was 2 hours (113 minutes). Adverse events, mostly nausea and anxiety, were reported in 12 patients.

The effect of the use of the on-demand approach on health care resources was remarkable. Although there was no difference in the overall number of episodes experienced in the group before and after instituting this approach, there was a great difference in the use of ER facilities (45.6 visits/month before vs 4.9 visits/month after) and hospitalizations (15/month vs 1.6/month). The researchers caution that patients who do not convert within 6 hours should go to the ER.

Alboni, P, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. New England Journal of Medicine**,** *Vol. 351, December 2, 2004, pp. 2384-91*

Editor's comment: Some practicing cardiologists feel it is safe to repeat the initial dose if conversion is not achieved after 5 hours, but the applicability of this approach clearly needs to be firmly established between doctor and patient.

Amiodarone – less is safer

MONTREAL, CANADA. The prolonged use of some antiarrhythmic drugs such as sotalol (Betapace) and amiodarone (Cordarone) has been associated with the development of bradycardia (excessively slow heart rate) and the subsequent need for a pacemaker implantation. Researchers at McGill University now report that the risk of bradycardia development associated with amiodarone use is highly dependent on the initial loading dose as well as on the maintenance dose.

Their study involved 1340 patients with AF and a prior heart attack who were given a first prescription for amiodarone. The patients (63% male) were all over the age of 65 years with an actual average age of 76 years. They were followed from their first exposure to amiodarone to the first of pacemaker implantation, death or end of follow-up at March 31, 2001 (an average of 1.8 years). During the follow-up, 53 patients received a permanent pacemaker. The incidence of implantation was significantly greater (5.2% per person-year) during the first 90 days of amiodarone exposure. The incidence of implantation was found to be 3 times higher during the first 90 days for patients whose daily dosage exceeded 200 mg and, over the whole study period, patients taking more than 200 mg/day had twice the incidence of pacemaker implantation than did patients taking 200 mg/day or less.

It is common to use high concentrations of amiodarone (660-1000 mg/day) in an initial "loading phase" when amiodarone therapy is first begun. Based on their findings of an exceptionally high incidence of pacemaker implantation during the first 90 days, the researchers question the wisdom of this practice at least when it comes to atrial fibrillation. They suggest that patients with paroxysmal AF or rate-controlled permanent AF may be better served by loading and maintenance dosages of 200 mg/day or less. This would apply particularly to elderly patients with a previous heart attack.

Essebag, V, et al. Effect of amiodarone dose on the risk of permanent pacemaker insertion. PACE, *Vol. 27, November 2004, pp. 1519-25*

Editor's comment: Other researchers have found that the benefits of amiodarone can be attained at significantly reduced dosage levels if the drug is taken with meals. Amiodarone has many more potential adverse effects than the development of bradycardia, so this is definitely one area

where doctor and patient need to work closely together to establish the minimum effective dosage for the individual patient.

Propafenone proves superior to sotalol

HERAKLION, GREECE. Greek researchers have carried out a long-term study to determine the relative effectiveness of sotalol (Betapace) and propafenone (Rythmol) in maintaining normal sinus rhythm in patients with recurrent atrial fibrillation. Their study included 245 afibbers who were randomly assigned to receive 300 mg/day of sotalol (in two divided doses), 450 mg/day of propafenone (in 3 divided doses), or placebo. After 18 months 81% of the patients on sotalol had relapsed into AF or experienced severe side effects as compared to 52% in the propafenone group after 26 months. In the placebo group 88% had relapsed into afib after 11 months. After a follow-up of 30 months the number of study participants in sinus rhythm was 47% in the propafenone group, 25% in the sotalol group, and 17% in the placebo group. The researchers conclude that propafenone is superior to sotalol for maintenance of sinus rhythm over the long term. Sotalol, on the other hand, is only slightly more effective than placebo.

Kochiadakis, GE, et al. Sotalol versus propafenone for long-term maintenance of normal sinus rhythm in patients with recurrent symptomatic atrial fibrillation. American Journal of Cardiology, *Vol. 94, December 15, 2004, pp. 1563-66*

Conversion to atrial flutter – A blessing in disguise?

FORLI, ITALY. The treatment with certain antiarrhythmic drugs, notably propafenone, flecainide and amiodarone, can result in the conversion of AF to typical right atrial flutter (AFL). AFL episodes are probably at least as uncomfortable as AF episodes, but could the conversion from AF to AFL actually be a blessing in disguise? Italian researchers believe so. Their study involved 46 AF patients (the majority with hypertension) whose AF episodes had converted to AFL episodes during treatment with propafenone, flecainide or amiodarone, or in whom AFL had been induced during an electrophysiological study. All study participants underwent radiofrequency ablation for AFL and were then followed for 1-78 months while on the same drugs prescribed for them prior to the ablation. The researchers found that 50% of participants remained AF-free, while 33% experienced a very marked improvement in their symptoms. The degree of improvement, however, declined significantly during the observation period and, after 35 months, only 8% of the patients were in stable sinus rhythm. The researchers conclude that AFL ablation and continuation of antiarrhythmic drugs may be a worthwhile first step in eliminating or reducing AF episodes in patients whose AF converts to atrial flutter either spontaneously (during drug treatment) or during an EP study.

Bandini, A, et al. Atrial fibrillation recurrence after drug-induced typical atrial flutter ablation. Italian Heart Journal, *Vol. 6, July 2005, pp. 584-90*

Catanzariti, D and Vergara, G. Lessons from catheter ablation: how a proarrhythmic effect has become a therapeutic chance. The case of class IC/II drugs in atrial flutter. Italian Heart Journal, *Vol. 6, July 2005, pp. 591-94*

Magnesium sulfate for rate control in AF

ADELAIDE, AUSTRALIA. At least seven published clinical trials have concluded that infusions of magnesium sulfate are effective in reducing heart rate (ventricular response rate) in patients with supraventricular arrhythmias including atrial fibrillation.

Emergency department physicians at the Royal Adelaide Hospital have now put these findings into practice in a major evaluation. Their study included 199 patients between the ages of 60 and 80 years who were admitted with rapid AF (heart rate above 120 bpm, average of 142 bpm). The patients were randomly assigned to receive intravenous infusions of magnesium sulfate (102 patients) or placebo. The magnesium infusion consisted of 40 mEq (5 g, 20 mmol) of magnesium sulfate in 100 mL of a 5% dextrose solution. Half the solution was infused over a 20-minute period followed by the other half being infused over the following 2 hours. The placebo solution (5% dextrose) was infused in a similar manner. In addition to the magnesium infusion most patients also received a rate-reduction drug such as digoxin (79%), beta-blocker (10%), or verapamil (3%). NOTE: The reason for the predominant use of digoxin is that beta- and calcium channel blockers may cause complications in patients with poor left ventricular function. In most cases, emergency physicians do not know the underlying cardiac status of the patients, so they err on the side of caution by using digoxin, which is safe for patients with low left ventricular ejection fraction.

The authors of the study observed that 65% of the patients given magnesium sulfate experienced a reduction in heart rate to below 100 bpm, while only 34% of placebo patients did so. It was also noted that 27% of the magnesium-treated patients reverted spontaneously to sinus rhythm during the infusion, while only 12% of those in the placebo group did so.

Several adverse side effects were, however, observed during magnesium treatment. Five patients experienced hypotension (systolic blood pressure below 100 mm Hg), two experienced bradycardia, while six complained of a flushing sensation. The researchers conclude that an infusion of magnesium sulfate helps reduce heart rate and increases the likelihood of spontaneous conversion in patients with rapid afib. They caution that treating physicians should watch for hypotension and bradycardia.

Davey, MJ and Teubner, D. A randomized controlled trial of magnesium sulfate in addition to usual care, for rate control in atrial fibrillation. Annals of Emergency Medicine, *Vol. 45, April 2005, pp. 347-53*

Editor's comment: I am not aware of any trials where orally administered magnesium has proven successful in reducing heart rate or speeding conversion to normal sinus rhythm. It is certainly possible that it could, but the quantities to be ingested would be quite larger since 20 mEq of magnesium is equivalent to 480 mg of elemental Mg, or 6 grams of magnesium citrate. Taking this much magnesium orally over a relatively short period of time is likely to lead to a serious case of diarrhea and, due to the risk of hypotension and bradycardia, should not be attempted without medical supervision. Another approach to increasing magnesium stores fairly rapidly would be to take a hot bath with Epsom salt (magnesium sulfate), but again, I am not aware of any evidence indicating that this may be effective.

Prevention & Treatment with Other Drugs

Treating hypertension helps prevent atrial fibrillation

GENEVA, SWITZERLAND. There is increasing evidence that essential hypertension (high blood pressure) is an important risk factor in the development of atrial fibrillation. What is less clear is whether treating the hypertension lessens the risk of afib. Swiss researchers now report that appropriate treatment does indeed reduce the risk and that the risk reduction is independent of the type of blood pressure reducing agent used. The study involved a group of 597 patients who, after having been diagnosed with hypertension (systolic blood pressure equal to or greater than 140 mm Hg and/or diastolic pressure equal to or greater than 90 mm Hg), were placed on antihypertensive therapy using ACE inhibitors (46%), angiotensin II receptor blockers (23%), calcium channel blockers (52%), and beta-blockers (21%) either alone or in combination.

After a 7-year follow-up the researchers found that the risk of developing atrial fibrillation decreased by 24% with a 12 mm Hg drop in systolic pressure after adjusting for age, gender, body mass, and pulse pressure (systolic blood pressure minus diastolic pressure). All blood pressure measurements were averages of 24-hour ambulatory measurements. Those of the patients who did develop atrial fibrillation were slightly older than those who did not, were more likely to be men, and to be overweight or obese. A decrease in pulse pressure also correlated with a decrease in AF risk, but this trend was not statistically significant. There was no indication that one class of blood pressure medications was superior in preventing the development of AF. The researchers conclude that an increased systolic pressure and pulse pressure may promote the onset of atrial fibrillation by modification of left ventricular diastolic function.

Ciaroni, S, et al. Prognostic value of 24-hour ambulatory blood pressure measurement for the onset of atrial fibrillation in treated patients with essential hypertension. American Journal of Cardiology, *Vol. 94, December 15, 2004, pp. 1566-69*

Angiotensin receptor blockers may increase risk of heart attack

TORONTO, CANADA. Angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin II type 1 receptor blockers (ARBs) are both widely used to control high blood pressure. Among the more common ACE inhibitors are enalapril (Vasotec), lisinopril (Zestril), ramipril (Altace),

and captopril (Capoten). The most popular ARBs are valsartan (Diovan), candesartan (Atacand), and irbesartan (Avapro). Both ACE inhibitors and ARBs inhibit the formation of aldosterone and are used interchangeably in the management of hypertension. There is also some evidence that both classes of drugs may be useful in preventing atrial fibrillation.

Cardiologists at two Toronto hospitals now point out that, while ACE inhibitors and ARBs may be equally effective in treating hypertension, their adverse effects are by no means equal. A clinical trial comparing the calcium-channel blocker amlodipine with valsartan found that patients in the valsartan group had a 13% higher incidence of stroke and a 19% higher incidence of heart attack. The CHARM trial showed that patients treated with candesartan had a 36% higher incidence of heart attack than did patients taking a placebo.

A study of diabetic patients with impaired kidney function found that irbesartan therapy was associated with a 36% increase in non-fatal myocardial infarction (heart attack) when compared to patients treated with amlodipine. In stark contrast to these findings are the findings regarding ACE inhibitors, which consistently produce a 20% reduction in the incidence of heart attack in patients with hypertension, atherosclerosis, diabetes, and renal insufficiency.

The Toronto cardiologists conclude that the potential adverse effects of ARBs are significantly greater than those of ACE inhibitors and that patients should be informed of this fact when discussing blood pressure lowering options with their physician.

Verma, S and Strauss, M. Angiotensin receptor blockers and myocardial infarction. British Medical Journal, *Vol. 329, November 27, 2004, pp. 1248-49*

Losartan helps prevent atrial fibrillation

COPENHAGEN, DENMARK. The risk of developing atrial fibrillation is increased in patients with uncontrolled high blood pressure (hypertension). A team of Scandinavian and US researchers has just released the results of a study aimed at determining whether blood pressure reduction treatment with angiotensin II receptor blockers (ARBs) is superior to treatment with beta-blockers in preventing AF.

Their study involved 8851 patients with hypertension but no AF at baseline. The patients were randomized to receive losartan (an angiotensin II receptor blocker) or atenolol (a beta-blocker) plus a diuretic, if necessary, as required to reach a target blood pressure below 140/90 mm Hg. During an average 4.8 years of follow-up, 150 patients (0.7%/year) in the losartan group developed AF as compared to 221

patients (1.1%/year) in the atenolol group; a relative risk reduction of 33% in the losartan group as compared to the atenolol group.

The incidence of stroke in the group that developed AF was 3 times higher than in the group that did not (3.2%/year versus 1.0%/year) and the incidence of heart failure was 5 times higher among AF patients than among patients who remained in sinus rhythm (2.7%/year versus 0.5%/year). The most important risk factor for the development of AF was increasing age, followed by male gender (56% increase in risk compared to women), and a high systolic blood pressure.

AF patients treated with losartan had half the incidence of stroke as compared to atenolol-treated patients, but there was no difference in overall cardiac mortality. However, atenolol-treated AF patients had fewer hospitalizations for heart failure and a lower incidence of sudden cardiac deaths. The researchers conclude that losartan (Cozaar) is superior to atenolol (Tenormin) in preventing the development of AF in patients with hypertension and that losartan is also superior when it comes to stroke prevention among hypertensive AF patients. NOTE: This study was funded by Merck and Co., the manufacturer of losartan.

Wachtell, K, et al. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol. Journal of the American College of Cardiology, *Vol. 45, March 1, 2005, pp. 712-19*

Bourassa, MG. Angiotensin II inhibition and prevention of atrial fibrillation and stroke. Journal of the American College of Cardiology, *Vol. 45, March 1, 2005, pp.720-21 (editorial)*

Alternative Means of Prevention

Fish oils and atrial fibrillation

AARHUS, DENMARK. There is impressive evidence that fish oils (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) can materially reduce the risk of sudden cardiac death (cardiac arrest). Researchers at the University of Washington found that men and women who consumed fatty fish just once a week reduced their risk of cardiac arrest by 50%. They believe that fatty fish consumption increases the levels of EPA and DHA in the membranes of red blood cells, which in turn, reduces platelet aggregation and the risk of fatal ventricular arrhythmias. Other researchers have confirmed the protective effect of fish oils against ventricular fibrillation, but very few, if any, studies have investigated the association between fish/fish oil intake and the development of atrial fibrillation.

A group of Danish researchers recently set out to fill in this gap in our knowledge. Their study included 22,528 men and 25,421 women (average age of 56 years) who were free of endocrine and cardiovascular diseases at baseline. All participants completed a detailed semi-quantitative food- and drink-frequency questionnaire and were then followed for an average of 5.7 years. At the end of the follow-up period 374 men (1.7%) and 182 women (0.7%) had been diagnosed with either atrial fibrillation or atrial flutter. About 10% of all participants were being treated for hypertension. Somewhat surprisingly, the researchers found that participants with a high consumption of fatty fish (herring, mackerel, sardines, trout, and salmon) had a significantly higher incidence of new-onset atrial fibrillation than did participants who rarely or never ate oily fish. After adjusting for age, gender, height, BMI, smoking, alcohol consumption, total daily energy intake, systolic blood pressure, treatment for hypertension, cholesterol level, and level of education, the researchers concluded that participants whose daily fish oil intake averaged 1290 mg had a 34% greater risk of developing AF than did those whose intake averaged only 160 mg/day. The difference was statistically significant ($p=0.006$). The researchers point out that the lack of an observed beneficial effect could have been because the consumption of fish oil was insufficient to prevent arrhythmias. They also say, “We cannot exclude the possibilities that fish oil may prevent the development of atrial fibrillation in patients with symptomatic heart disease or that fish oil may prevent relapses of atrial fibrillation in patients with paroxysmal atrial fibrillation.”

Finally, they point out that they did not collect information regarding the use of fish oil supplements and also emphasize that they do not know whether fish oil would have a protective effect against the development of AF in populations with a low intake of fatty fish (such as the United States). Their overall conclusion was that, "Consumption of omega-3 fatty acids from fish is not associated with a reduction in the risk of developing atrial fibrillation or flutter."

Frost, L and Vestergaard, P. n-3 fatty acids consumed from fish and risk of atrial fibrillation or flutter: the Danish Diet, Cancer, and Health Study. American Journal of Clinical Nutrition, *Vol. 81, January 2005, pp. 5-54*

Editor's comment: The conclusions of the Danish study are fully in line with the results of the two LAF surveys, which investigated the association between afib severity and fish oil intake. None of our surveys have ever found that a high fish oil intake is associated with fewer or shorter episodes. This, as pointed out by the Danish researchers, could be due to the fact that the fish oil intake was not high enough to provide a benefit. However, this would seem unlikely since the highest intakes were well above those required to provide excellent protection against ventricular fibrillation. The finding that heavy fish consumers have a statistically significant 34% greater risk of developing atrial fibrillation or flutter is worth noting. It is possible that this could be due to the higher mercury intake associated with higher fish consumption. Several studies have shown that people with a high consumption of certain fish have higher mercury levels in their blood and toenails. The lesson here is that the safest way to obtain a high intake of EPA and DHA is through the consumption of a high quality, molecular distilled fish oil supplement. In conclusion then, even though there may be no scientific evidence that fish oils can prevent the development of AF, there are still numerous reasons for ensuring an adequate intake (1-2 grams/day). The evidence that they help prevent cardiac arrest, reduce triglyceride levels, combat inflammation, and help prevent stroke and heart attack makes fish oils a must supplement for all, whether an afibber or not.

'Western diet' may have numerous consequences for health

FORT COLLINS, COLORADO. Ten thousand years ago the agricultural revolution began a dramatic change in the human diet that continues to the present day. Estimates suggest that over 70% of dietary calorie intake in Western populations comes from foods which our Paleolithic ancestors rarely or never ate.

A group of experts from Colorado State University have assembled evidence to support their theory that this dietary change has produced many of the so-called diseases of civilization, such as cardiovascular

disease, cancer, diabetes, osteoporosis, arthritis, and gastrointestinal disease. In a recent commentary they propose that changes in food production 10,000 years ago occurred too recently for the human genome (genetic code) to adjust. Instead, it is still adapted to the environment of our ancestors, as 10,000 years is short on an evolutionary time scale. The authors explain that intakes of dairy products, cereals, refined sugars, vegetable oils, alcohol, fatty meat and salt have risen significantly, and highlight seven main nutritional characteristics of our diet which have altered drastically. Intake of foods with a high glycemic load (blood glucose raising potential) has increased, raising insulin levels and increasing rates of the metabolic syndrome. Fatty acid intake has altered, with an excess of saturated and trans fats, raising cholesterol and contributing to cardiovascular disease.

Macronutrient composition has also shifted, as evidence suggests we consume less protein and more carbohydrate than our ancestors. This could explain some of the increase in cardiovascular disease, say the authors. Micronutrient density has also changed, with a greater consumption of refined grains containing fewer vitamins and minerals, producing deficiencies and subsequent illness. The acid-base balance of the 'Western' diet has altered in favor of acid, which may have a damaging effect on the kidneys and other organs. A huge rise in sodium through salt intake has modified the sodium-potassium ratio, which is linked to a wide range of chronic illnesses, the authors believe. Finally, fiber content has dropped to the extent that it could play a role in many gastrointestinal and circulatory problems.

The authors conclude that our genome clashes with our modern lifestyle, and together with genetic and environmental elements, virtually all of the 'diseases of civilization' have multifactorial dietary causes.
Cordain, L et al. Origins and evolution of the Western diet: health implications for the 21st century. American Journal of Clinical Nutrition*, Vol. 81, February 2005, pp. 341-354*

Editor's comment: Several afibbers have found that adhering to a diet similar to that of our ancestors (the Paleo diet) is effective in eliminating or reducing the incidence of afib episodes.

Fish oils help prevent AF after bypass surgery

ROME, ITALY. Atrial fibrillation is a common complication of coronary artery bypass graft surgery. Treatment with beta-blockers, sotalol or amiodarone can reduce the risk of AF development somewhat, but these drugs have several undesirable side effects.

Italian researchers now report that fish oil supplementation is highly effective in preventing post-operative atrial fibrillation. Their randomized clinical trial involved 160 patients (136 men and 24 women) scheduled for elective bypass surgery. The average age of the patients was 66 years and one of them had a previous history of AF. Half the patients were randomized to receive 2 grams/day of ethyl esters of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) for at least 5 days prior to their operation and for the remainder of their hospital stay. The other half just received usual post-operative care.

All patients underwent continuous rhythm monitoring for the first 4 to 5 days after surgery. During this monitoring period, 27 patients in the control group (33%) experienced afib episodes lasting an average of 24 hours. In contrast, only 12 patients in the fish oil group (15%) experienced episodes and they lasted an average of only 15 hours. Non-fatal post-operative complications occurred in 7 patients in the control group and in 5 patients in the fish oil group; 2 patients died after the operation in the control group versus 1 patient in the fish oil group.

The researchers speculate that the beneficial effects of fish oil are associated with its documented ability to reduce inflammation as well as with its direct effect on cardiac myocytes (muscle cells), specifically in regard to resting membrane potential and an increase in phase 4 refractory period. They conclude that fish oil supplementation can safely be administered to all patients undergoing bypass surgery and that it is at least as effective as medication with beta-blockers, sotalol or amiodarone.
Calo, L, et al. N-3 fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery. Journal of the American College of Cardiology, *Vol. 45, May 17, 2005, pp. 1723-28*

Editor's comment: The findings of the Italian researchers support those of several afibbers who have found fish oils beneficial in dealing with their afib. I suspect fish oils would be most effective if inflammation is the underlying cause of the afib and prior to extensive remodelling. Fish oils have also been found effective in the prevention of ischemic stroke and, for this reason alone, should be part of every afibber's supplementation program.

Ablation - Procedures

Haissaguerre's method explained

BORDEAUX, FRANCE. In 1998 Dr. Michel Haissaguerre and colleagues at the Hopital Cardiologique du Haut-Leveque in Bordeaux reported that 94% of the points (foci) triggering paroxysmal atrial fibrillation were to be found inside the pulmonary veins (about 2-4 cm from where the veins exit into the left atrium)[1]. This discovery led to the techniques of pulmonary vein ablation (ablation of foci inside the vein), pulmonary vein isolation (isolation of the veins from the atrium through the placement of ring-shaped lesions around each vein), and more recently, circumferential pulmonary vein ablation (Pappone method) where ablation lines are drawn so as to encircle the left pulmonary veins within one ring of scar tissue and the right veins with a separate ring – the two rings are connected with a line on the back wall of the left atrium.

Since 1998 Dr. Haissaguerre and his team have continually refined their pulmonary vein isolation (PVI) procedure and have now performed several thousand procedures on patients with paroxysmal, persistent or permanent atrial fibrillation. Dr. Haissaguerre recently outlined the details of his procedure in an article published in the *Journal of Cardiovascular Electrophysiology*. Following are the highlights:

- Patients are considered for ablation if they have suffered frequent afib episodes for more than one month and have proven resistant to at least two class I (propafenone, flecainide, disopyramide) or class II (amiodarone, sotalol, dofetilide) antiarrhythmics. Patients are accepted for treatment whether their afib is paroxysmal, persistent or permanent and are not excluded based on the presence of structural heart disease, left ventricular dysfunction, enlarged left atrium, prior stroke or advanced age.

- All antiarrhythmic drugs are discontinued at least 5 half-lives prior to the ablation except for amiodarone which must be discontinued 3 months prior to the procedure. All patients are anticoagulated to an INR of between 2 and 3 for at least a month prior to the procedure and a check for left atrial thrombi (blood clots) is performed via transesophageal echocardiography (TEE) in the week prior to ablation. The oral anticoagulation is replaced with heparin 48 hours before

and all anticoagulation is withdrawn 6 hours before the procedure.

- The first step in the procedure, following appropriate sedation, involves the insertion of three catheters through sheaths inserted in the right femoral vein. A quadripolar steerable catheter is placed in the coronary sinus, a circumferential mapping (Lasso) catheter and a 4-mm-tip externally irrigated ablation catheter (Celsius Thermocool) are advanced through the septum into the left atrium. Different navigation systems such as the LocaLisa, NavX and CARTO systems are used to help in navigation and reduce fluoroscopy exposure.

- Once the left atrium, specifically the area around the pulmonary veins, has been mapped the ablation catheter is used to create rings of lesions around each pulmonary vein outlet usually at least 1 cm from the edge so as to avoid pulmonary stenosis. The RF generator is limited to deliver a maximum of 30-35 W when ablating outside the veins and the maximum allowable temperature is 50^{o}C. Ablation is also performed at the cavotricuspid isthmus (in the right atrium) and a lesion line is drawn between the left inferior pulmonary vein and the neck of the mitral valve in cases where simple PVI and cavotricuspid ablation do not prevent atrial fibrillation from recurring after pacing.

- In a recent series of 368 patients, the total procedural time for PVI and cavotricuspid ablation was about 70 minutes, of which about 44 minutes involved fluoroscopy exposure and 35 minutes involved the application of RF energy.

- The overall success rate for the initial ablation (no afib, no drugs) was 69% for paroxysmal afibbers undergoing just PVI and cavotricuspid ablation and 87% for patients having the added mitral isthmus ablation. The procedural time with the added mitral isthmus ablation was about twice that of the basic procedure.

- Severe symptomatic pulmonary vein stenosis (more than 70% narrowing) has been observed in 0.2% of over 2000 patients. No deaths or strokes were reported.

Hocini, M, et al. Techniques for curative treatment of atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 15, December 2004, pp. 1467-71*

Editor's comment: I can highly recommend this article to anyone contemplating a RF ablation. Dr. Haissaguerre's original 1998 paper also provides fascinating insights into the original research leading to today's PVI procedures.

[1] Haissaguerre, M, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. New England Journal of Medicine, Vol. 339, September 3, 1998, pp. 659-66

Natale's method explained

CLEVELAND, OHIO. Dr. Andrea Natale and his team at the Cleveland Clinic Foundation have, by now, performed several thousand radiofrequency (RF) ablations with the purpose of curing atrial fibrillation. Their technique has evolved rapidly over the past few years and is now producing impressive results with very few adverse effects. Dr. Natale recently outlined his latest pulmonary vein isolation procedure in an article published in the *Journal of Cardiovascular Electrophysiology*. Here are the highlights:

- Patients are considered for pulmonary vein isolation or, more specifically, pulmonary vein antrum isolation (PVAI) if they have symptomatic atrial fibrillation and have not responded to at least one antiarrhythmic drug. Patients are accepted regardless of whether AF is of the paroxysmal, persistent or permanent variety and advanced age, enlarged left atrium or low left ventricular ejection fraction are not causes for exclusion.

- All antiarrhythmic drugs are withdrawn at least 5 days prior to the procedure except in the case of amiodarone which must be discontinued at least 4 months before, because it interferes with the accuracy of mapping. All patients are anticoagulated with warfarin to an INR of 2-3 for 6 to 8 weeks prior to the procedure. More recently, an INR range of 2.0-2.5 has been targeted with no significant complications. Warfarin is stopped 2 days before the procedure.

- All patients have a 12-lead ECG, 24-hour Holter monitoring, and an echocardiogram (transthoracic) prior to the procedure. Some patients also have a CT scan of the left atrium to determine the anatomy of the pulmonary veins, but this is not mandatory. Patients who are in AF the day before undergo transesophageal echocardiography (TEE) to ensure the absence of a blood clot (thrombus) in the left atrial

appendage. If a clot is found, the procedure is postponed for 3-4 weeks during which time anticoagulation is resumed.

- Heparin is injected before the procedure and as required during to maintain an activated clotting time of 350-400 seconds. After the procedure, patients are again anticoagulated with warfarin for at least 4 months (twice the usual dose is given for the 3 days immediately following the procedure).

- After appropriate sedation, 4 catheters are placed in the heart. One (a 14-pole, non-deflectable recording catheter) is inserted through the right internal jugular vein and placed in the coronary sinus; one (a 64-element phased-array ultrasound catheter) is inserted through the left femoral vein and is positioned in the middle of the right atrium; one (a 10-pole Lasso mapping catheter) is inserted through the right femoral vein and advanced through the septum into the left atrium. The fourth and last catheter (an 8-mm-tip ablation catheter) is inserted through the right femoral vein and advanced through the septum into the left atrium.

- Once all catheters are in place the mapping to establish electrically active areas (PV potentials) in the pulmonary veins using the 10-pole Lasso catheter begins. Once an active area has been located its pathway to the left atrium is ablated guided by the 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. The mapping and ablation can be done during sinus rhythm, atrial fibrillation or artificial pacing. RF energy is set at 30 W and 55^{o}C and is increased by 5 W every 5 seconds until satisfactory lesion formation is obtained or microbubbles (a sign of overheating) are observed on the ICE monitor.

- All four pulmonary veins as well as the superior vena cava (in the right atrium) are isolated during the procedure. When isolation is deemed complete another round of Lasso catheter mapping is performed in order to ensure that no PV potentials have been missed.

- The procedure is deemed a success if there are no further afib episodes and no antiarrhythmic drugs required beyond the first 2 months after the procedure. During the 2 months immediately following, afib episodes are common while the

heart heals. Patients with an original diagnosis of persistent or permanent AF are placed on sotalol (Betapace) or dofetilide (Tikosyn) for the 2 months immediately following the procedure. The current success rate of the initial procedure is about 80% with higher rates in young, paroxysmal afibbers. A second (touch-up) procedure brings the final success rate to 90-94%. The success rate among afibbers with previous heart surgery or an impaired ejection fraction is somewhat lower at about 73%.

- Patient follow-up involves 24-hour Holter monitoring on the day following the procedure as well as 3, 6 and 12 months after. An event monitor is used for the first 3 months after the procedure and a contrast-enhanced multi-slice CT scan of the left atrium is performed 3 months after to check for stenosis.

- The rate of moderate-to-severe stenosis has been 0.25% for the last 400 cases, the rate of thromboembolic complications 0.8%, and the rate of cardiac tamponade (penetration of the heart wall) 0.5%. No cases of atrial-esophageal fistula have occurred.

Verma, A, et al. Pulmonary vein antrum isolation: intracardiac echocardiography-guided technique. Journal of Cardiovascular Electrophysiology, *Vol. 15, November 2004, pp. 1335-40*

Editor's comment: An excellent description of the PVI procedure currently used at the Cleveland Clinic can be found at www.clevelandclinic.org/heartcenter/pub/atrial_fibrillation/pulmonaryvein_ablation.htm

US test run of cryoablation

DES MOINES, IOWA. Cryoablation, that is, ablation using a catheter cooled with liquid nitrogen rather than one heated with radiofrequency energy, is fairly well established in certain centers in Europe, but has had a slow start in the US. Despite the fact that, CryoCor Inc., the developer of the nitrogen-cooled catheter, is located in San Diego.

Now electrophysiologists from 6 American cardiac centers report on their experience with the procedure. Their trials involved 32 afibbers (75% men, average age of 57 years [range of 32-73 years]). All but one of the patients had paroxysmal afib; the remaining patient had the persistent variety. Afib episodes were documented on event recorders for 1 month prior to the procedure and 6 months after. The cryoablation procedure was immediately successful in 29 of 31 patients (93.5%). The total

procedure time was 5 to 8.5 hours with a fluoroscopy time of 47 minutes to 3.5 hours (average of 131 minutes).

Seven of the initially successfully ablated patients experienced serious afib breakthroughs within 3 months of the procedure and underwent a touch-up using regular RF ablation. The average incidence of afib episodes over the first 3 months for the remaining 22 patients who only had the cryoablation was 4.9/month, but this declined to 2.8/month in the 3- to 6-month period after ablation. At the end of 6 months 18 patients experienced no afib episodes at all. This corresponds to an 82% success rate among those afibbers who did not need a RF touch-up and a 62% success rate when considering the whole group. There were no indications of stenosis in CT scans performed 3 and 6 months after the initial cryoablation. However, there were a rather astonishing number of side effects reported. Among them – respiratory depression during conscious sedation, transient leg weakness, transient asymptomatic sinus pauses, femoral pseudoaneurysm, atrial defibrillator implantation, and bacterial endocarditis.

Among the 7 patients who underwent a touch-up ablation with RF, one TIA, one femoral pseudoaneurysm, and one femoral hemorrhage was observed.

The participating electrophysiologists conclude with this somewhat surprising statement, "For paroxysmal AF, the clinical efficacy of cryoablation was comparable to RF segmental PV isolation, with repeat procedures required for AF recurrence in up to nearly 50% of patients. These results underscore the limitations of the segmental PV isolation approach, regardless of the energy source." NOTE: This study was funded by CryoCor Inc.

Hoyt, RH, et al. Transvenous catheter cryoablation for treatment of atrial fibrillation. PACE, *Vol. 28, suppl 1, January 2005, pp. S78-S82*

Editor's comment: Only one of the participating institutions made it to the "A List" in my recent tabulation of top-notch ablation centers (see *Lone Atrial Fibrillation: Towards A Cure – Vol. II*). This certainly shows in the results. A 62% initial success rate is well below expectations and the radiation exposure from fluoroscopy would also seem to be unacceptably high at an average of 131 minutes. The average fluoroscopy time at the Bordeaux Clinic in France is only 57 minutes and that at the Cleveland Clinic somewhere between 51 and 110 minutes. I would conclude that cryoablation, in the US at least, is still in its infancy and unless you fancy being a guinea pig you would be better off waiting or going for a RF ablation at one of the institutions on my "A List".

More extensive ablation required for persistent and permanent AF

Catheter ablation, whether radiofrequency (RF) or cryo, is generally much less successful in persistent and permanent afibbers. Italian researchers now report that the creation of additional ablation lines (including disconnection of the superior vena cava) in the right atrium markedly improves the success rate of RF ablation in persistent and permanent afibbers. Their study involved 60 patients, 35 with persistent AF and 25 with permanent, who were randomized to receive the standard pulmonary vein ablation (including cavotricuspid isthmus ablation) or the standard plus additional ablation in the right atrium. After an average 12 months of follow-up, 87% of the patients who were ablated in both the left and right atria were afib-free as compared to 63% in the conventional left atrium ablation group.

ACC, 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 847-8, p. 121A

Effectiveness of anatomically guided PVA

BAD KROZINGEN, GERMANY. The pulmonary veins are the main sources of the ectopic beats and tachycardias responsible for the initiation of AF. The rogue cells creating the ectopics are found in the myocardial sleeves extending from the left atrium into the veins. Current ablation practices therefore focus on electrically isolating the pulmonary veins from the atrium through the creation of lesions (with radiofrequency energy or freezing [cryoablation]), which interrupt the electrical pathways between the veins and the left atrium. There are two main approaches to achieving the isolation:

- The electrophysiological approach in which the electrical pathways are located using a mapping catheter (Lasso or similar) and then isolating by ablation.

- The anatomical approach in which the veins are isolated guided by an electroanatomical (non-fluoroscopic) mapping system (CARTO or Astronomer). In this method, the offending pathways are not specifically identified, but rather a contiguous, circumferential lesion is created which presumably stops all conduction between the pulmonary veins and the atrium.

German researchers now report that the anatomical approach, on its own, is not effective in preventing recurrence of AF. Their study involved 34

afib patients (average age of 52 years, 76% male) who had all proven resistant to at least 3 antiarrhythmic drugs. The majority (76%) had lone AF – 22 patients the paroxysmal variety (2 or more episodes per week) and the remaining 12 the persistent form. All patients underwent anatomically guided pulmonary vein ablation (PVA) after which the extent of remaining conduction between the veins and the atrium was measured with a 64-pole basket catheter. Only 46% of the isolated veins showed complete conduction block indicating that sole dependency on electroanatomical mapping during PVA is not sufficient to ensure a cure.

The remaining pathways were then isolated using electrophysiological guidance (basket catheter) and at the 12-month follow-up, 21 of the 34 patients (62%) were in sinus rhythm without the use of antiarrhythmics. Another 8 patients (24%) were in sinus rhythm with the aid of antiarrhythmics, which had been ineffective prior to the ablation. Nine patients (26%) needed a touch-up and 6 patients (18%) developed atrial flutter after the procedure.

The researchers conclude that the use of a combined anatomical/electrophysiological approach does not result in better clinical success than the use of the electrophysiological approach on its own. They also point out that the occurrence of left atrial flutter after ablation is highly unusual when the electrophysiological approach is used on its own, so the 18% incidence during their study was probably associated with the initial creation of the contiguous, circumferential lesion. NOTE: Electrophysiologists at the Hopital Cardiologique du Haut-Leveque in Bordeaux have also found that purely anatomically guided ablation leaves residual conduction in 45% of the supposedly isolated pulmonary veins[1].

[1] Hocini, M, et al. Prevalence of pulmonary vein disconnection after anatomical ablation for atrial fibrillation: consequences of wide atrial encircling of the pulmonary veins. European Heart Journal, Vol. 26, April 2005, pp. 696-704 www.eurheartj.org/cgi/content/full/26/7/696

Arentz, T, et al. Effects of circumferential ostial radiofrequency lesions on pulmonary vein activation recorded with a multipolar basket catheter. Journal of Cardiovascular Electrophysiology, *Vol. 16, March 2005, pp. 302-08*

AV node ablation versus PVI

TAIPEI, TAIWAN. The discomfort associated with atrial fibrillation is not primarily due to the fibrillation of the atria, but rather to the fact that the fibrillation affects the AV (atrio-ventricular) node and causes the ventricular rate (pulse rate) to be fast and irregular. An obvious solution to this problem is to isolate the AV node (the ventricular beat controller) from the chaotic impulses originating in the atria from any extraneous impulses and feed it “its marching order” from an implanted pacemaker. This procedure has three major drawbacks:

- It does nothing to stop the fibrillation of the atria, which in itself can be quite uncomfortable, and necessitates continuing anticoagulation (warfarin) therapy.
- It makes the patient entirely dependent on the pacemaker. If it malfunctions or the batteries run out the patient dies.
- It does nothing to remedy the fatigue and reduced exercise capacity caused by the fibrillation of the atria.

AV node ablation is performed in much the same way as a RF ablation except that it is the area around the node that is ablated.

Taiwanese researchers have now compared the long-term efficacy of AV node ablation and pacemaker implantation with pulmonary vein isolation. Their study included 69 elderly patients with AF not controllable with medications. The patients were given the choice of a PVI or the AV node ablation. Thirty-two chose the AV ablation and 37 the PVI. All patients were followed for an average of 52 months after their procedure. At the end of the follow-up, all members of the AV node group experienced a regular pulse rate as compared to 81% in the PVI group. However, the prevalence of persistent AF was substantially higher in the AV node group than in the PVI group (69% versus 8%). The prevalence of heart failure was significantly higher in the AV node group (53% versus 24%) and a decline in left ventricular ejection fraction was also noted in the AV node group (from 51% to 44%), but not in the PVI group. The researchers conclude that AV node ablation and pacemaker implantation is superior to PVI in maintaining a steady ventricular rate, but carries with it an increased prevalence of persistent AF, atrial enlargement, heart failure, and decreased left ventricular ejection fraction.

Hsieh, MH, et al. Catheter ablation of atrial fibrillation versus atrioventricular junction ablation plus pacing therapy for elderly patients with medically refractory paroxysmal atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 16, May 2005, pp. 457-61*

Editor's comment: The Taiwanese study confirms that AV node ablation with pacemaker implantation should be the very last resort for atrial fibrillation patients, particularly for those with the lone variety.

New developments in AF ablation

MILANO, ITALY. Dr. Carlo Pappone and his colleagues at the San Raffaele University Hospital have published a fascinating review of the current and future status of radiofrequency ablation for AF. Some of the highlights of the article are:

- The San Raffaele Hospital treats afibbers who fulfill the following criteria:
  - At least one weekly episode of paroxysmal AF, or
  - At least one monthly episode of persistent AF, or
  - Permanent AF
  - At least one failed trial of antiarrhythmic drugs, or more than one antiarrhythmic drug needed to control symptoms.

- They do not treat patients over the age of 80 years or those with a life expectancy of less than one year. They also exclude patients with serious heart failure (NYHA functional class IV), those with a thyroid dysfunction, contraindications to anticoagulation, thrombi in the left atrium or a left atrial diameter at or above 65 mm. Patients with mitral and/or aortic metallic prosthetic valves are not excluded.

- A review of the outcome for 589 patients who were recently treated with circumferential pulmonary vein ablation yielded the following results: –
  - Total procedure time – 162 minutes
  - Mapping time (using CARTO or NavX) – 75 minutes
  - Fluoroscopy time – 29 minutes
  - Number of patients needing reablation – 30 (6%)
  - Extent of ablated area – 4.9 sq cm (28% of total left atrial area)
  - Procedural success rate – 98.5%
  - Freedom from afib after 29 months – 81% for paroxysmal and 76% for chronic afibbers
  - Procedure related mortality – 0%
  - Transient ischemic attack – 0.2%
  - Stroke – 0.03%
  - Tamponade – 0.1%
  - Atrio-esophageal fistula – 0.03%
  - Pulmonary vein stenosis – 0%
  - Left atrial tachycardia – 6%

- Overall mortality (from any cause) in this group of ablated afibbers was similar to that found among age- and gender-matched persons in the Italian population.

- It is clear that there is a steep learning curve in developing expertise in performing a successful circumferential pulmonary vein ablation and complications are significantly

more common when the EP has done less than 150 procedures.

- There are many exciting new developments on the horizon. Among them: –

- Integration of anatomical mapping (CARTO and NavX) with magnetic resonance imaging or CT scans.
- Remote control of mapping and eventually ablation catheters, largely eliminating the need for extensive operator experience.
- Denervation of vagal ganglia in the left atrium to further improve ablation outcome.

The above summary gives the gist of Dr. Pappone's article in the *Italian Heart Journal*, but for anyone seriously interested in a thorough review of the current and future status of pulmonary vein ablation this article is a must read. It can be found at www.italheartj.org

Pappone, C, et al. Atrial fibrillation ablation. Italian Heart Journal, *Vol. 6, March 2005, pp. 190-99*

Comparison of Haissaguerre and Pappone methods

MUNICH, GERMANY. After the discovery in 1998, by Professor Michel Haissaguerre, that atrial fibrillation originates mainly in the pulmonary veins ablation techniques have focused on electrically isolating these veins from the left atrium. Two different techniques are now widely used for the purpose – the segmental pulmonary vein isolation method (Haissaguerre method) and the circumferential anatomical pulmonary vein isolation method (Pappone method).

In the Haissaguerre approach 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.

In the Pappone approach 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. The Pappone method is somewhat quicker and easier to perform since it does not require the complex interpretation of pulmonary vein electrogram end points. Early results from Dr. Pappone and colleagues were highly

encouraging with success rates of 85% for paroxysmal and 68% for permanent afibbers.

Dr. Hakan Oral and colleagues at the University of Michigan compared the Haissaguerre and Pappone methods directly in a series of 80 patients and found that 88% of patients in the Pappone group were free of afib during a 6- to 12-month follow-up as compared to 67% in the Haissaguerre group. It is important to bear in mind that only symptomatic episodes were considered in these two trials. It is now known that many afib episodes occurring after pulmonary vein isolation (PVI) are completely asymptomatic.

Researchers at the German Heart Center have just completed a comparison of the efficacy and safety of the two methods. Their study included 100 afib patients with highly symptomatic episodes (an average [median] of 10 episodes a month) despite the use of an average (median) of two antiarrhythmic drugs. The majority (89%) of patients had paroxysmal episodes with the remainder having persistent episodes. About 40% of the patients had lone AF. The study participants were randomly assigned to undergo either segmental PVI (Haissaguerre method) or circumferential PVI (Pappone method) and were then followed for 6 months. Twelve patients (24%) in the circumferential PVI group had a follow-up ablation within the first 6 months, as did 8 patients (16%) in the segmental group.

During the 6-month follow-up 82% of patients in the segmental (Haissaguerre) group were free of afib symptoms as compared to 54% in the circumferential (Pappone) group. Six months after the initial ablation all participants underwent 7-day Holter monitoring. Sixty-six per cent of patients in the segmental group were found to be in constant sinus rhythm during the 7 days as compared to only 42% in the circumferential group. Atypical atrial flutter was observed in 9 patients after circumferential PVI, but in only 1 in the segmental group. There were no incidences of pericardial tamponade (piercing of the heart wall) in either group, but pericardial effusion (leakage) was noted in 44% of circumferential ablatees versus 10% of segmental ablatees. Transient ischemic attacks (TIAs) occurred in 2 patients after circumferential ablation and in 1 patient after segmental ablation. Asymptomatic pulmonary vein stenosis was observed in 6% of circumferential ablatees and in 12% of segmental ablatees.

The German researchers conclude that circumferential PVI is not superior to segmental PVI. Dr. David Callans of the University of Pennsylvania School of Medicine, in an accompanying editorial, concurs with the observation, "... it is strange and unprecedented to expect that less electrophysiological investigation will triumph over more."

Karch, MR, et al. Freedom from atrial tachyarrhythmias after catheter ablation of atrial fibrillation: a randomized comparison between 2 current ablation strategies. Circulation, *Vol. 111, June 7, 2005, 2875-80*
Callans, DJ. Comparing different strategies for catheter ablation of atrial fibrillation, Circulation, *Vol. 111, June 7, 2005, 2866-68*

Editor's comment: The German study confirms my own feelings about the relative efficacy of the two procedures. The circumferential PVI (Pappone method) relies more on technology (CARTO anatomical mapping system) than on skill, so it is probably easier to learn and perform than is the segmental PVI procedure. However, in skilled hands, the segmental PVI (Haissaguerre method) produces superior results. It is of interest that Dr. Andrea Natale at the Cleveland Clinic uses a modified segmental PVI approach and has found the circumferential approach to be inferior.

New developments in ablation

CLEVELAND, OHIO. The current standard for the pulmonary vein isolation (PVI) procedure involves the use of radiofrequency (RF) energy (0.3 - 3.0 MHz) to create lesions around the pulmonary veins so as to isolate the left atrium from any aberrant impulses originating in the veins. Most RF delivery systems consist of a "pinpoint" catheter electrode and a second large-surface electrode (ground pad) placed underneath the patient's back. The main problem with this system is that the current density declines very rapidly with increasing distance from the catheter. This makes it difficult to produce deep enough lesions (burns) to ensure adequate isolation without at the same time risking carbonization, steam popping and coagulum formation – all risk factors for stroke.
Several approaches are being evaluated to overcome this problem. Electrodes where the current flows between two closely opposed small electrodes contained within the catheter are used extensively in electro-surgery, but have not yet been evaluated in RF ablation. Cooled or irrigated catheters allow a deeper burn without surface carbonization and are becoming increasingly popular. Other methods of energy delivery for ablation are based on microwaves, lasers, ultrasound, and freezing (cryoablation).

Microwaves (0.3 – 300 GHz) induce oscillation of water molecules which, in turn, create enough heat to "cook" the tissue at the desired spots. There are still significant problems in creating an antenna catheter that will work inside the atrium, but microwave ablation has been used successfully in maze procedures.

Laser beams produce photon energy that can heat tissue and create a lesion. Laser technology for pulmonary vein isolation is still very much in the developmental stage. Some very exciting work is currently underway

to develop a laser balloon that would produce a ring of laser energy which, in turn, would completely isolate a pulmonary vein in one application.

High intensity ultrasound (2 – 20 MHz) can be used to create lesions and has been extensively evaluated in prostate surgery. Ultrasound can be focused in much the same fashion as light beams making it possible to target a specific area for ablation. Work is underway to develop a balloon delivery system, but so far results have been disappointing. There is also some indication that current ultrasound delivery systems are associated with a higher incidence of phrenic nerve paralysis.

Cryoablation makes use of a hollow catheter whose tip is cooled to -75^{o}C through the use of liquid nitrogen. The cryo-catheter produces ice formation inside and outside the cells, a mechanism of irreversible cellular injury. Cryoablation is slower than RF ablation (4-8 minutes per lesion versus 1 minute or less), but does avoid the complications (charring, steam popping, thrombus formation) associated with RF ablation. There is also some indication that it is less likely to produce pulmonary vein stenosis. There is some concern that the risk of afib recurrence is higher with cryoablation; however, new catheter developments are expected to overcome this problem and could well make cryoablation the preferred form of pulmonary vein ablation.
Cummings, JE, et al. Alternative energy sources for the ablation of arrhythmias. PACE, *Vol. 28, May 2005, pp. 434-43*

Highlights from Atrial Fibrillation Symposium

DUBLIN, IRELAND. The 10th annual Atrial Fibrillation Symposium was held in Boston January 14-15, 2005. An illustrious group of cardiologists and EPs exchanged information concerning remaining problems and current research into the catheter ablation of AF. Among the distinguished contributors were Pierre Jais MD, Fred Morady MD, Koonlawee Nademanee MD, Andrea Natale MD, Carlo Pappone MD, and Marcus Wharton MD. Following are highlights of the discussions:

- It is becoming increasingly clear that just isolating the pulmonary veins during an ablation may not be sufficient to result in a cure. It may also be necessary to create lesions specifically aimed at disrupting the dominant rotors in the left and right atria, or to target vagal nerve endings or ganglionated autonomic plexi in the epicardial fat pads. These approaches are currently under intensive study.

- There is intensive debate as to just how far from the edge of the pulmonary veins the ablation lesions should be placed. Placing them too close to the edge increases the risk of

stenosis, while placing then too far away necessitates a greater number of "burns" in order to complete the isolation.

- There is some indication that the segmental PVI (Haissaguerre method) is more effective than the circumferential PVI (Pappone method) in reducing ectopic activity, but that the Pappone method may be more effective in inactivating the rotors responsible for maintaining AF.

- Ablation techniques at advanced centers have now reached the stage where patients with permanent AF and heart failure patients can be successfully treated. There is actually some evidence that a successful ablation may improve left ventricular function and the quality of life in patients suffering from both heart failure and AF.

- There is considerable variation in the way different centers report their success rates depending mainly on the type and duration of electrocardiographic follow-up and on the definition of success. There is recognition that success should perhaps be based on the perceived improvement in patients' quality of life. Thus, "for a patient who is transformed from a predominant pattern of highly symptomatic persistent atrial fibrillation with occasional spontaneous terminations preablation to a pattern of asymptomatic or symptomatic short-lived episodes of transient atrial fibrillation (lasting 30 seconds or 1 minute) postablation, the procedure could be deemed clinically successful."

- There is still no consensus as to the optimum type and size of ablation catheters. There is some indication that the use of an 8 mm catheter is more likely to cause blood clots than is the use of an irrigated tip catheter. The use of the intracardiac echocardiography (ICE) does not totally exclude the occurrence of the steam popping associated with excessive tissue healing.

- The creation of a fistula (hole) between the back wall of the left atrium and the esophagus is now recognized as a potential complication with often fatal consequences. It is estimated that approximately 20 cases of atrio-esophageal fistula have occurred so far worldwide. Numerous suggestions for avoiding this serious problem were discussed.

- The danger of blood clot formation at the time of penetration of the wall (septum) between the right and left atrium is high so heparin is now routinely administered immediately prior to penetration. Most centers continue anticoagulation with warfarin 3-6 months post-ablation depending on the age and risk factors of the patient and on whether or not the ablation was successful.

- New developments in the field of ablation include the combination of three-dimensional MRI and CT scans with real-time three-dimensional electroanatomical mapping. This approach could potentially eliminate the use of fluoroscopy during the procedure.

- Closure or removal of the left atrial appendage may be a viable alternative to anticoagulation for patients with persistent AF who have had a failed ablation.

Keane, D, et al. Emerging concepts on catheter ablation of atrial fibrillation from the Tenth Annual Boston Atrial Fibrillation Symposium. Journal of Cardiovascular Electrophysiology, *Vol. 16, September 2005, pp. 1025-28*

Editor's comment: Much of the above information is clearly highly technical, but the fact that these topics are still being intensely debated indicate that catheter ablation still has a ways to go before being entirely successful, and that much research effort is being invested in solving the remaining problems.

PVI not enough in persistent AF

BORDEAUX, FRANCE. Pulmonary vein isolation (PVI) has been shown highly effective in eliminating paroxysmal (intermittent) atrial fibrillation with some specialized centers showing cure rates of close to 90%. The elimination of persistent and permanent afib has, however, proven much more difficult with success rates closer to 60%. Researchers at the Hopital Cardiologique du Haut Leveque in Bordeaux now report the development of a new ablation procedure resulting in a cure rate of 95% for patients with persistent afib.

Their study involved 53 patients with persistent afib (episodes longer than 7 days, but amenable to electrical cardioversion) and 7 patients in permanent afib. The patients were between the ages of 44 and 62 years (mean age of 53 years) and had endured afib for a median of 12 months. They also had failed an average of 3.3 antiarrhythmic drugs. The patients underwent a highly complicated procedure in which several distinct areas of the left and right atria were ablated in random order. The ablations

were all carried out using the *Thermacool* catheter (an irrigated tip ablation catheter with a distal 3.5 mm tip and three 1-mm electrodes separated by 2-5-2 mm interelectrode spacings). Maximum power used inside venous structures was 20-30 watts, while 30-40 watts was the maximum when atrial structures were ablated.

The initial ablation step in 22 patients was a PVI, isolation of the superior vena cava and the coronary sinus (thoracic veins) was the initial step for 19 patients, and the remaining 19 patients started out with ablation of areas in the left atrium showing unusual electrical activity. After this first "round", 3 patients (5%) converted to sinus rhythm. It is noteworthy that only 1 out of the 22 patients (5%) having the PVI achieved sinus rhythm as a result of just this procedure. Seventeen of the remaining 57 patients still in afib were then treated with a PVI (assuming they had not undergone one in the first step), 19 received thoracic vein ablation, and 21 received an atrial ablation. This brought another 12 patients into sinus rhythm for an overall success rate of 25%. The third step for the remaining 45 patients was a PVI in 15 patients, thoracic vein ablation in 17, and atrial ablation in 13. This resulted in termination of afib in 17 patients increasing the success rate to 53%.

Finally, linear ablation (involving the cavotricuspid isthmus and the left atrial roof) of the remaining 28 patients brought 20 into sinus rhythm resulting in a total success rate of 87%. In most cases the conversion to sinus rhythm went through a stage of atrial tachycardia, which had to be ablated during the procedure as well. Total average procedure time was 264 minutes (4.5 hours) with an average fluoroscopy time of 84 minutes.

The ablation site resulting in conversion to sinus rhythm or atrial tachycardia was the pulmonary veins in 18% of patients, the coronary sinus region in 17%, anterior left atrium in 15%, atrial roof in 10%, mitral isthmus in 8%, and the septum in 10%. Only 3% of patients converted after ablation around the superior vena cava.

Based upon their results the Bordeaux researchers propose the following sequence for ablation of persistent afibbers. PVI followed by linear ablation of the left atrial roof and then atrial ablation along the left atrial appendage and the coronary sinus. If afib persists then other atrial locations should be targeted with the final site being the mitral isthmus line.

Five of the 8 patients whose first ablation was unsuccessful underwent a successful second ablation bringing the total cure rate to 95%. All study participants were hospitalized for 1 day at 1, 3, 6 and 12 months after the last procedure for clinical review and ambulatory monitoring. Twenty-four patients developed atrial tachycardia during the first 3 months of follow-

up and were successfully ablated for this after-effect. None of the patients developed pulmonary vein stenosis. The Bordeaux center has now performed ablations on over 4000 patients and has experienced no incidences of atrio-esophageal fistula.

Haissaguerre, M, et al. Catheter ablation of long-lasting persistent atrial fibrillation: Critical structures for termination. Journal of Cardiovascular Electrophysiology, *Vol. 16, November 2005, pp. 1125-37*

Haissaguerre, M, et al. Catheter ablation of long-lasting persistent atrial fibrillation: Clinical outcome and mechanisms of subsequent arrhythmias. Journal of Cardiovascular Electrophysiology, *Vol. 16, November 2005, pp. 1138-47*

Tse, Hung-Fat and Lau, Chu-Pak. Catheter ablation for persistent atrial fibrillation: Are we ready for "prime time"? Journal of Cardiovascular Electrophysiology, *Vol. 16, November 2005, pp. 1148-49*

Editor's comment: This study clearly shows that the elimination of persistent and permanent afib requires a far more comprehensive and complicated approach than does the elimination of paroxysmal (intermittent) afib where a simple PVI is usually enough to do the job. This may, at least partially, explain the wide variation in success rates reported by various centers. It would seem that the extensive destruction of atrial tissue resulting from this comprehensive procedure could affect the atria's efficiency in acting as booster pumps for the ventricles. The Bordeaux researchers are currently evaluating this aspect, but so far have found no indication that exercise capacity (duration and maximum workload) are decreased following the comprehensive procedure. My own conclusion would be that persistent and permanent afibbers need to seek out the very best EPs and centers if they are to have a half decent chance of being cured.

Ablation - Complications

Atrial flutter after pulmonary vein isolation

CLEVELAND, OHIO. It is estimated that about 10% of afibbers undergoing pulmonary vein isolation (PVI) develop left atrial flutter (LAFL) or tachycardia as a result of the procedure. If the LAFL 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 after the 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.

Electrophysiologists (EPs) at the Cleveland Clinic recently completed a study involving 730 afibbers who had undergone pulmonary vein antrum isolation guided by intracardiac echocardiography (ICE). Twenty-three patients (3.1%) developed LAFL after the procedure. All underwent a second procedure during which veins that had regained electrical conductivity were again isolated. During the procedure electroanatomical mapping (CARTO) was also carried out to determine the location of the flutter circuits and the presence of scar tissue in the left atrium.

After an average 496 days of follow-up 61% of the LAFL patients were free of all arrhythmias without the use of antiarrhythmic medication, 21% were able to maintain sinus rhythm with the use of previously unsuccessful antiarrhythmics, 2 patients (9%) required a third procedure during which linear lesions were made to interrupt the flutter circuit, and the remaining 2 patients (9%) developed recurrent persistent LAFL.

Imaging carried out during the initial PVI showed that 48% of the 23 LAFL patients had pre-existing scar tissue in their left atrium – possibly caused by fibrosis induced by long-term AF. The success rate for these patients was significantly poorer than for those without scar tissue. Only 36% were free of arrhythmia without antiarrhythmics, 27% had partial success (free of arrhythmia with the use of antiarrhythmics), and 36% experienced "complete failure". In comparison, 83% of the patients without scars remained free of arrhythmia without antiarrhythmics and the remaining 17% were free of arrhythmia with the use of antiarrhythmics.

The researchers conclude that most cases of post-PVI LAFL can be resolved by a second PVI, but that patients with pre-existing scar tissue may need additional linear lesions to resolve the problem. They also point

out that in patients with coexisting AF and right atrial flutter, a standard PVI is often sufficient to resolve both arrhythmias, eliminating the need for the creation of ablation lines in the right atrium.

In an accompanying editorial Italian EPs question the routine use of linear lesions (usually between the mitral valve and the left inferior pulmonary vein) to reduce the risk of post-procedure LAFL. They point out that creating these lesions lengthens procedure and fluoroscopy time and may be less effective than a second PVI in resolving potential LAFL problems.

Cummings, JE, et al. Left atrial flutter following pulmonary vein antrum isolation with radiofrequency energy: linear lesions or repeat isolation. Journal of Cardiovascular Electrophysiology, *Vol. 16, March 2005, pp. 293-97*

Raviele, A, et al. Iatrogenic postatrial fibrillation ablation left atrial tachycardia/flutter: how to prevent and treat it? Journal of Cardiovascular Electrophysiology, *Vol. 16, March 2005, pp. 298-301*

Left atrium changes after ablation

While radiofrequency (RF) ablation can be highly effective in eliminating AF, it is not clear what effect the creation of extensive lesions on the atrium wall has on the function and performance of the left atrium. American researchers have used contrast-enhanced magnetic resonance angiography and cine magnetic resonance of the left atrium to measure changes occurring in 11 patients who underwent RF ablation. They found that the left atrium volume had decreased by an average 8% 3 months after the ablation. This positive remodeling change, however, was offset by a 17% reduction in left atrial ejection fraction (from an average 52% to 38%). The researchers conclude that left atrial function may worsen after an extensive ablation.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1164-248, p. 123A

Asymptomatic AF common after ablation

LEIPZIG, GERMANY. Most afibbers experience very obvious symptoms when they experience an episode with palpitations being the most common. Perhaps 20% of afibbers have no symptoms at all during an episode and thus suffer from what is called asymptomatic or silent AF. German researchers now report that the incidence of asymptomatic AF increases substantially after a radiofrequency ablation using the Pappone method (circumferential anatomical pulmonary vein isolation). Their study involved 114 patients with highly symptomatic AF who had experienced at least 3 documented episodes and had suffered from the condition for at least 18 months. The patients had a 7-day Holter monitoring session just

prior to their ablation, immediately following, and after 3, 6 and 12 months of follow-up.

Prior to the ablation the study participants experienced a median of one episode (range of 1-3) during the 7-day Holter monitoring period. The average duration of these episodes was 38 (10-133) hours. Immediately after ablation the median number of episodes experienced over 7 days was 2 (1-5) and the duration was 36 (22-79) hours. The corresponding numbers after 3, 6 and 12 months were:

- After 3 months – 2 (1-6) episodes for a total of 23 (8-41) hours
- After 6 months – 2 (1-4) episodes for a total of 17 (8-43) hours
- After 12 months – 2 (1-5) episodes for a total of 10 (3-25) hours

The number of episodes that were asymptomatic was substantially higher after the ablation than before.

- Percentage of asymptomatic episodes before ablation – 0% (0-25)
- Percentage of asymptomatic episodes after ablation – 50% (0-89)
- Percentage of asymptomatic episodes after 3 months – 50% (0-100)
- Percentage of asymptomatic episodes after 6 months – 50% (0-100)
- Percentage of asymptomatic episodes after 12 months – 58% (0-100)

The proportion of time spent in asymptomatic AF as a percentage of total time spent in AF also increased slightly with time.

- Time spent in asymptomatic AF before ablation – 62% (6-88)
- Time spent in asymptomatic AF after ablation – 70% (10-98)
- Time spent in asymptomatic AF after 3 months – 73% (23-96)
- Time spent in asymptomatic AF after 6 months – 77% (8-100)
- Time spent in asymptomatic AF after 12 months – 77% (34-88)

Combining this information shows that the total mean duration of symptomatic AF decreased from 12 hours (during a 7-day period) prior to

ablation to 2.3 hours 12 months after the ablation. A very noticeable improvement particularly in view of the fact that the researchers considered any period of rapid, irregular heart beat as an AF episode if it lasted more than 30 seconds. Nevertheless, the fact that 50% or more of AF episodes after the ablation were asymptomatic is disconcerting. It clearly impacts on success rates, which actually may be significantly lower than generally claimed. It also raises the question as to whether continued aspirin usage or anticoagulation is advisable after a circumferential, anatomical PVI.

The researchers point out that the use of beta-blockers increased substantially from prior to the ablation when 57% of participants took them to after the ablation when 77% took them. Even after 12 months 72% of participants were still on beta-blockers. It is possible that this may have reduced the intensity of episodes to the point whereby the afibber did not perceive any symptoms during an episode resulting in the episode being classified as asymptomatic.

Hindricks, G, et al. Perception of atrial fibrillation before and after radiofrequency catheter ablation. Circulation, *Vol. 112, July 19, 2005, pp. 307-13*

Editor's comment: The main expectation of an afibber having an ablation is that he/she will come out of it having no more symptomatic episodes. While the procedures performed in Leipzig clearly did not totally eliminate AF in all cases, they certainly made a vast improvement in regard to the average time spent in symptomatic AF. Nevertheless, the continued presence of asymptomatic episodes is disconcerting. It is possible that his phenomenon is related to the type of PVI procedure used. Another long-term study involving 165 afibbers having undergone a segmental PVI (Haissaguerre method) found that successfully ablated afibbers had very few asymptomatic episodes (only 12% of total episodes in a 30-day period) after 2 years.

Cryoablation associated with lower stroke risk

Researchers at the University of Hong Kong report that the use of cryoablation rather than radiofrequency ablation significantly reduces the risk of thromboembolic complications during the procedure. They measured the platelet and coagulation activation before and during the procedure and found that both were elevated immediately after the transseptal puncture. However, the increase in platelet activation was considerably less during cryoablation indicating that this procedure may have an inherently lower risk of TIAs and stroke.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 847-3, p. 120A

Heart rate increase after ablation

COPENHAGEN, DENMARK. Several studies and indeed our own LAF surveys have observed that many afibbers experience an increase in heart rate after a pulmonary vein isolation (PVI) procedure. Electrophysiologists at the Danish Heart Centre now confirm these observations in a study involving 62 patients with paroxysmal or persistent afib. The average age of the patients was 55 years; 29% were women and 63% had hypertension or associated cardiovascular disease. The patients were divided into two groups with one group of 37 undergoing segmental PVI (Haissaguerre method) and the remaining 25 undergoing circumferential PVI (Pappone method). A Lasso catheter was used for mapping in the segmental group, while the CARTO system was used in the circumferential group.

Successful isolation of the pulmonary veins was achieved in 97% of cases; however, a repeat ablation was required in 72% of patients having the circumferential procedure and in 73% of patients in the segmental group. A substantial number of patients (55%) required ablation in areas other than the pulmonary veins with isolation of the superior vena cava (right atrium) being the most common extra procedure (required by 26 patients). The procedure time for the segmental method was somewhat longer than for the circumferential method (166 versus 138 minutes). The procedure times for the second ablations were somewhat shorter at 115 and 99 minutes respectively. During a follow-up of 8.8 months, 35 of the 62 patients (56%) experienced recurrent afib corresponding to an overall success rate of 44%. At the 12-month follow-up point 29% of the study participants were still on antiarrhythmic drugs.

The researchers observed a significant increase in the average heart rate (in sinus rhythm) of the ablatees. One month after the ablation the average rate had increased from 58 bpm at baseline to 67 bpm and further increased to 71 bpm after 3 months; at the final measuring point 12 months after the ablation, the average heart rate was still 70 bpm. Three patients had mean heart rates of 99 bpm going as high as 140 bpm and had to be prescribed a calcium channel blocker and digoxin to reduce their heart rate to a comfortable level. The researchers noted that those patients who did not experience a recurrence of afib had a significantly greater increase in heart rate than did those whose ablations were unsuccessful (13 bpm versus 6 bpm).

Other electrophysiologists have observed increases in heart rate after PVIs, but in most cases these have been transient. The Danish researchers conclude that the increases may not be transient and that up to 5% of ablatees may need long-term medication to control symptoms associated with the uncomfortably high heart rate. They suggest that the reason for the heart rate increase is that they used deeper lesions

resulting in a more extensive destruction of vagal nerve fibers and thus partial elimination of the heart's built-in slowdown mechanism. They recommend that patients undergoing PVI should be informed of this possible complication.

Nilsson, B, et al. Increased resting heart rate following radiofrequency catheter ablation for atrial fibrillation. **Europace**, *Vol. 7, September 2005, pp. 415-20*

Editor's comment: It is always rewarding to see the findings of our LAF surveys confirmed by other studies. The following is taken from the September 2005 issue of *The AFIB Report.*

"*Changes in heart rate after the procedures were quite common as indicated in the table below*.

	Complete Success	Partial Success	Failure	Average
Increase in heart rate	58%	59%	20%	44%
No change in rate	34%	27%	52%	40%
Decrease in rate	8%	14%	27%	16%
TOTAL	100%	100%	100%	100%

The most frequent change was an increase in heart rate (experienced by 44%). This change was most common among afibbers who had undergone successful procedure(s) (58%) and least common among those whose procedures had failed to cure the afib (20%). Statistically, the difference was very significant (p=0.0015).

The reason for the increase in heart rate after an ablation is that a significant portion of vagal nerve endings are 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.

The increase in heart rate is usually temporary and abates as the vagal nerve endings heal."

My own heart rate increased to about 95 bpm after my PVI in Bordeaux; it is now, 6 months later, down to 80 bpm and will hopefully return to my normal 60 or 65 bpm within the next 6 months. Dr. Jais suggested that increased physical activity might hasten the process towards normalcy.

Atrial flutter after PVI

CLEVELAND, OHIO. Atrial fibrillation and atrial flutter often co-exist in the same patient with one readily converting to another. Studies have shown that a successful pulmonary vein antrum isolation (PVAI – Natale method) often is effective in controlling both afib and aflutter in patients who have not undergone previous cardiac surgery. However, it is not known whether patients who have had cardiac surgery are more likely to develop flutter after a PVAI than are those with no previous cardiac surgery (controls).

Researchers at the Cleveland Clinic analyzed data from 1125 patients who had undergone a PVAI. The majority (1062 patients) had no history of cardiac surgery, while the remaining 63 had undergone such surgery. The afib recurrence rate among surgery patients (after about 1.5 years of follow-up) was 21% (success rate of 79%) versus 19% (success rate of 81%) for controls; in other words, no significant difference. The rate of recurrence of atrial flutter, however, was much higher (33%) in surgery patients than in controls (4%). All 21 aflutter patients in the surgery group underwent an ablation procedure for atrial flutter with an immediate success rate of 86% and a long-term success rate of 76%. The immediate success rate for controls was 100% with a long-term rate of 95%.

The researchers point out that incision lines, cannulation sites, scars, etc. may make surgery patients more prone to develop aflutter. They also point out that among patients not exposed to previous cardiac surgery the PVAI cured pre-existing afib in 94% of cases as compared to only 63% among cardiac surgery patients. It is also noteworthy that, while 18% of controls experienced atrial flutter within the first two months after the PVAI, only 4% continued to do so long term (1.2% experienced left atrial flutter). In the group of former heart surgery patients 60% experienced aflutter during the first two months and 33% needed an ablation to eliminate it.

The researchers conclude that patients who have undergone cardiac surgery previous to their PVAI should be warned of the possibility of developing atrial flutter after the procedure.

Kilicaslan, F, et al. The need for atrial flutter ablation following pulmonary vein antrum isolation in patients with and without previous cardiac surgery. Journal of the American College of Cardiology, *Vol. 45, March 1, 2005, pp. 690-96*

Ablation - Outcome

Afib recurrence after pulmonary vein isolation

BERGEN, NORWAY. Researchers at the Haukeland University Hospital have carried out a study to determine the afib recurrence rate after a PVI and the change in quality of life (QOL) associated with the procedure. Their study involved 59 men and 13 women with a mean age of 52 years who had been unsuccessfully treated with two or more antiarrhythmic drugs. Most (89%) had lone atrial fibrillation and 49% of all participants had an enlarged left atrium.

The patients underwent a PVI using a 10-polar Lasso catheter for mapping and a *Celsius* deflectable 7F quadripolar catheter for recording and ablating. An average of 3.1 veins were isolated per patient. A single procedure was performed on 60 of the patients, two procedures on 10 patients, and three procedures on 2 patients. The second procedure (touch-up) was done within 48 hours of the first procedure in 5 patients. One patient experienced cardiac tamponade, one had a stroke, and one later developed stenosis.

During an average follow-up of 10 months 27 patients experienced more than one afib episode. Quality of life was judged very good in 26 patients who had not experienced a recurrence; it was judged to be better in 30 patients (15 with recurrences), unchanged in 11 patients of which 10 had recurrences, and worse in 2 patients who both had recurrences.

The researchers noted that the risk of recurrence increased sharply with age and the number of years the afib had been present. As a matter of fact, they suggest that patients who have suffered from AF for more than 10 years may need a more extensive procedure than the standard PVI to resolve their problem. Overall, 60% of all patients involved in the study were free of afib during the 10 months follow-up and 72% reported that they were satisfied with the procedure.

Chen, Jian, et al. A clinical study of patients with and without recurrence of paroxysmal atrial fibrillation after pulmonary vein isolation. PACE, *Vol. 28, suppl 1, January 2005, pp. S86-S89*

Remodeling after successful PVI

TAIWAN, REPUBLIC OF CHINA. Researchers at the Columbia University Medical College of Physicians and Surgeons recently concluded that patients with atrial fibrillation tend to have significantly larger ostial

pulmonary vein (PV) diameters than do people without AF. They also noted that larger PV diameters were associated with enlarged left atria.

Taiwanese researchers now report that successful pulmonary vein isolation (PVI) gradually remodels the heart toward normal by decreasing the diameter and degree of eccentricity of ablated veins while, at the same time, reducing the size of the left atrium.

Forty-five afibbers participated in the study which involved magnetic resonance angiographic (MRA) imaging one month before and 12 months after the PVI. Thirty-five (78%) of the patients experienced no AF recurrence, while 10 experienced afib episodes more than one month after ablation. The researchers found that the diameters of the superior PVs in successfully ablated patients had decreased significantly one year after the PVI and also showed less eccentricity. They also noted a slight reduction (8%) in left atrium volume.

Among patients whose PVI had been unsuccessful the story was quite different. Twelve months after the PVI the right superior PV had increased in diameter by about 21% and the volume of the left atrium had increased by about 29%. The researchers conclude that a successful PVI is associated with desirable structural remodeling of the superior PVs and the left atrium. An unsuccessful PVI resulting in late recurrence of afib is, however, associated with continued left atrium enlargement.

Tsao, HM, et al. Morphologic remodeling of pulmonary veins and left atrium after catheter ablation of atrial fibrillation. Journal of Cardiovascular Electrophysiology, *Vol. 16, January 2005, pp. 7-12*

Worldwide survey on ablation

MILAN, ITALY. A group of 10 prominent electrophysiologists (EPs) has just completed a worldwide survey of ablation procedures for afib to determine success rates and complications. The survey included 181 centers that had performed catheter ablations between 1995 and 2002. The number of procedures done at the centers varied from fewer than 30 to more than 300 and the success rates reflected this. Overall success rate (no afib, no medication) in 90 centers having treated 8745 patients was 52% after a 1-year follow-up with 27.3% of patients requiring a touch-up procedure to achieve this result. Another 23.9% were able to control their afib with antiarrhythmic drugs after the ablation although these drugs had been ineffective prior to the ablation. For centers having performed less than 30 procedures the average success rate (no afib, no medication) was 29.8% as compared to 63.8% among centers having done 300 or more. Adequate control with antiarrhythmic drugs was achieved among 30.1% of the patients treated at the smaller institutions versus 15.8% in the larger ones.

The type of procedure used was found to have evolved rapidly between 1995 and 2002. Between 1995 and 1997 simple compartmentalization was the predominant technique, searching for and ablating triggering foci was the favorite technique between 1998 and 1999, and pulmonary vein ablation or isolation became the standard in the year 2000. The total number of patients undergoing catheter ablation for atrial fibrillation rose from 15 in 1995 to 5050 in 2002. All centers reported treating paroxysmal AF, 53% also treated persistent AF, but only 20% treated permanent AF. Most centers (64%) would not treat patients with prior heart surgery, impaired left ventricular ejection fraction (between 30 and 35%) or a grossly enlarged left atrium (46%).

The most commonly used mapping techniques involved the use of the Lasso catheter (77%) and the CARTO system (43%). The most frequently used energy sources used in ablation were radiofrequency (84%), cryoablation (4%), ultrasound ablation (2%), and laser ablation (2%). Most centers (83%) required their patients to be on oral anticoagulation for between 1 and 6 months post-procedure, while 17% prescribed aspirin.

Major complications occurred in 524 patients (6%). The most common complications were chronic pulmonary vein stenosis experienced by 1.31% of patients, tamponade (piercing of the heart wall) experienced by 1.22%, and stroke or transient ischemic attack (TIA) experienced by 0.94%.

Success rates were found to vary with time. During the first 6 months post-ablation a cumulative total of 34% of ablatees became afib-free. This percentage rose to 66% after 12 months, but then declined again to 43% for those who had gone more than 2 years since their ablation. This decline in cumulative success rates is likely due to the less effective protocols used in the early years of AF ablation, but could also reflect on adverse evolution of the atrial substrate with time.

Cappato, R, et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circulation, *Vol. 111, March 8, 2005, pp. 1100-05*

Editor's comment: In my own survey of 112 afibbers who had undergone radiofrequency ablation (www.afibbers.org/sample.htm) I found that the 9 top-rated centers (in my estimation) had an average success rate of 68% in the first attempt and 76% with a touch-up. In comparison, the "B-class" centers had success rates of 21% and 29% (with touch-up) respectively. These results are quite similar to the ones reported in *Circulation* and, once again, emphasize the importance of lots of experience as the prime determinant in the outcome of an ablation.

Real success rate of PVAs

MIRANO, ITALY. The outcome of a pulmonary vein ablation (PVA) is usually determined by the results of a Holter recording and standard electrocardiogram (ECG) taken 1 to 4 months after the ablation. If no AF is observed during these tests the procedure is deemed to have been a success.

Italian researchers now question the validity of this approach. In a study of 72 patients who had undergone a seemingly successful PVA the researchers found that 13.9% of them showed evidence of AF episodes on Holter recordings or ECGs taken 30 or 120 days post ablation. However, when patients used a trans-telephonic electrocardiographic monitor (TT monitor) for a 90-day period (one 30-second recording per day plus recordings when palpitations were felt) it was clear that 27.8% of participants had evidence of AF episodes. Of particular interest is the finding that 8 of the 20 patients showing AF episodes were completely asymptomatic, while 10 patients had at least one asymptomatic episode.

The researchers conclude that TT monitoring is superior to Holter recordings and periodic ECGs in evaluating AF relapses after ablation. In this particular case, the short-term success rate of the PVA was only 72% when using TT monitoring as compared to 86% when using ECGs and Holter recordings. They also point out that 50% of the patients with relapses where completely asymptomatic during at least one AF episode.

Senatore, G, et al. Role of transtelephonic electrocardiographic monitoring in detecting short-term arrhythmia recurrences after radiofrequency ablation in patients with atrial fibrillation. Journal of the American College of Cardiology, *Vol. 45, March 15, 2005, pp. 873-76*

Prediction of PVI success

MESTRE, ITALY. Pulmonary vein isolation (PVI) is now the standard when it comes to radiofrequency ablation for atrial fibrillation. There are two major methods for performing a PVI; the electrophysiologically guided segmental ablation (Haissaguerre method), and the circumferential anatomical ablation (Pappone method). Some electrophysiologists use a combination of the two methods. The Haissaguerre method specifically locates the pathways conducting aberrant impulses from the pulmonary veins and isolates those, while the Pappone method completely encircles the veins with lesions aided by anatomical mapping. The Haissaguerre approach has the advantage of requiring less application of radiofrequency energy, but usually does result in longer fluoroscopy exposure.

Italian researchers using the circumferential anatomical ablation approach have just completed a study aimed at determining if early recurrence of AF after a PVI predicts the long-term success of the

procedure. Their study involved 143 consecutive patients who had undergone a PVI using the Pappone method. All patients were followed for an average of 19 months after the PVI at which time 102 (71%) were in sinus rhythm. The majority (62%) was still on antiarrhythmic drugs that had not been effective prior to their ablation. Twenty-two per cent of the 143 patients relapsed into AF during the first 48 hours following their PVI, another 20% had a relapse after the first 48 hours, but before a month had gone by, and another 3% experienced a relapse during the second and third months. Patients who did not relapse during the first 3 months had a 95% probability of long-term success as compared to only 43% among afibbers who did relapse. Only 10% of those ablatees who relapsed during the first month and continued to have episodes during the second and third month eventually achieved long-term success. However, 45.5% of patients who just relapsed during the first month achieved long-term success. The researchers conclude that the presence of structural heart disease and incomplete isolation of the pulmonary veins are the main predictors of the early relapse into AF.

Bertaglia, E, et al. Predictive value of early atrial tachyarrhythmias recurrence after circumferential anatomical pulmonary vein ablation. PACE, *Vol. 28, May 2005, pp. 366-71*

Editor's comment: This study shows that afibbers who have no relapse of afib during the first 3 months following their ablation have a 95% probability of having achieved a long-term cure. However, afibbers who have a relapse during the first month have a less than 50% chance of remaining afib-free in the long term, while those who have relapses in both the first, second and third months have only a 10% probability of a long-term cure.

Decrease in left atrium size predicts PVI success

ZWOLLE, THE NETHERLANDS. Dutch researchers have released the results of a study designed to determine the association between post-ablation left atrial size and the medium-term success of PVIs. Their study involved 105 afibbers (70% male) with an average age of 52 years (range of 27-75 years). The patients had endured afib for an average 6 years (1-11 years) with 49.5% having the paroxysmal form and 50.5% the persistent form. Only 6% had underlying structural heart disease, but 26% had hypertension.

The patients underwent a PVI using the circumferential anatomical method (Pappone method). Average procedure time and fluoroscopy time were 211 minutes and 57 minutes respectively. Twenty-two per cent of the ablatees experienced recurrent afib episodes 3 to 6 months after the initial procedure and underwent a second procedure (22% repeat rate). The patients were followed for an average of 14.6 months (6-24 months).

At the last follow-up 86.5% of paroxysmal afibbers and 77% of persistent afibbers were still in normal sinus rhythm. However, 34% of afibbers in sinus rhythm needed antiarrhythmic drugs to maintain sinus rhythm. Thus the overall full success rate (no afib, no drugs) was 54%.

The researchers measured left atrium diameter (PSLAX view) before and 6 months after the ablation. They found that the average LA diameter decreased from 40.5 to 37.5 mm in successfully treated paroxysmal afibbers and noted a similar decrease in successfully treated persistent afibbers (from 44.0 to 40.0 mm). In contrast, patients who reverted to afib experienced an increase in LA diameter from an average 45 mm to 49 mm. (Editor's note: Unsuccessfully ablated afibbers would seem to have had an enlarged LA even prior to the ablation).

The researchers also found that patients with an elevated troponin T level (average 1.6 microgram/L) 16 hours after the ablation were more likely to be in sinus rhythm at long-term follow-up than were those with lower levels (average 0.87 mcg/L). Troponin T level is an indicator of the extent of damage done to the heart during the ablation and the normal range is 0-0.5 mcg/L. These findings support the contention that the more aggressive an ablation is the greater the chance of success. The Dutch researchers conclude that elevated troponin T level 16 hours post-ablation and a reduction in LA diameter 6 months after the procedure are both predictors of a successful outcome.
Beukema, WP, et al. Successful radiofrequency ablation in patients with previous atrial fibrillation results in a significant decrease in left atrial size. **Circulation**, *Vol. 112, October 4, 2005, pp. 2089-95*

Editor's comment: It is interesting to compare some of the above findings with those of the LAF Survey-9. The average age at ablation in the Dutch study was 52 years (27-75 years) compared to 55 years (27-85 years) in LAFS-9. Six per cent of participants in the Dutch study had underlying heart disease versus 7% in LAFS-9. Thirty per cent of ablatees in the Dutch study were female versus 26% in LAFS-9. Thus, the two groups would seem to be quite comparable. Success rates compared as follows:

	Dutch Study	LAFS-9 Average	LAFS-9 "Top 9"
Full success (NSR, no drugs)	54%	41%	62%
Partial success (NSR, antiarrhythmics)	29%	17%	14%
Failure (recurrent afib)	17%	42%	24%
Repeat rate	22%	30%	20%

It is interesting to note that 16% of the patients still on antiarrhythmics were taking amiodarone thus partially accounting for the quite low failure rate in the Dutch study.

Ablation improves heart function

BORDEAUX, FRANCE. Conventional medical wisdom has it that left ventricular dysfunction can be a causative factor in atrial fibrillation (AF). Now researchers at the Hopital Cardiologique du Haut Leveque provide tantalizing evidence that it may actually be the other way round, ie. that AF can result in left ventricular dysfunction.

Their study included 38 men and 10 women with paroxysmal or chronic (persistent or permanent) symptomatic AF. Their type of AF was classified as isolated, that is AF in the absence of moderate or severe mitral regurgitation and/or mitral stenosis, mitral annular calcification, coronary artery disease, chronic pulmonary disease, systemic hypertension (greater than 140/90 mm Hg), thyroid disease, and diabetes.

This classification would seem to be quite similar to "lone" afib or perhaps more precisely "idiopathic" AF. The participants were studied in sinus rhythm (when possible) prior to undergoing a PVI procedure with additional lesion lines as required. The researchers observed a pronounced tendency to left ventricular dysfunction in the AF patients as compared to controls. They found a significant reduction in lateral early diastolic peak velocity in 37% of paroxysmal afibbers and in 48% of chronic afibbers when compared with healthy controls.

Twenty-nine (78%) of the 37 paroxysmal patients and 6 (54%) of the 11 chronic patients were successfully treated without AF recurrence. All patients with recurrence were classified as partial success and pooled with patients with complete success. None of them were considered to have had a failure of ablation (defined as less than 70% improvement) and none required a second procedure. The patients were followed for 12 months after their PVI. The following major changes were observed at the final (12-month) examination:

- Left atrium diameter had decreased by an average of 11% in both paroxysmal and chronic afibbers.
- Left atrium area had decreased by an average of 18% in paroxysmal and by 23% in chronic afibbers.
- Left ventricular diastolic function had improved significantly with an average increase in lateral early diastolic peak velocity of 29% in paroxysmal afibbers and a 46% increase in chronic AF patients.
- Left ventricular ejection fraction also increased significantly over the observation period (by an average of 7.7% in paroxysmal afibbers and 18.8% in chronic ones).

The researchers conclude that remodeling of the left atrium and ventricle does indeed take place after a successful PVI and that this may suggest that afib may be partly the cause rather than a consequence of diastolic dysfunction.

Reant, P, et al. Reverse remodeling of the left cardiac chambers after catheter ablation after 1 year in a series of patients with isolated atrial fibrillation. **Circulation**, *Vol. 112, November 8, 2005, pp. 2896-2903*

Antiarrhythmics improve ablation success

While success rates for pulmonary vein isolation (PVI) now approach 80% or better for paroxysmal afibbers, the success among persistent afibbers is still relatively poor. Researchers at St. Luke's-Roosevelt Hospital Center in New York now report that electrical cardioversion and pre- and post-treatment with antiarrhythmics (dofetilide, amiodarone or sotalol) for one month before and after the PVI can markedly improve long-term success rate of PVI among persistent afibbers. They found that 81% of 43 persistent afibbers were still in sinus rhythm almost 2 years after their ablation compared to 88% among 142 paroxysmal afibbers.

ACC, 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1164-250, p. 124A

Stroke Risk Factors

Embolic risk markers in LAF patients

PARIS, FRANCE. The presence of SEC (spontaneous echocardiographic contrast) in a transesophageal echocardiogram has been shown to predict the ischemic stroke risk in patients with AF. A team of French and Italian researchers has just completed a study aimed at determining the extent of SEC and other thromboembolic risk markers in patients with AF. Their study included 82 patients with lone atrial fibrillation (LAF) and 289 patients with AF and underlying heart disease. The definition of LAF used by the researchers differed somewhat from the conventional one in that it excluded AF with any of the following features – a history of stroke, coronary artery disease, congestive heart failure, valvular heart disease, cardiomyopathy, cardiomegaly, hypertension (controlled or uncontrolled), hyperthyroidism, diabetes, chronic obstructive pulmonary disease (emphysema and chronic bronchitis). The definition of LAF also excluded AF occurring only during trauma, surgery, or an acute medical illness. The definition used for persistent AF was AF that required electrical or pharmacologic cardioversion or lasted more than 7 days.

Paroxysmal AF was defined as episodes that self-terminated within 48 hours or lasted less than 7 days. Left atrial appendage (LAA) abnormalities were defined as a LAA area greater than 5 square centimeters, an emptying or filling velocity less than 25 cm/second, or the presence of a clot (thrombus) in the LAA or left atrium. All patients underwent conventional transthoracic echocardiography as well as transesophageal echocardiography (TEE) in which the ultrasound probe is placed in the esophagus rather than on the outside chest wall.

The researchers found that 29.3% of LAF patients showed signs of SEC as compared to 49.8% of non-LAF patients. They also observed that LAF patients over the age of 60 years were more likely to have SEC (39.5%) than were patients 60 years or younger (17.9%). Paroxysmal LAF patients were least likely to show SEC (5.9%), while 45.8% of persistent LAF patients had signs of SEC. It was also clear that paroxysmal LAF patients had a significantly smaller left atrial diameter (37.4 mm) than did persistent lone afibbers (40.9 mm). In general, the researchers found the lowest incidence of thromboembolic risk markers in paroxysmal lone afibbers below the age of 60 years. Older age, persistent afib, and the presence of cardiovascular disease or other risk factors markedly increased the incidence of SEC and LAA abnormalities.

Di Angelantonio, E, et al. Comparison of transesophageal echocardiographic identification of embolic risk markers in patients with lone versus non-lone atrial fibrillation. American Journal of Cardiology, *Vol. 95, March 1, 2005, pp. 592-96*

Stroke Prevention

Viable alternative to warfarin?

CHIETI, ITALY. Warfarin therapy is recommended for AF patients at high risk of ischemic stroke. Despite this, its actual use is limited for a variety of reasons, including the difficulty in maintaining INR within prescribed limits (usually 2.0 to 3.0), the substantial risk of internal bleeding and hemorrhagic stroke, contraindication, interactions with herbs and other drugs, and the inconvenience of periodic blood testing. Thus, the search for viable alternatives to warfarin therapy is actively pursued.

Researchers at the Universities of Pisa and Chieti recently evaluated the combination of aspirin and clopidogrel (Plavix) versus warfarin in preventing thromboembolic complications in persistent and permanent afibbers. Their clinical trial included 30 afibbers between the ages of 45 and 75 years (11 women), 12 of whom had non-high-risk permanent afib and 18 of whom had persistent afib and were awaiting electrical cardioversion.

The study participants underwent transesophageal echocardiography (TEE) at the beginning of the trial to check for thrombi and dense spontaneous echo-contrast (SEC), a forerunner of thrombi. None of the participants had any indication of thrombi or SEC. The participants were then randomly assigned to receive warfarin (INR 2.0-3.0) or aspirin/clopidogrel. Warfarin was given once daily before dinner; aspirin (100 mg) was given after lunch, and clopidogrel (75 mg) after dinner. For the first week of the trial aspirin was given alone followed by 3 weeks of the combination.

After 3 weeks on the assigned regimen all participants had another TEE, blood tests for INR and thromboxane B2 (an indicator of platelet activity), and determination of bleeding time. None of the participants had any evidence of SEC or left atrial thrombi. Patients on warfarin, as expected, showed no change in thromboxane B2 level or bleeding time. Patients on aspirin/clopidogrel, as expected, showed no change in INR, but an average 98% decrease in thromboxane B2 and an average 319% increase in bleeding time (from 4 to 16 minutes). Aspirin, on its own, increased bleeding time by 71% with clopidogrel adding an additional 144% increase.

Fourteen of the 18 persistent afibbers underwent successful electrocardioversion (7 in each group) and no SEC or left atrial thrombi occurred in either group during a 3-month follow-up. The researchers conclude that a combination of aspirin and clopidogrel is as effective as warfarin in preventing thromboembolic complications over the short term in low-risk permanent and persistent afibbers. A larger trial (ACTIVE) is now underway with the purpose of evaluating a combination of aspirin, clopidogrel and irbesartan (Avapro) in the prevention of vascular events in AF. NOTE: This study was partially funded by Bristol-Myers Squibb, Italy, a manufacturer of clopidogrel.

Lorenzoni, R, et al. Short-term prevention of thromboembolic complications in patients with atrial fibrillation with aspirin plus clopidogrel. American Heart Journal, *Vol. 148, July 2004, pp. 11-18*

Complications in lone atrial fibrillation

GRONINGEN, THE NETHERLANDS. Dutch researchers involved in trials to determine the relative merits of rate control versus rhythm control in AF have studied the results in a subgroup of lone afibbers. They define lone atrial fibrillation as AF not associated with hypertension or any underlying heart disease. Their study group included 522 patients with AF of which 89 had the lone variety (persistent). The lone afibbers were more likely to be men, tended to be younger (average of 65 years versus 69 years), and had fewer complaints of fatigue and breathing difficulties. During a mean follow-up of 2.3 years three lone afibbers (3%) died from internal bleeding or hemorrhagic stroke. They were all on warfarin at the time of their death with an INR in excess of 3.5. Two patients suffered non-fatal bleeding (also on anticoagulants) and 2 experienced an ischemic stroke or TIA. The two lone afibbers having a stroke or TIA were not taking anticoagulants at the time even though they had one or more additional risk factors for stroke. Among non-lone afibbers, 6 (1%) died from bleeding, while another 16 (4%) suffered serious bleeding. Thirty-three (8%) had a stroke or TIA even though 70% of them were on anticoagulation at the time of their stroke.

None of the lone afibbers suffered severe adverse effects from their antiarrhythmic drugs, while 3% of the non-lone afibbers did so. None of the lone afibbers died from heart disease or heart failure, while 5% of the non-lone afibbers did. Overall, death or serious adverse effects were significantly more common among lone afibbers using rate control than among those using rhythm control, but due to the small sample size the researchers could not conclude whether rate control is an acceptable alternative for patients with persistent lone AF. They do conclude though that lone AF is a far more benign disorder than is AF with underlying heart disease.

Rienstra, M, et al. Clinical characteristics of persistent lone atrial fibrillation in the RACE Study. American Journal of Cardiology, *Vol. 94, December 15, 2004, pp. 1486-90*

Editor's comment: Although the sample size was small, it is clear that the most serious complication facing lone afibbers is death or serious bleeding from inadequately controlled anticoagulation (warfarin) therapy. The study provided no evidence that lone afibbers with no additional risk factors for stroke would benefit from warfarin therapy – actually quite the opposite.

Effectiveness of warfarin questioned

TORONTO, CANADA. The anticoagulant warfarin (Coumadin) is routinely prescribed for elderly patients who have a prosthetic heart valve, have suffered a prior stroke or TIA (transient ischemic attack), or have been diagnosed with atrial fibrillation, diabetes, coronary artery disease, hypertension or heart failure. Although several studies have shown warfarin to be effective in preventing ischemic stroke in high-risk patients, it is also clear that anticoagulation increases the risk of internal bleeding and hemorrhagic stroke.

Researchers at the University of Toronto have just completed an investigation aimed at determining if patients (aged 66 years and older) are at increased risk of stroke if they discontinue warfarin therapy after suffering major trauma. Their study involved 8450 warfarin-taking individuals who had sustained major traumas (82% due to falls) in the period 1992 to 2001. During the 6 months following the trauma, 78% of the study participants resumed anticoagulation with warfarin, while the remaining 22% did not. During an average 3.3 years of follow-up a total of 592 patients (2.2% a year) sustained an ischemic stroke and 399 (1.5% a year) experienced a heart attack (myocardial infarction). There was no difference in the incidence of ischemic stroke and heart attacks between the patients on warfarin and those who had discontinued anticoagulation therapy.

The long-term risk of major hemorrhage (hemorrhagic stroke and internal bleeding requiring blood transfusion) was significantly higher among patients on warfarin (1.9% a year) than among those who had discontinued the drug (1.3% a year). The incidence of deep vein thrombosis was, however, almost twice as high among patients not on warfarin, but was fairly low overall (0.4% a year). There was no difference in the incidence of pulmonary embolism in the two groups. The researchers conclude that discontinuing warfarin in patients prone to falls will not increase their risk of stroke and heart attack, but will materially

reduce the risk of major hemorrhage at the expense of a fairly small increase in the risk of deep vein thrombosis.
Hackam, DG, et al. Prognostic implications of warfarin cessation after major trauma. Circulation, *Vol. 111, May 3, 2005, pp. 2250-56*

Editor's comment: This study certainly casts considerable doubt on the wisdom of routinely anticoagulating elderly patients at risk for ischemic stroke, particularly if they are prone to falls. The slight increase in deep vein thrombosis could easily be counteracted by giving nattokinase to patients not on warfarin. At least one clinical trial has found nattokinase to provide very effective protection against deep vein thrombosis.

Vitamin K stabilizes INR in warfarin therapy

NEWCASTLE, UNITED KINGDOM. Maintaining an INR (International Normalized Ratio) in the therapeutic range (usually 2.0-3.0) when on warfarin (Coumadin) therapy can be problematical. Some studies have concluded that patients on warfarin are out of range at least a third of the time. Too low an INR increases the risk of an ischemic stroke, while too high a reading increases the risk of a hemorrhagic stroke or a major internal bleeding event. Warfarin works by reducing the amount of vitamin K available for the synthesis of clotting factors II, VII, IX and X. Patients on warfarin are therefore often counseled to avoid dark green leafy vegetables (the major dietary source of vitamin K) and to strictly avoid vitamin K-containing supplements.

British researchers now report that minimizing vitamin K intake while on warfarin might be precisely the wrong thing to do. Their study involved 26 patients (stable) whose INR had remained within the therapeutic range for at least 6 months without a change in warfarin dosage. The daily vitamin K intake of these patients was compared to that of 26 patients (unstable) whose INR had been varying considerably (standard deviation of INR values greater than 0.5) over a 6-month period and thus requiring continuous adjustment of warfarin dosage. All participants carefully weighed their food intake for two 7-day periods and completed detailed food diaries. Analysis of the data showed that the unstable patients had a significantly lower average daily intake of vitamin K (K_1) than did stable patients (29 versus 76 micrograms/day). As a matter of fact, the daily vitamin K intake of the unstable patients was significantly lower than the daily intake of 60-80 micrograms estimated for the general UK population.

The researchers conclude that INR levels can be stabilized by increasing daily vitamin K intake. They point out that even a daily increase in vitamin K intake of 100 micrograms has comparatively little effect on INR (reduction of about 0.2). While it would be theoretically possible to

improve the consistency of daily vitamin K intake through a strictly controlled diet, it is unlikely that this would be a viable solution. The researchers conclude their report with the statement, "Daily supplementation with vitamin K could be an alternative method in stabilizing anticoagulation control, lessening the impact of variable dietary vitamin K intake. We are currently evaluating this possibility."

Johannes Oldenburg, a German medical researcher, concurs and suggests that a continuous low-dose intake of vitamin K may stabilize the INR and subsequently reduce risk of bleeding complications.

Sconce, E, et al. Patients with unstable control have a poorer dietary intake of vitamin K compared to patients with stable control of anticoagulation. Thrombosis and Haemostasis, *Vol. 93, May 2005, pp. 872-75*

Oldenburg, J. Vitamin K intake and stability of oral anticoagulant treatment. Thrombosis and Haemostasis, *Vol. 93, May 2005, pp. 799-800*

Editor's comment: This is indeed a revolutionary study. The idea of avoiding vitamin K when taking warfarin is firmly entrenched in the medical community. So firmly in fact that vitamin K supplements and multivitamins containing vitamin K are banned in Canada, so as to "protect" the small minority of the Canadian population who are on warfarin therapy. Seemingly no thought has been given to the thousands and thousands of Canadians who may develop osteoporosis due to a lack of vitamin K. Hopefully, this will all change now! The immediate practical implication of the study is for anyone who has trouble controlling their INR to supplement with 50-75 micrograms/day of vitamin K – with their doctor's approval, of course.

Warfarin therapy in very old people

CHELTENHAM, VICTORIA, AUSTRALIA. Warfarin therapy is recommended for afibbers over the age of 75 years in order to lessen the risk of an ischemic stroke. However, there is some concern that the reduced risk of ischemic stroke may be offset by an increased risk of hemorrhagic stroke and internal bleeding. Australian researchers recently addressed this concern in a study involving 933 patients (aged 76 years and older) admitted to hospital with atrial fibrillation during the period July 1, 2001 to June 30, 2002. All the patients had at least one other risk factor for stroke (previous stroke, diabetes, hypertension or heart failure) and all were quite frail (average age of 81 years). About 25% (228 patients) were prescribed warfarin upon discharge (INR between 2.0 and 3.0). The researchers followed these patients until October 1, 2003 at which time 158 (69%) were still alive and 70 (31%) had died. (Editor's note: It is indeed unfortunate that the remaining 705 patients not on warfarin were excluded from the study. Having followed them as well would have provided a baseline against which the efficacy of warfarin could have been compared.)

During the follow-up there was a total of 17 strokes affecting 16 people. Five of the strokes occurred among patients who were within the specified INR range of 2.0 to 3.0 at the time of the stroke, 6 occurred while patients had an INR below 2.0, and the remaining 6 occurred while the patients had stopped taking warfarin. The total follow-up period for the study was 530 person-years corresponding to an annual ischemic stroke rate of 2.6%. During this period 41 patients experienced 53 episodes of major bleeding. The annual event rate of major hemorrhage was 10% and that of fatal hemorrhage was 0.9%. Forty-five per cent of the 53 major bleeding events were classified as serious, 45% as life threatening, and 10% as fatal. Most of the hemorrhages (64%) occurred in patients who had been on warfarin for more than a year. Two gastrointestinal hemorrhages, 2 intracranial hemorrhages (hemorrhagic stroke), and 1 acute anemia caused the 5 fatal bleeding events. The researchers conclude by recommending that warfarin be used in preventing ischemic stroke in an older, frail population.

Johnson, CE, et al. People aged over 75 in atrial fibrillation on warfarin: the rate of major hemorrhage and stroke in more than 500 patient-years of follow-up. Journal of the American Geriatrics Society, *Vol. 53, April 2005, pp. 655-59*

Warfarin interactions with food and drugs

TORONTO, CANADA. Warfarin (Coumadin) is prescribed for the prevention of ischemic stroke and deep venous thrombosis in patients with atrial fibrillation, prosthetic heart valves, venous thromboembolism, and coronary artery disease. The major potential adverse effects of warfarin are hemorrhagic stroke and internal bleeding. The blood level of warfarin must be controlled within very narrow limits in order to ensure that clots don't form while avoiding internal bleeding. It is becoming increasingly clear that controlling warfarin levels is not a simple matter and that many drugs and foods either potentiate warfarin's effect making bleeding more likely, or reduce warfarin's effect making thrombosis and stroke more likely.

A team of Canadian medical doctors and pharmacists recently reviewed the medical literature from 1993 to March 2004 in order to compile a verified list of important interactions between warfarin and foods, supplements, and other drugs. The most probable and best-verified interactions are presented in the tables below.

Interactions that **inhibit** warfarin's effect

Highly probable

Drugs	Foods & Herbs
Cholestyramine	
Mercaptopurine	
Mesalamine	
Ribavirin	
Trazodone	

Probable

Azathioprine	Ginseng
Bosentan	
Dicloxacillin	
Ritonavir	

Interactions that **potentiate** warfarin's effect

Highly probable

Drugs	Foods & Herbs
Acetaminophen (Tylenol)	Boldo/fenugreek mixture
Ciprofloxacin	Fish oil
Citalopram	Mango
Diltiazem	Quilinggao
Entacapone	
Fenofibrate	
Miconazole	
Sertraline	
Voriconazole	
Zileuton	

Probable

Amoxicillin	Danshen
NSAIDs	Dong quai
COX-2 inhibitors	Grapefruit juice
Fluorouracil	
Fluvastatin	
Fluvoxamine	
Gemcitabine	

There are no credible studies supporting an interaction between warfarin and the following drugs and foods – alcohol, antacids, atenolol, clopidogrel, fluoxetine (Prozac), metoprolol, naproxen, psyllium, ranitidine, vitamin E, atorvastatin (Lipitor), coenzyme Q10, ginkgo biloba, ibuprofen, and influenza vaccine.

The researchers point out that there are now so many potential interactions between warfarin and other drugs that it would be impossible for a physician or pharmacist to remember them all. They recommend that doctors prescribing other drugs to patients on warfarin keep in mind that many drugs in the following groups can increase or inhibit the effect of warfarin:

- Antibiotics and antifungal agents
- Cardiovascular drugs (including propafenone, amiodarone, and cholesterol-reducing drugs)
- Painkillers
- Anti-inflammatories
- Central nervous system drugs (citalopram, sertraline)
- Gastrointestinal drugs (cimetidine, omeprazole)
- Anabolic steroids

Holbrook, AM, et al. Systematic overview of warfarin and its drug and food interactions. Archives of Internal Medicine, *Vol. 165, May 23, 2005, pp. 1095-1106*

Editor's comment: It is of particular interest that this latest study found no credible evidence that supplementing with vitamin E, ginkgo biloba, or coenzyme Q10 has any effect on the efficacy or safety of warfarin therapy. The study did, however, note that concomitant use of fish oils is likely to potentiate warfarin.

Benefits and risks in warfarin therapy

SAN FRANCISCO, CALIFORNIA. A team of researchers from the University of California, the Massachusetts General Hospital and Boston University School of Medicine has just completed a study aimed at determining whether women with afib have a higher risk of ischemic stroke than do men. The study included 13,559 adults with atrial fibrillation. The majority of the study participants had one or more recognized risk factors for stroke, such as hypertension (57.7%), congestive heart failure (26.7%), coronary artery disease (23.9%), or diabetes (14.2%). Only 15.8% of women and 23.8% of men could be classified as non-hypertensive lone afibbers.

The overall incidence of ischemic stroke during 15,494 person years was 2.4%. The annual average rate on warfarin was 1.5% for women and 1.2% for men as compared to 3.5% and 1.8% when not on warfarin. However, the rate among lone afibbers (not on warfarin) with no additional risk factors for stroke was only 0.6% for women and 0.5% for men – in other words, no higher than would be expected in the general population.

The incidence of major hemorrhage (fatal bleeding, blood transfusion requiring two units or more of packed blood cells, or bleeding into a critical anatomical site) was 1.0% a year among warfarin-treated women and 1.1% among men. Of the major hemorrhages 0.36% among women and 0.55% among men were intracranial (hemorrhagic stroke). The authors of the study point out that, "the health consequences of intracranial hemorrhage are worse than those resulting from the ischemic strokes we seek to prevent through anticoagulation."

Fang, MC, et al. Gender differences in the risk of ischemic stroke and peripheral embolism in atrial fibrillation. Circulation, *Vol. 112, September 20, 2005, pp. 1687-91*

Editor's comment: These recent findings confirm earlier ones that neither men nor women with LONE atrial fibrillation and no other risk factors for stroke benefit from warfarin therapy. As a matter of fact, for this group the risk of major hemorrhage is almost twice as high as the risk of ischemic stroke and the risk of hemorrhagic stroke for men on warfarin is actually higher than the risk of ischemic stroke when not on warfarin. Even for lone afibbers with one additional minor risk factor such as hypertension, diabetes or age over 75 years, the benefits of warfarin therapy are not at all clear-cut. Women with one additional risk factor would have an annual ischemic stroke risk of 1.8% if not on warfarin. On warfarin this risk would be reduced to 0.7%, but would be accompanied by a 1.0% risk of major hemorrhage of which 0.36% would be associated with hemorrhagic stroke. For men the ischemic stroke risk when not on warfarin would be 1.2%. On warfarin this would be reduced to 0.7%, but would be accompanied by a 1.1% risk of major hemorrhage of which 0.55% would involve hemorrhagic stroke – in other words, pretty well a toss-up.

Age-related risk of warfarin therapy

LEIDEN, THE NETHERLANDS. The risk of a thromboembolic event [ischemic stroke (cerebral infarction), heart attack (myocardial infarction), or peripheral arterial embolism] increases sharply with age, especially in patients with mechanical heart valve prostheses, atrial fibrillation, or a prior heart attack. These patients, especially older ones, are commonly prescribed warfarin in order to reduce the risk of a thromboembolic event. Unfortunately, warfarin therapy is associated with an increased risk of major hemorrhage (mainly gastrointestinal) and hemorrhagic stroke.

Researchers at the Leiden University Medical Center have recently completed a study to determine the relative risks of thromboembolic and bleeding events in patients treated with warfarin. The study included 4202 patients treated at a regional anticoagulation clinic. Half of these patients were on warfarin because of atrial fibrillation and their target INR

was 2.5 to 3.5. The remaining patients were on warfarin because they had experienced a heart attack or had a mechanical heart valve. At baseline about 13% of patients in the entire study group was under the age of 60 years, 24% were between the ages of 60 and 70 years, 40% between 71 and 80 years, and the remaining 23% were over the age of 80 years.

Overall, the warfarin-treated patients were within their INR target range 61-68% of the time. The incidence (%/year) of ischemic stroke (fatal and non-fatal), heart attack (fatal and non-fatal), hemorrhagic stroke, and major bleeding are listed below for the various age groups.

	Less than 60 years	61-70 years	71-80 years	80+ years
Fatal ischemic stroke	0%	0%	0%	0%
Non-fatal ischemic stroke	0.1%	0.4%	0.2%	0.5%
Fatal heart attack	0.3%	0.3%	0.3%	0.5%
Non-fatal heart attack	0.6%	0.7%	1.0%	1.3%
Total thromboembolic incidence	**1.0%**	**1.4%**	**1.6%**	**2.4%**
Fatal hemorrhagic stroke	0.1%	0.3%	0.3%	0.2%
Non-fatal hemorrhagic stroke	0%	0.2%	0.4%	0.4%
Fatal major bleeding	0%	0.04%	0.07%	0.09%
Non-fatal major bleeding	0%	1.5%	1.8%	3.6%
Total bleeding incidence	**1.5%**	**2.1%**	**2.5%**	**4.2%**

From the above results it is indeed hard to conclude that warfarin therapy confers any overall benefit at any age, especially when considering only fatal strokes. It is of considerable concern that the incidence of fatal hemorrhagic strokes was about 0.3% versus 0% for ischemic stroke.

A detailed breakdown is not available for atrial fibrillation patients, but the following summary data again point to a distinct disadvantage of warfarin therapy at any age.

	Less than 60 years	61-70 years	71-80 years	80+ years
Incidence of thromboembolism	0.3%	1.6%	1.4%	1.8%
Incidence of hemorrhage	0.5%	1.9%	3.0%	4.5%

The researchers conclude that anticoagulant treatment in elderly patients presents a major clinical dilemma and state that, "The question is whether an overall benefit remains for elderly patients who are treated with oral anticoagulants."

Torn, M, et al. Risks of oral anticoagulant therapy with increasing age. Archives of Internal Medicine, *Vol. 165, July 11, 2005, pp. 1527-32*

Editor's comment: Although the target INR of 2.5 to 3.5 employed in this study is higher than the standard range (2.0 to 3.0) used in North America the results certainly cast considerable doubt on the benefits of warfarin therapy for stroke prevention in atrial fibrillation patients, especially those with LONE atrial fibrillation. The Dutch results also cast doubt on the generally accepted idea that afibbers over 75 years need to be on warfarin. With the incidence of hemorrhagic events being 2.5 times higher than the incidence of ischemic events for patients 80 years or older the benefits are not easy to discern.

Odds and Ends

Pacemakers – longevity versus size

NEW YORK, NY. For the last few years manufacturers of pacemakers and implantable cardioverter defibrillators (ICDs) have made great strides in miniaturizing their products so as to make the implant less noticeable. This size reduction has, however, to a large extent come from the use of smaller and less durable batteries. Researchers at the Albert Einstein College of Medicine in New York recently completed a survey to determine if patients would prefer a smaller implant with a smaller battery and a commensurate shorter period before battery replacement surgery or a larger device with longer battery life.

The answer to the survey involving 156 patients was pretty unanimous – 90% preferred a larger device with a battery life of 5-9 years rather than a smaller one with a battery life of 3-7 years. There was no significant different in preference between men and women nor between younger and older patients, nor between patients with a first or replacement implant. The researchers conclude that the message is clear. Device longevity is more important than size.

Wild, DM, et al. Pacemakers and implantable cardioverter defibrillators: device longevity is more important than smaller size. PACE, *Vol. 27, November 2004, pp. 1526-29*

Atenolol in the treatment of hypertension

GOTHENBURG, SWEDEN. Atenolol (Tenormin) is a popular beta-blocker used widely in the treatment of high blood pressure (hypertension). It is also used to lower heart rate in atrial fibrillation patients.

Swedish researchers recently released a report comparing atenolol to placebo and other antihypertensive drugs. The 4 studies comparing atenolol to placebo or no treatment found that atenolol was quite effective in lowering blood pressure, but had no effect in preventing heart attack, cardiovascular death, or death from any cause. One of the 4 studies did, however, conclude that atenolol reduced the risk of stroke. The 5 studies (involving 17,671 patients followed up for a mean of 4.6 years) comparing atenolol to other antihypertensives (hydrochlorothiazide, captopril, losartan and lacidipine) found that all drugs lowered blood pressure to a similar degree, but that atenolol-treated patients had a 13% higher overall mortality, and a 30% higher risk of stroke than did patients treated with the other drugs. Other studies have shown that other beta-blocking agents such as metoprolol, propranolol, and timolol significantly

increase survival time after a heart attack, while atenolol has no such effect.

The researchers conclude that their meta-analysis casts doubt on the suitability of atenolol as a first-line antihypertensive drug and as a reference drug in the evaluation of other antihypertensive drugs. NOTE: Most of the authors of this study had received grants from pharmaceutical companies including AstraZeneca, the manufacturer of Tenormin.
Carlberg, B, et al. Atenolol in hypertension: is it a wise choice? The Lancet, *Vol. 364, November 6, 2004, pp. 1684-89*

Editor's comment: This study basically concludes that, while atenolol does not increase overall or cardiovascular mortality compared to placebo or no treatment, there are other antihypertensive drugs that do indeed reduce mortality compared to atenolol.

PVA in patients with mitral valve prostheses

MILAN, ITALY. Many patients with artificial mitral valves have or will eventually develop AF. Up until now pulmonary vein ablation (PVA) in these patients has been thought to be a somewhat dicey proposition due to the inherent danger of damaging the valve during the PVA and also because patients with artificial valves tend to have enlarged and scarred atria.

Dr. Carlo Pappone and his colleagues at San Raffaele Hospital now report that PVAs can be successfully performed in patients with mitral valve prostheses (MVP). Their study involved 26 MVP patients and 52 controls matched for age, gender, left atrial diameter, type of afib (paroxysmal or chronic), history of hypertension, and left ventricular ejection fraction. Thirteen of the MVP patients had paroxysmal AF and 13 had the permanent (chronic) variety. A transesophageal echocardiogram (TEE) was performed prior to the procedure to ensure the absence of thrombus in the left atrial appendage.

The patients and controls all underwent circumferential pulmonary vein ablation with 81% of patients in both groups receiving additional linear lesions between the lateral mitral valve annulus and the left inferior pulmonary vein as well as posterior lines joining the contralateral superior and inferior veins. The procedure was performed in whatever rhythm (sinus or fibrillation) the patient was in at the start of the procedure.

At the 12-month follow-up 73% of the MVP patients were in sinus rhythm as compared to 75% among controls. Fluoroscopy times were, however, longer for MVP patients than for controls – 35 minutes versus 21 minutes, and 3 complications (one TIA) were observed in the MVP

patients versus none in the controls. MVP patients were also more likely to develop atrial tachycardia after the procedure (6 MVP patients versus 1 control) and 3 MVP patients needed a repeat procedure to correct this problem. The Italian EPs conclude that the presence of a MVP does not affect the success rate of a circumferential pulmonary vein ablation, but is associated with longer fluoroscopy time and a greater risk of complications and the subsequent development of atrial tachycardia.

Lang, CC, et al. Transcatheter radiofrequency ablation of atrial fibrillation in patients with mitral valve prostheses and enlarged atria. Journal of the American College of Cardiology, *Vol. 45, March 15, 2005, pp. 868-72*

Aspirin at bedtime reduces blood pressure

SANTIAGO DE COMPOSTELA, SPAIN. Low-dose aspirin (acetylsalicylic acid) is widely used on a daily basis to help prevent cardiovascular events such as stroke and heart attack. Spanish researchers now report that 100 mg aspirin taken at bedtime is also effective in reducing blood pressure in patients with untreated hypertension. Their clinical trial involved 113 men and 215 women (average age of 44 years, range of 23-79 years). The participants had all been diagnosed with mild essential hypertension defined as a systolic blood pressure between 140 and 159 mm Hg or a diastolic pressure between 90 and 99 mm Hg. Heavy drinkers, smokers, and heavy exercisers were excluded from the study.

The patients were randomized into three groups and were all given appropriate diet and lifestyle instructions. The first group of 169 received no drugs, the second group of 77 patients received 100 mg aspirin upon awakening, and the third group received 100 mg aspirin before bedtime. At baseline the participants all had similar blood pressures (systolic average of 147 mm Hg, diastolic average of 85 mm Hg) and no statistically significant difference in a wide range of other variables measured. The blood pressure and heart rate of each participant were automatically measured every 20 minutes from 7 AM to 11 PM and every 30 minutes during the night for 48 hours, both at baseline and again after 3 months of the aspirin regimen.

Comparing baseline results with results after 3 months revealed no difference in blood pressure or heart rate in the control group (no aspirin). The group receiving aspirin upon awakening experienced a slight, but significant INCREASE in blood pressure during sleep (3.4 mm Hg increase in systolic and 2.0 mm Hg increase in diastolic). The group taking aspirin before bedtime, on the other hand, experienced a significant DECREASE in blood pressure, which was evident both during the day and at night (average 6.8 mm Hg drop in systolic and 4.6 mm Hg drop in diastolic). None of the groups experienced any significant differences in heart rate or a wide variety of other variables measured.

The researchers speculate that aspirin may be more effective if taken at bedtime because it inhibits both angiotensin II and renin production,

which tends to peak at night. It is also possible that aspirin works by inhibiting the production of superoxide and thereby promotes the synthesis of the blood vessel wall relaxing nitric oxide. They also point out that taking aspirin in the evening rather than in the morning has been found to result in 37% fewer gastrointestinal hemorrhages. Administering aspirin at bedtime rather than in the morning has also been found beneficial in the prevention of preeclampsia, gestational hypertension, intrauterine growth retardation, and preterm delivery in high-risk pregnant women. Of course, there is also considerable evidence that daily aspirin is effective in preventing stroke and a second heart attack.

Hermida, R, et al. Aspirin administered at bedtime, but not on awakening, has an effect on ambulatory blood pressure in hypertensive patients. Journal of the American College of Cardiology, *Vol. 46, September 20, 2005, pp. 975-83*

Editor's comment: The finding that aspirin reduces blood pressure when taken at bedtime, but not in the morning, was reported earlier by PeggyM, one of our regular Bulletin Board contributors – it is nice to see this confirmed. The observation that aspirin "works" (for blood pressure control) when taken at bedtime, but not in the morning, is a typical example of chronobiology in action. It is to be hoped that it will give a shot in the arm to emerging field of chronopharmacology, which aims to determine the most effective time to administer common drugs. NOTE: Chinese medicine has used chronopharmacology for thousands of years. In any case, there would seem to be much to gain and nothing to lose by taking one's daily aspirin before bedtime rather than in the morning.

Pretreatment improves conversion rates

Afibbers with the persistent variety require electrical cardioversion in order to regain normal sinus rhythm (NSR). Greek researchers now report that pretreatment (for 4 weeks) with amiodarone (Cordarone) or the beta-blocker carvedilol (Coreg) prior to cardioversion improves the acute success rate and lengthens the time in NSR after the conversion. Their randomized study of 145 patients with persistent AF found that the conversion rate among those pretreated with amiodarone was 93.3% as compared to 91.5% for carvedilol-treated patients and 73% for those given a placebo. The percentage of patients whose afib recurred within the first month after cardioversion was 16.6% for amiodarone, 27.9% for carvedilol, and 39.4% for placebo. The researchers noted that patients on amiodarone experienced significantly fewer ectopic beats after conversion than did those in the other two groups.

ACC 54th Annual Scientific Session. Journal of the American College of Cardiology, Vol. 45, Suppl. A, No. 3, February 1, 2005, Abstract 1021-253, p. 92A

Research Reports

P Cells and Potassium

by Patrick Chambers, MD

Introduction

The late great French cardiologist Philippe Coumel, a giant in the field of arrhythmias who also wrote the foreword for *Lone Atrial Fibrillation: Towards A Cure* by Hans Larsen, was the first to describe vagally mediated atrial fibrillation (VMAF) about 20 years ago. His seminal patient went into AF upon reclining but could terminate the episode upon standing. It is difficult to believe that such a dramatic disease could go unnoticed prior, unless, of course, it didn't exist prior. This suggests that environment plays a significant role in its genesis. To quote from Hans' new book *Lone Atrial Fibrillation: Towards A Cure - Volume 2*, Coumel "developed the concept of the triangle of arrhythmogenesis". "There are always three main ingredients required for the production of a clinical arrhythmia, the arrhythmogenic substrate, the trigger factor and the modulation factors of which the most common is the autonomic nervous system." The role of the ANS in the genesis of AF is obvious to all. Identification of the arrhythmogenic substrate (the tissue in which the arrhythmia starts and propagates) and the trigger factor have been more problematic.

Arrhythmogenic Substrate (P Cells)

Many LAFers are consumed by the search for their AF trigger, some specific item present or absent from their diet. Although this search will undoubtedly improve their general health, for the vast majority frustration will be a constant companion. And this is because of the arrhythmogenic substrate that all LAFers share.

P is for pole cells and they are the pacemaker cells of the heart. These have traditionally been described only in nodal tissue (SA node and AV node). However, in August of 2003 the Cleveland Clinic group was the first to describe P cells in human pulmonary veins (PVs) near their entry into the left atrium. They were found at autopsy in 4/4 AF patients and in 0/6 controls (one without history of tachyarrhythmia and five heart transplant donors). To date they have not been described anywhere else in the heart outside of nodal tissue.

Pacemaker cells are unique in that they slowly depolarize by themselves, hence their greater inherent automaticity. This is due to their unique Na (sodium) and K (potassium) ion channels. They are regulated by the opposing influence of sympathetic (adrenergic) and parasympathetic

(vagal) stimulation. Both of these, but especially the vagus, cause shortening of the effective refractory period (ERP). The refractory period is the rest period following a contraction of the heart muscle. Individual heart cells do not respond to stimulation during this period so ectopic beats or afib cannot be initiated during the ERP. A shortened ERP thus increases the risk of ectopics and afib.

In September of 1998 the Bordeaux group published an electrophysiologic (EP) study of 45 patients with frequent paroxysmal AF. They looked at the location of the triggering atrial ectopic beats and found that 94% were located in the PVs (2-4 cm inside the veins). I'm not sure what per cent of those with paroxysmal AF qualify as lone (LAF), but I would guess that if one accepts any degree of hypertension in the definition of LAF, it would be a clear majority.

In October of 2002 this same group published another EP study of 28 patients with paroxysmal AF (average age about 50) v. 20 age-matched controls. They evaluated the effective refractory period (ERP) of cells in the pulmonary veins and the atrial ERP (AERP) in both groups. First they found that AERP did not differ between the two groups. However, in the AF group the PV ERP was SHORTER than the AERP, whereas in the control group it was LONGER. Furthermore, they found that there was greater dispersion of PV conduction velocity in the AF patients, and that in these same patients AF was more easily induced (by fast pacing) in the PVs (22/90) than in the left atrium (1/81). Consequently, this PV refractoriness and dispersion of conduction properties create a substrate favorable for reentry. It would appear to me that these PVs represent the oft-quoted but elusive "defective substrate" or "arrhythmogenic substrate" of LAF. This is what is responsible for "the loss of physiologic rate adaptation" present in AF, e.g., conditions that should slow down the heart (slower conduction velocity, shortened refractory period) often result in a tachyarrhythmia instead.

Putting these studies together paroxysmal AFers appear to have a problem with their PVs. It would seem logical to implicate P cells in this process. The increasingly successful reports of catheter ablation via pulmonary vein isolation (PVI) for LAF are certainly consistent with this interpretation. Whether these P cells have been damaged by free radicals or not remains to be determined, although delayed onset of LAF is suggestive of this. Free radical damage to PVs is further supported by the frequent occurrence of AF after surgery. The mechanism involves lipid peroxidation (damage to cell walls caused by ROS or reactive oxygen species, especially peroxynitrite). It is also called ischemic reperfusion injury. Please see pp. 137-138 of Hans' book *Lone Atrial Fibrillation: Towards A Cure* for an eloquent description of how this relates to AF and the PVs. Furthermore, the demonstrated abnormalities in refractory

period, conduction velocity, and dispersion in the PVs of LAFers involves many sodium, potassium and calcium channels. This finding is much more consistent with indiscriminate damage to cell membranes due to ROS than that rendered by some specific genetically determined channelopathy. The $64 question: We all know that LAF is more frequently encountered in endurance athletes (five times more in one study). Is their primary problem an arrhythmogenic substrate created by such action of ROS or is enhanced vagal tone more contributory to their VMAF (or both)? Vitamin C and magnesium have both been shown to be instrumental in preventing damage due to ROS.

Trigger Factor (Low Potassium)

Information on a diurnal rhythm for potassium, if any, is hard to find in the medical literature. I initially assumed that because blood potassium is so intimately associated with aldosterone, any possible diurnal rhythm would follow that of aldosterone (and ACTH/cortisol). But such is not the case.

The diurnal rhythm of aldosterone secretion in healthy individuals parallels that of cortisol and is ACTH dependent. The lowest values are observed from midnight to 4AM. Values peak in the morning around 8AM after which there is a gradual decline throughout the day (assuming a normal sleep-wake cycle).[1]

Furthermore, cortisol and ACTH are not always secreted uniformly throughout the day. Episodic spikes can occur when the body is stressed, e.g., fasting, anxiety, etc. Otherwise, in humans, urinary potassium excretion peaks in the early morning between 0530 and 0730 with a minimum at night from 2100 to 0530. Therefore, the diurnal rhythm of urinary potassium excretion seems to be controlled by the diurnal rhythm of cortisol and/or aldosterone. Not so for blood potassium.

Plasma potassium follows a diurnal rhythm with a peak at noon and a trough at midnight with an average peak-to-trough difference of 0.62 +/- 0.05 mmol/L.[2]

In other words blood potassium is lowest when aldosterone secretion is lowest and blood potassium climbs as blood aldosterone/cortisol are peaking. This seems somewhat contradictory. Is this excreted potassium coming from inside the cells? If aldosterone/cortisol are not driving this drop in blood potassium, what is? A partial answer may be insulin.

As an aside, blood magnesium peaks around 0330 and reaches its lowest point around 1530. Its diurnal variation is greater than that of blood potassium. We all know how critical magnesium is to the maintenance of intracellular potassium.[3]

According to one study, the frequency of hypokalemia (potassium less than or equal to 3.5 mmol/L) is related to the time at which the blood potassium is measured.[4]

Not many blood samples for evaluation of potassium are drawn in the evening, especially around midnight (its diurnal nadir). How many people with lower range blood potassium values on specimens drawn during a daytime visit to the doctor's office are frankly hypokalemic at midnight?

Blood potassium values decrease postprandially because of insulin released in response to an ingested carbohydrate load. Blood potassium after our largest meal of the day (dinner in America) slowly declines due to insulin.

Insulin induced cellular uptake of glucose affects blood potassium in the following manner: Similar to Na, entry of glucose into a cell brings water with it, thereby decreasing the concentration of intracellular potassium. The ATP (requires magnesium) sensitive Na+/K+ pump is then stimulated to increase intracellular potassium. Blood potassium consequently drops.

This insulin-induced uptake of glucose (and potassium) occurs primarily in fat, liver and muscle, including cardiac muscle. However, cardiac muscle (v. skeletal muscle) is relatively less dependent on glucose generated ATP and relatively more dependent on oxygen generated ATP. This latter process occurs in the mitochondria and is called cellular respiration. Heart muscle cells have the greatest concentration of mitochondria at about 5,000 per cell. By weight 40% of each heart cell is mitochondria. [This is one reason why CoenzymeQ10 (protects mitochondria from oxidative damage) deficiency associated with statin therapy is causing an epidemic of heart failure.] Also, the cell membrane of the heart is HIGHLY permeable to potassium ions (there are many passive potassium channels). Therefore, it would seem that beneficial glucose and potassium uptake by the heart is relatively less helpful and that the potassium concentration gradient for the heart becomes relatively more problematic (v. skeletal muscle, smooth muscle, liver and fat cells). For spontaneously depolarizing P cells (specialized nerve cells) gradient rules!

Furthermore, aerobic training is associated with enhanced insulin sensitivity in skeletal muscle but diminished insulin-stimulated glucose (and potassium) uptake in the heart.[5]

Perhaps such conditioning enhances oxygen exchange so much so that glucose is relegated to an even less significant role as an energy substrate for the heart. Aging further diminishes this insulin sensitivity in the heart. So, especially in the physically fit and the elderly, low blood potassium is more likely to cause arrhythmia.

In one study comparing response to orthostatic challenge between those with high vagal tone and those with low vagal tone “a significant increase in plasma renin activity was found during LBNP (lower body negative pressure) in the HI responders only”.[6]

In other words prolonged standing or the equivalent causes a greater release of aldosterone in those with high vagal tone. During this time, e.g., a round of golf, aldosterone secretion is increased. In VMAFers this is a mixed bag, aldosterone is vagolytic (lengthens ERP) but the potassium loss it induces shortens ERP. While relaxing afterward blood aldosterone drops and its protective effect is lost but not the damage it has done to the potassium gradient. Combine this with a concomitant drop in blood glucose and AF risk is maximized. Much of this was discussed in Session 33 of the Conference Room Proceedings.[7]

Since a one mmole reduction in blood potassium generally translates to a deficit of about 300 mmoles of total body potassium, about 7 grams of potassium must move from the intracellular compartment to the extracellular compartment between its blood concentration trough and its peak.[8]

Part of the intracellular deficit so created is addressed by dietary potassium, but the RDA for potassium is only 3.5 gm in both America and Europe. And this dietary intake is offset by that lost in the urine.

This diurnal nadir of blood potassium certainly correlates well with the preponderance of night time episodes. Indeed the diurnal contribution of the PNS (vagal tone increases during the night, assuming a normal sleep wake cycle) seems to have camouflaged the diurnal contribution of low blood potassium to night time episode.

What to do about it?

Last year Hans brought to my attention an article by Dr Allan Struthers (“What Is the Optimum Serum Potassium Level in Cardiovascular Patients?” - 2004) in which he states that potassium supplementation is pretty useless at least in heart failure patients in the absence of an aldosterone antagonist, e.g., spironolactone or eplerenone. "A serum potassium increase of 0.25 mmol/L elevates serum aldosterone concentrations by 50% or 100%.” Since most of supplemental potassium is absorbed and then distributed in the blood (total blood volume is about 5 liters), just over 1 mmole or about 50 mg of ingested potassium should result in a 50-100% increase in aldosterone.

According to Struthers et al., "Clinicians can be comforted by the fact that hyperkalemia does not typically occur in patients with normal renal status, because large potassium loads are efficiently and rapidly excreted."[9]

Dr. Michael Lam (www.lammd.com) on p. 246 of his book *How to Stay Young and Live Longer* indicates 15 gm daily potassium as safe in a healthy adult. In a study of eight patients with long QT syndrome the equivalent of 250 mg of spironolactone and 9 gm of supplemental potassium daily (70 kg person) increased blood potassium from 4.0 to 5.2 mmoles/L. Four weeks of this therapy resulted in no serious complications.[10]

So, the combination of an aldosterone antagonist with potassium is certainly effective and does not seem to pose excessive risk. However, although I'm a physician, I'm not your physician and this is not a blank endorsement of the above combination.

Furthermore, these aldosterone antagonists appear to be more effective in increasing blood potassium in the morning and ineffective in the evening. This latter finding is certainly consistent with the diurnal rhythm of aldosterone. It's hard to block aldosterone, if it's not being secreted (evening). Angiotensin converting enzyme inhibitors (ACEIs) decrease urinary potassium excretion and, according to most studies, increase blood potassium.[11]

Although decreased urinary potassium excretion translates to increased blood potassium, changes in blood potassium directly stimulate aldosterone secretion without the renin angiotensin system (RAS). And ACTH, responsible for the diurnal rhythm, also works independently of the RAS.

As another aside, simultaneous supplementation of magnesium with potassium and an aldosterone antagonist increases cellular uptake of both potassium and magnesium.

It is important to remember that blood potassium levels may vary for reasons other than diurnal variation. Insulin and catecholamines cause transcellular shifts of potassium. The latter also causes urinary potassium wasting. Orthostatic challenge, e.g., prolonged standing or exercise, can also cause urinary potassium wasting via increased RAAS induced aldosterone. This would be more common amongst VMAFers, since they hyper respond with aldosterone during such activities (see above). And, of course, stress does the same for ALAFers (adrenergic lone atrial fibrillation).

On pp. 63-64 of Hans' book it is reported that excessive vagal tone is associated with a flat GTT (glucose tolerance test) curve. In other words VMAFers may have a more prolonged response to insulin. Perhaps the explanation for this lies in hepatic insulin sensitizing substance (HISS). This substance is secreted by the liver under the control of the vagus nerve.[12]

Increased insulin sensitivity would certainly be useful in those whose caloric intake was occasionally insufficient for their daily energy expenditure (endurance athletes). Many LAFers have reported an increase in episodes during weight loss.

So, in VMAF insulin or hypoglycemia (transcellular shifts or urinary potassium wasting respectively) may be the predominant determinant for triggering a daytime episode. In ALAF it might be stress-induced cortisol/aldosterone. All appear to work by increasing the potassium gradient. Emphasis on steady potassium supplementation throughout the day from the moment we arise to bedtime would seem to be a good idea for all LAFers. Decreasing salt intake might also prove beneficial, since it causes urinary potassium wasting. Addition of a potassium sparing diuretic might improve not only this gradient but also magnesium balance as well. In ALAF the contribution of the potassium gradient may be relatively greater than in VMAF, where vagal tone is more critical (see below equation). Obviously under appropriate conditions (a round of golf – see above) aldosterone may aggravate VMAF and insulin can do the same for ALAF.

One brief word on "Waller water". This is an aqueous magnesium preparation divined by our own Erling Waller. He was one of the first to realize that many LAFers may owe their malady to magnesium deficiency, at least in part, since it is inextricably entwined with maintenance of intracellular potassium. He created the recipe (soda water and milk of magnesia), which can be found at www.afibbers.org/Wallerwater.pdf One word of caution concerning supplementing KCl or any powdered organic potassium preparation with magnesium. Potassium inhibits magnesium absorption and you may easily exceed your bowel tolerance for magnesium.

In my opinion the common denominator linking VMAF and ALAF appears to be low potassium, at least in part. P cells, as described above, would be the other link. As the Bordeaux group has shown, those with paroxysmal AF have inexplicably low PV ERP. Both arms of the ANS cause shortening of the ERP, as does low blood potassium. So either arm in combination with low potassium can trigger an episode in the arrhythmogenic heart. ERP x (P cells + Potassium + ANS) => AF Risk

My own personal experience with LAF episodes suggests that vagal tone and low potassium work in concert. My 9AM potassium values are usually 4.5 or less. That would put me well under 4 during the night. The simultaneous appearance of high vagal tone and low potassium would accentuate the shortening of ERP. This would conveniently explain my typical middle of the night episodes.

However, during the late morning or afternoon I've had occasional episodes (less than 10% of the total) that appear to be related to possible dehydration and/or hypoglycemia. Both of these stimulate not only catecholamine but also ACTH and aldosterone release (as does physical or emotional stress). Oftentimes I've had just a pastry for breakfast. Talk about an open invitation to an insulin surge. My HR is usually over 70 with low vagal tone at the time, but the episode is nonetheless triggered by a vagal maneuver. Presumably the insulin and fasting state induce the hypoglycemia. According to one study, ERP is shortest under hypoglycemia (v. hyperglycemia) in the left atrium (v. the right atrium).[13]

Might this be P cell related? A greater potassium gradient would presumably augment this shortening. Another study in rats has shown that insulin-induced hypoglycemia directly stimulates vagal neurons in the brainstem.[14] Perhaps hypoglycemia can induce AF via both vagal stimulation and increased potassium gradient (catecholamine induced).

On very rare occasions I've triggered an episode by a short sprint. Here again, the timing of the episodes suggests low blood sugar and underscores the arrhythmogenic risk posed at the extremes of autonomic tone. During heart attacks the humoral catecholamine surge that can occur causes a rapid, transient transcellular shift of potassium, resulting in a short-lived but dramatic fall in blood potassium of approximately 0.5-0.6 mmol/L or more.[15] Although these shifts are evanescent and readily reversible, the transient drop in blood potassium can trigger PACs (and PVCs) and sometimes AF. This, of course, is in addition to the urinary potassium wasting that catecholamines cause.

I've also had episodes that are postprandial, but only in the evening (presumably because there is more reinforcing vagal tone at this time). Initially I thought this was due primarily to the alkaline tide associated with a meal (production of gastric acid by the stomach reflexively causes blood alkalosis) and subsequent urinary potassium loss (low blood potassium both causes and is caused by alkalosis). Then I thought that it was due to the effect of insulin and loss of cardiac intracellular potassium due to the increased concentration gradient. Then I thought I might have a mild problem with gastroesophageal reflux (GERD)/lower esophagal sphincter (LES). GERD is increased in athletes, especially in those that run, which I do (no more marathons, however). However, now I'm inclined

to think that evening meals with poor K/glucose and K/Na ratios are the primary problem. I once thought that seafood (lots of salt) at dinner was a trigger. Looking back on such episodes, these meals were often low on the veggies and high on the simple carbs (love my desserts).

Hans went from typical stress related ALAF to typical vagally mediated AF, when he briefly took spironolactone, which has a vagotonic effect (in addition to being a potassium sparing diuretic). So, it seems that LAF can appear anywhere along the spectrum of autonomic tone. And remember, Hans always ran right at the lower limit of normal with his blood potassium. And his aldosterone, a vagolytic, and cortisol were always elevated (both aldosterone and cortisol bind to mineralocorticoid receptors, i.e., cause urinary loss of potassium). Furthermore, although there was never much change in his blood potassium (daytime values of 3.5 – 3.7 mmoles/L), his urinary potassium (and magnesium) excretion continued to escalate, as he approached the next episode. Obviously there was continual leakage of potassium from the intracellular compartment to maintain the constant blood potassium concentration in the face of escalating urinary loss.

Many LAFers have commented on what seems to be a repeating periodicity to their episodes. It seems that the length of my episodes was directly proportional to the time interval before the next episode. On the Bulletin Board (BB) in late 2002 before choosing the inaugural topic for the Conference Room.[16] Hans queried as to why there always seemed to be an abundance of PACs just prior to an episode and none just after termination. He surmised that ANP (atrial natriuretic peptide) might explain this. ANP is secreted during episodes via a mechanism that involves atrial cell stretch. ANP inhibits aldosterone synthesis and renin release thereby conserving blood potassium and helping replete intracellular levels. At some point ERP shortening due to the potassium gradient is sufficiently lengthened and the episode terminates. This point is usually in the AM when vagal tone is low and its associated ERP has also lengthened.

During this natriuresis (sodium in urine) the consequent drop in blood volume and increase in blood K/Na stimulates aldosterone secretion to oppose circulating ANP. Additionally during AF cardiac output drops by about 30% and with it the hydrostatic pressure sensed by the renal baroreceptors (the juxtaglomerular apparatus). This is another reason why aldosterone should be elevated at the end of an episode. I've often noticed on my Polar S810 HR monitor that immediately after termination of an episode my HR albeit NSR is always inappropriately high and my HRV is always inappropriately low for several hours. The vagolytic state caused by elevated aldosterone would easily explain this. It would also explain the complete absence of PACs. The half-life of aldosterone is

about 15 minutes. The more aldosterone (vagolytic) present at the end of an episode, i.e., the longer the episode of AF, the longer this post episode PAC free period will last. But it comes with a cost and that is accelerated urinary potassium wasting after the protection of ANP has been removed. Life style and diet might then combine to slowly deplete these intracellular potassium stores until blood potassium level cannot be maintained and some threshold gradient value (for P cells) is breached and another episode is triggered. In this scenario the potassium gradient may be more integral in triggering ALAF episodes and vagal tone may be more integral in triggering VMAF episodes.

If one assumes the potassium gradient as vital to triggering an episode, then one can continue further along this line of thinking. Typical night time (vagally mediated) episodes rebalance potassium stores and protect against typical daytime (adrenergic) episodes and vice versa. However, if vagal tone in VMAF is lowered by medication, then daytime episodes should become relatively more frequent. And if potassium loss in ALAF is lowered by medication, then night time episodes should become relatively more frequent. I've experienced the former with disopyramide and Hans has experienced the latter with spironolactone.

LAFers exist all along the spectrum of both autonomic tone and the potassium gradient. Our arrhythmogenic substrate is a given and separates us from "normals". Some LAFers have minimal tone or gradient problems (fortunate) but enough of both to trigger LAF (unfortunate). They are fortunate because either by medication for autonomic tone or lifestyle and diet for potassium gradient they have been able to avoid the beast. Counter-regulating mechanisms (RAS, blood K/Na, ACTH) otherwise make the latter a very difficult proposition. The real question is could this "fortunate" category of LAFers be expanded by addition of medication for better potassium balance? Inbred resistance to combining increased potassium intake with a potassium sparing diuretic makes this a very difficult proposition. Triamterene or amiloride and NOT spironolactone or eplerenone would seem to be the best choices on this count (see below). Neseritide (synthetic BNP) or carperitide (synthetic ANP) might be even better, but are only available by the intravenous route. According to the medical literature ACEIs are vagotonic, but perhaps not all are. For example, enalapril but not captopril significantly inhibits plasma aldosterone concentration and urinary aldosterone excretion. Since aldosterone is vagolytic, perhaps enalapril is vagotonic and captopril is not.[17]

Another interesting question is why proton pump inhibitors (PPI) not only relieve GERD but also appear to relieve AF. Is it only because there is less irritation of the lower esophagus (and less vagal stimulation)? Or is it also because of an improvement in the potassium gradient? Gastric acid

production causes a simultaneous blood alkalosis (alkaline tide). Hypokalemia both causes and is caused by alkalosis. By inhibiting the proton pump (H+ is no more than a proton) less H+ is lost in the gastric juice. Less potassium is lost in the urine, because the blood is less alkaline (since the gastric fluid is less acidic).

Jackie Burgess, well known and respected by all of us that frequent the BB and CR, has suggested a balanced snack of protein, complex carbohydrate and healthy fat two hours before bedtime. And, of course, magnesium and potassium are always welcome at anytime. This approach would impede any insulin induced hypokalemia/hypoglycemia and possibly AF as well. She also has reiterated for us an old adage "if you can feel your heart beating at night when lying in bed, you may be low in potassium". This undoubtedly is due to the mild BP elevating effects of low blood potassium. The heart has to work just a little harder, enough to make you aware of its beating, when all else is quiet.

Due to the insulin induced drop in blood potassium that occurs after a carbohydrate meal, it would seem prudent to always ingest potassium with your carbohydrates. Jackie has also pointed out that KCl can cause gastric irritation, at least if taken on an empty stomach. It can also elevate blood pressure in the salt sensitive. However, potassium in fruit without chloride is less absorbable. According to one source only 40 percent of the potassium in a banana is retained. This is one reason why MDs prescribe potassium as KCl (about 800mg K as KCl per tab of K-Dur). KCl also addresses hypochloremia, which often accompanies hypokalemia. If KCl irritates your stomach, then you should never let a meal go by without potassium supplementation, thereby exploiting its buffering effect in this regard. K-Dur is also a sustained release formulation, most convenient at bedtime to address the midnight diurnal nadir of blood potassium.

I heartily agree with the general recommendation to shift from simple to complex carbohydrates in our diets. I used to think this advice was better directed at those that struggle with their weight. However, given my problems with episodes being triggered when I skip or delay meals, I think thin people can also benefit from it. Eat properly and don't skip meals. Graze rather than gorge. Earlier is better than later.

In a past post on the BB I suggested that a portable potassium meter might be a very useful item for a LAFer. Horiba and Hoskin Scientific make good ones, but they are not quite ready for prime time, at least not in humans. I recently purchased an Omron BP monitor (less than $50 at Costco) and have found that relative evening BP (slightly higher systolic than normal) and/or the presence of PACs when lying on my right side both provide feedback on probable intracellular potassium.[18] Although

this is only an indirect approach at best, it may be the difference between PM AF and normal sinus rhythm (NSR).

Being on top of my daily potassium supplementation definitely decreases my evening PACs and BP. This also requires awareness of activities that cause transcellular shifts of potassium and sometimes urinary potassium (and magnesium) wasting as well. Appropriate countermeasures are needed, i.e., more fluid intake, small potassium rich complex carb snacks, e.g., a banana, etc.

My Experience with Spironolactone

I have experimented extensively with potassium and spironolactone. A combination of 3 g/day of potassium and 100 mg/day of spironolactone increased my blood level of potassium to 4.7 mEq/L. Increasing my potassium intake to 6 g/day and my spironolactone to 200 mg/day (blood potassium over 5 mmoles/L) increased the frequency and duration of my afib episodes despite also taking 500 mg/day of disopyramide (Norpace). I have now concluded, and Hans' experience supports this, that spironolactone is unlikely to be beneficial for either adrenergic or vagal afibbers for the simple reason that its detrimental vagotonic effect clearly outweighs its positive effect in regard to potassium conservation. I have therefore terminated my experiment with spironolactone. My next experiment will involve aggressive potassium supplementation starting in the afternoon and escalating until bedtime as well as taking K-Dur (800 mg of elemental potassium in a sustained release formulation) at bedtime. If that produces insufficient improvement I plan on investigating triamterene (Dyrenium) and amiloride (Midamor). *Most, if not all,* ACE inhibitors and angiotensin receptor blockers (ARBs) are decidedly vagotonic so I intend to give them a miss.

Triamterene and amiloride, both potassium-sparing diuretics, work at the level of the distal convoluted tubule in the kidneys, but do not bind to mineralocorticoid receptors. They impair sodium reabsorption in exchange for potassium and hydrogen. Thus, unlike spironolactone and eplerenone, they should not directly increase vagal tone. In fact, they may modestly increase blood potassium and thereby elevate the K/Na ratio. This would increase aldosterone secretion and thereby increase vagolysis. This, in turn, would increase the component of total blood aldosterone due to K/Na compared to the other two sources of aldosterone (RAAS, major and ACTH, minor). This might prove beneficial because increased potassium and decreased sodium intake would have greater impact on aldosterone secretion, in effect providing greater control over aldosterone secretion via diet and/or supplements (especially useful for a VMAFer).

Conclusion

You can't directly control the arrhymogenic substrate (PVs) except through PVI. You can't effectively control vagal or sympathetic tone except through meds. That leaves low potassium. If you want to get serious about controlling your episodes, then you must get serious about your potassium intake. You must address not only how much you ingest but when you ingest it. Either avoid those situations that assault your blood potassium gradient (stress, hypoglycemia, dehydration, etc) or increase your daily potassium (and magnesium) intake with appropriately time-targeted supplementation. Although food sources are best for most of what we need, for potassium repletion IMHO supplements are superior (fish oils and omega 3s are another such exception). Intake of potassium through diet alone is less convenient, less quantifiable and less absorbable. And then there's the glycemic load problem posed. Presently there is great resistance within mainstream medicine to combining potassium supplementation with a potassium sparing diuretic. Hyperkalemia and life threatening ventricular arrhythmias are of great concern. However, with the pioneering work of Drs. Struthers, MacDonald and others this overemphasized concern may soon take a back seat to a rational combination regimen. In my view it is quite plausible that this LAF epidemic might be reversed, if such an aggressive regimen were pursued by those afflicted. The study that needs to be done is one similar to that referenced above on LQTS (long QT syndrome), but with amiloride or triamterene and on LAF patients instead. But until then please remember my above disclaimer and make sure you have good renal function. My BUN (blood urea nitrogen) and creatinine are well within normal limits, but I still routinely monitor my blood potassium.

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Left Atrial Appendage: Useless or Priceless?

by Hans R. Larsen

There is considerable evidence that the left atrial appendage (LAA) is an important source of blood clots (thrombi) in afibbers with underlying heart disease. There is, however, no evidence that the LAA harbours blood clots in lone afibbers. The fact that the LAA may be a source of blood clots has spawned the practice of routinely removing it during maze and mini-maze procedures. German researchers now suggest that this may not be such a great idea[1]. What is the evidence for and against this practice?

Anatomy and Function of the LAA

The LAA is a remnant of the original embryonic left atrium formed during the third week of gestation. The LAA lies within the pericardium in close contact with the free wall of the left ventricle. It is therefore likely that blood flow, in and out of the LAA, depends to a significant degree on a properly functioning left ventricle. The LAA empties into the left atrium through an orifice located between the left upper pulmonary vein and the left ventricle. The diameter of the opening varies between 10 and 40 mm, the overall volume of the LAA varies between 0.77 and 19.27 cubic centimeters (mL), and its length can vary between 16 and 51 mm[1-3].

The LAA has several important physiological functions[1-3]:

- As it is more distensible than the left atrium itself it can act as a decompression chamber when left atrial pressure is high. Animal experiments have shown that eliminating access to the LAA results in an increase in the size and mean pressure in the left atrium.

- The LAA is known to mediate thirst (at least in animals). Thus people without a LAA might have a greater tendency to become dehydrated.

- Removal of the LAA has been shown to reduce stroke volume and cardiac output and may thus promote heart failure. Its removal could be particularly detrimental in patients with existing heart failure as it would further reduce their cardiac output and perhaps promote pulmonary congestion.

- The LAA is a major endocrine organ and is the main producer of ANP (atrial natriuretic peptide) in the human heart. The ANP concentration is 40 times higher in the LAA walls than in the rest of the atrial free wall and in the ventricles. A study of patients having undergone the maze procedure and associated LAA removal found a significantly lower ANP secretion and a commensurate increase in salt and water retention. Whether this could eventually lead to hypertension is not known.

Reasons for Removal

The LAA is a known incubator of blood clots in atrial fibrillation patients with underlying heart disease; thus the idea of removing it to eliminate one potential source of thrombi that could ultimately precipitate an ischemic stroke. Although an important one, the LAA is by no means the only source of embolic thrombi. Ventricular thrombi, aortic, carotid or vertebral arterial plaques are other possible sources, as are venous thrombi entering the left atrium via right-to-left shunting.

Japanese researchers checked 50 patients with permanent non-valvular atrial fibrillation and 12 patients with atrial flutter for the presence of thrombi in the left atrial appendage (LAA) using transesophageal echocardiography (TEE). They found no thrombi in patients with atrial flutter nor in those with lone atrial fibrillation; however, they did observe thrombi in 17% of afibbers whose AF did not fall in the category of "lone"[4]. Another group of Japanese researchers investigated 50 permanent afibbers with a history of prior cardioembolic stroke and found that 38% had thrombi in the LAA[5].

The developers of the PLAATO system for sealing off the LAA evaluated 15 permanent afibbers with severe cardiovascular disease and a high risk for stroke. They found LAA thrombi in 90% of the patients[6].

Researchers at the University of Louisville in the USA carried out a large study to determine the association between having a thrombus in the LAA and suffering a subsequent transient ischemic attack (TIA, mini-stroke). Their study involved 261 men and women who had been in atrial fibrillation for at least 4 days. About 70% had hypertension. Using transesophageal echocardiography (TEE) the researchers found that 18% of the participants had a thrombus in the LAA. The patients with thrombi were far more likely to have congestive heart failure (67% versus 30%), permanent afib (91% versus 67%) or to have suffered a prior cardiovascular event to TIA (52% versus 27%) than were patient without a discernible thrombus.

Clearly, the presence of thrombi in the LAA is related to the severity of the afib (permanent versus paroxysmal), the presence of heart failure, and a prior history of cardiovascular events. However, even among these quite sick people, thrombi were only found in 18% and the TIA rate among them was 9.2% per year as compared to 1.9% per year in the group without thrombi. The researchers noted that 75% of the participants with thrombi were on warfarin, but still had a total embolic event rate of 13.8% per year. They conclude that warfarin is not very effective in preventing or eliminating LAA thrombi in AF patients[7,8].

Other researchers have, however, found that prolonged anticoagulation with warfarin eventually resolves up to 90% of atrial thrombi[9].

It is clear that estimates of the incidence of thrombi in the LAA of permanent afibbers varies widely from 0-90% depending on prior stroke history and severity of underlying heart disease. However, it would seem that the incidence of LAA thrombi in otherwise healthy afibbers is negligible, particularly in the case of paroxysmal afibbers.

A landmark study, by cardiologists at the Medical College of Virginia, found that blood flow through the appendage was quite adequate (average ejection fraction of 46%) during normal sinus rhythm, but declined significantly (average ejection fraction of 26%) during an afib episode thus resulting in blood stagnation. Blood stagnation can promote thrombus formation because the concentration of coagulation factors tends to increase when blood flow is reduced and the blood is not regularly "cleaned up" by passing through the liver. The Virginia researchers also observed a very strong inverse correlation between heart rate during atrial fibrillation and LAA ejection fraction. They reason that a slower heart rate gives the left ventricle a better chance to fill up before it ejects its contents into the arteries. The wall of the left ventricle abuts the LAA so a more distended ventricle would tend to compress the LAA and then let it expand again when the ventricle empties. This would increase the blood flow in and out of the LAA and thus prevent stagnation[10]. These findings underscore the importance of keeping the heart rate under control, ie. below 100 or, better still, below 90 bpm in order to avoid thrombus formation in the LAA. They also explain why emboli in the LAA are more common among afibbers with severe heart disease and reduced left ventricular ejection fraction[6].

Italian researchers have confirmed that the blood flow through the LAA is significantly lower during afib than during sinus rhythm and that thrombus formation in the LAA is associated with an exceptionally low rate of flow through the LAA[11]. American researchers have found that blood flow through the LAA is lower in older patients with heart disease-related atrial fibrillation than in younger patients[12]. Japanese researchers have

found that blood flow through the LAA decreases with age in people with normal sinus rhythm[13]. Fortunately, a recent study also carried out by Japanese researchers concludes that lone afibbers (afibbers without underlying heart disease) and people with atrial flutter are at very low risk for thrombus formation in the LAA[4].

Conclusion

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 mini-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"[3], while a just-published study by German researchers concluded, "Elimination of the LAA may impeded 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."[1]

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.

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Post Ablation Care

by Hans R. Larsen

Recently I have noticed several postings from afibbers who are having a rough time post ablation. I believe there are two important aspects that could be contributing to this.

1. **Low potassium** levels may occur after surgery. My own level after my recent ablation was 3.2 mmol/L; well below my normal level and also outside the normal range of 3.5 – 5.0 mmol/L. A low potassium level is likely to increase the number of PVCs (premature ventricular complexes) and PACs (premature atrial complexes). The PACs can set off afib episodes and the PVCs, if frequent enough, can result in very uncomfortable palpitations. The way to overcome this problem is to increase your potassium intake. This can be done through the diet (www.afibbers.org/conference/session32.pdf), through supplementation with potassium chloride or potassium gluconate, or through consumption of low sodium V8 juice or a potassium-rich drink such as the PAC-Tamer (www.afibbers.org/conference/session38.pdf). It is a good idea to have your serum potassium level measured just after the ablation. If it is below about 4.1 mmol/L (mEq/L) then an increase in potassium intake is definitely needed.

2. **Ongoing inflammation** – It is almost certain that the serious trauma experienced by the heart during the ablation will result in an inflammation of the heart tissue (myocardium). My own C-reactive protein (CRP) level went from 0.3 mg/L to 7.0 mg/L after my ablation indicating the presence of a serious inflammation. The Cleveland Clinic has recognized this problem and used to prescribe statin drugs to help prevent inflammation. I believe they are now using prednisone to prevent and, if necessary, treat the inflammation. I am not entirely sure of this, but in any case, a course of prednisone post ablation would probably be a good idea. For those of us who are not keen on pharmaceutical drugs, there are lots of alternative means of combating an inflammation. My own anti-inflammatory regimen (for one month after the ablation) consisted of:
    - Fish oil (3 x 2 grams daily)
    - Beta-sitosterol (3 x 113 mg daily)

- *Zyflamend* (2 capsules with dinner)
- This in addition to my normal supplementation with vitamins, minerals and antioxidants.

I am sure there are other just as effective natural protocols.

Perhaps the most important anti-inflammatory measure you can take is to avoid strenuous exercise for at least 4-6 weeks after the ablation. Strenuous and prolonged physical activity will markedly "fan the flames" of an inflammation and may also deplete you of important electrolytes, especially potassium and magnesium. Swedish sports medicine experts are adamant that exercise should be totally avoided whenever myocarditis (inflammation of the heart tissue) is suspected[1]. Very recently Greek researchers found that participants in a 36-hour long distance run experienced a 152-fold increase in CRP levels and an 8000-fold increase in the level of interleukin-6 (IL-6), another important marker of systemic inflammation. They conclude that the increases in the inflammation markers noted, "amount to a potent systemic inflammatory response"[2].

While not many afibbers will run a 36-hour marathon following their ablation, the Greek study, nevertheless, clearly supports the contention that prolonged, heavy exercise is very detrimental when it comes to preventing or combating an inflammation. I would suggest that no exercise at all would be the best approach for the first two weeks after the ablation followed by one or two daily walks for the next month or so. Jumping right into a strenuous physical activity program right after an ablation is, in my opinion, a very unwise thing to do.

In conclusion, I strongly believe that ensuring an adequate potassium intake, following a suitable anti-inflammatory protocol, and going very easy on the exercise for the first month, at least, can go a long way to preventing a miserable recovery period and may even help ensure the success of the ablation.

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LAF Survey 9

LAF Survey 9

Introduction

The evaluation of LAF survey-9 (September 2005) turned out to be a very major undertaking indeed. With 193 afibbers responding to almost 100 questions about their ablation, maze or other procedures close to 20,000 data points had to be extracted, arranged and evaluated. The volume of data is clearly good as far as being able to draw valid conclusions, but less desirable as far as being able to present the data and conclusions in a readable and comprehensible format. I am fairly certain that the LAF survey-9 is the largest ablation survey ever done in the "real world". In other words, a survey in which the information is provided by the patients who underwent the procedures rather than by the EPs or institutions that performed them.

This report has been divided into five major sections: –

- Update to Afib Database
- Definition of Terms
- Background Data
- RF Ablation for Atrial Fibrillation
- Performance Rating for RF Ablation
- Maze Surgery and Other Procedures
- Update to Performance Ratings

Update to Afib Database

A total of 193 afibbers responded to LAF Survey-9 – our 3rd survey designed to determine the success and complication rates of ablation and surgical procedures for curing atrial fibrillation. Adding the 193 responses to our current database brings the total number of afibbers for whom basic demographic data is available to 625. This is clearly a valuable information source and it is therefore of interest to evaluate this data so as to shed further light on the make-up of the afib population.

The total database now consists of 492 male (79%) and 133 female (21%) afibbers. The distribution of the different types of AF is as follows:

Distribution of AF types

	#	%
Male afibbers		
Adrenergic	50	10%
Mixed	171	35%
Vagal	175	36%
Total paroxysmal[1]	396	80%
Permanent	70	15%
Unknown	26	5%
Grand total	492	100%
Female afibbers		
Adrenergic	9	7%
Mixed	64	48%
Vagal	36	27%
Total paroxysmal[1]	109	82%
Permanent	15	11%
Unknown	9	7%
Grand total	133	100%
All afibbers		
Adrenergic	59	9%
Mixed	235	38%
Vagal	211	34%
Total paroxysmal[1]	505	81%
Permanent	85	14%
Unknown	35	5%
Grand total	625	100%

[1] including persistent

Mixed (random) paroxysmal afib is the most common variety of AF at 38% of total. It is more common among women (48%) than among men (35%). Vagal afib is the next most common at 34% of total. It is somewhat more common among men (36%) than among women (27%). Permanent afib was reported by 15% of male respondents and by 11% of female respondents. Pure adrenergic afib was fairly rare at 10% among male afibbers and 7% among female. Only 5% of respondents were not aware of what type of AF they had, perhaps indicating that most cases are symptomatic.

The age of diagnosis or first episode is presented in the following table:

Age at Diagnosis, years

	Mean	Median	Range
Male afibbers			
Adrenergic	49	49	16-77
Mixed	47	48	18-75
Vagal	45	46	14-74
Total paroxysmal[1]	46	47	14-77
Permanent	46	47	14-75
Unknown	49	50	30-81
Grand total	47	48	14-81
Female afibbers			
Adrenergic	50	51	36-68
Mixed	43	47	8-68
Vagal	50	53	12-79
Total paroxysmal[1]	46	49	8-79
Permanent	50	53	8-71
Unknown	50	51	36-68
Grand total	47	49	8-79
All afibbers			
Adrenergic	48	49	16-77
Mixed	46	48	8-75
Vagal	46	47	12-79
Total paroxysmal[1]	46	47	8-79
Permanent	49	50	8-75
Unknown	49	50	30-81
Grand total	47	48	8-81

[1] including persistent

The average (median) age at diagnosis was 48 years for a sample of 619 afibbers who knew their year of diagnosis or first episode. The average age of onset did not differ significantly between men (48 years) and women (49 years). Only the difference between age at diagnosis for mixed female afibbers (47 years) and vagal female afibbers (53 years) was statistically significant. There was also a trend for vagal female afibbers to be diagnosed later than vagal male afibbers (53 years vs 46 years), but the difference was not quite statistically significant (p=0.057). Nevertheless, these findings might indicate that female hormones could somehow help protect against vagal AF.

With an average age at onset of 48 years, lone atrial fibrillation is clearly not an old age disease, but rather a condition that strikes in what, for most people, is their most productive years. Only 7% of the 619 afibbers in our sample group were diagnosed as late as 65 years of age or older, while 10% were diagnosed before reaching the age of 30 years. A massive 60% were diagnosed at or before the age of 50 years. The number of years that respondents had been dealing with afib varied from an average (median) of 7 years (range of 1-65 years) for women and 6

years for men (range of 1-49 years). Although these numbers are somewhat arbitrary in that they depend on how early in their afib "career" the respondents participated in a survey, they do show that many afibbers have lived a very long time with their condition.

In conclusion, an evaluation of data from 625 afibbers shows that:

- Men are more likely to develop AF than are women (79% vs 21%).
- Mixed (randomly occurring) AF is the most common type with 48% of women and 35% of men having it.
- Vagal AF is the second most common type with a prevalence of 36% among men and 27% among women.
- The average age at diagnosis or first episode is 48 years with 60% of all afibbers having been diagnosed by age 50 or earlier. Only 7% are diagnosed at age 65 or older.
- The average age at diagnosis for mixed female afibbers (47 years) is significantly lower than that for female vagal afibbers (53 years) perhaps pointing to a protective effect of female hormones against vagally-mediated AF.
- The average number of years that the survey respondents had been dealing with AF was 6 years for men and 7 years for women ranging from a few months to 65 years.

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 occurring anytime and do not consistently fit the adrenergic or vagal pattern.

Procedures

- **Focal ablation** – The original radiofrequency 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. This procedure is not used much anymore since it carries a high risk of pulmonary stenosis.
- **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** – This procedure involves open-heart surgery. After making a foot long incision and cracking open the ribs, scar tissue is surgically created (by cutting and sewing) on the surface of the heart to make pathways

connecting the sinus node and the AV node and to eliminate the possibility of aberrant impulses initiating atrial fibrillation.

- **Mini-maze procedure –** This procedure is similar to the maze procedure in that scar tissue is created on the outside of the heart rather than on the inside as is done in ablation procedures. Access to the heart is through two or more small incisions between the ribs and it is not necessary to stop the heart during the procedure. Lesions are created via radiofrequency ablation rather than by cutting and sewing.

Statistical Terms

- **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 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, not successful, or too early to tell

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

- Success – No afib episodes, no antiarrhythmics or beta-blockers, consistent sinus rhythm
- Partial success – No afib episodes, but on antiarrhythmics or beta-blockers
- Failure – Afib episodes still occurring
- Uncertain – Cases where insufficient data was available or where less than 3 months had gone by since the procedure and afib episodes were still occurring.

Background Data

Distribution of Procedures

One hundred and ninety-three afibbers responded to the survey and provided details of a total of 288 procedures distributed as follows:

	Number of Procedures				
Procedure	1st	2nd	3rd	Further	Total
Focal ablation	17	5	3	0	25
Pulmonary vein ablation (PVA)	46	23	3	0	72
Segmental PVA	20	12	2	0	34
Circumferential PVA	19	6	2	2	29
Pulmonary vein antrum isolation	36	9	1	1	47
RF procedure not specified	18	10	2	0	30
Total RF ablation procedures	156	65	13	3	237
Cryoablation	2	0	0	0	2
Maze procedure	5	0	1	0	6
Mini-maze procedure	6	1	0	0	7
Right atrial flutter	17	2	1	0	20
Left atrial flutter	2	3	0	0	5
AV node ablation + pacemaker	2	0	0	0	2
Other procedures	3	4	2	0	9
TOTAL	**193**	**75**	**17**	**3**	**288**

The majority of procedures (81%) were radio frequency (RF) ablation procedures aimed at curing atrial fibrillation. Thirty-nine per cent of the 193 respondents underwent a second procedure, 9% a third procedure, and 2% underwent a fourth procedure. The most widely used AF ablation procedure was the 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

Demographics	Male	Female	Total
Gender distribution	76%	24%	100%
Average (median) age*	57	57	57
Age range (present)	29-74	29-86	29-86
LAF confirmed by diagnosis	95%	87%	93%
Underlying heart disease	8%	9%	8%
Mitral valve prolapse	7%	9%	7%
Mitral valve regurgitation	12%	19%	13%
Median age at diagnosis	46	49	47
Age range (at diagnosis)	16-72	8-79	8-79

* at time of completing survey

There are no significant differences between males and females as far as demographic variables are concerned, nor are there any major differences between this group of 193 afibbers and the total base of 625 afibbers.

Afib Type

A total of 172 respondents had provided information regarding their type of AF. The distribution was as follows:

Type of AF	Male	Female	Total
Adrenergic	11%	2%	8%
Mixed	45%	50%	47%
Vagal	22%	33%	25%
Total Paroxysmal	78%	85%	80%
Permanent	22%	15%	20%
TOTAL	**100%**	**100%**	**100%**

The majority of respondents (80%) had paroxysmal or persistent AF, while 20% were in permanent AF. The proportion of permanent afibbers in this sample would thus seem to be somewhat higher than in the general AF population, while the prevalence of vagal AF is somewhat lower. Mixed (random) AF was the most common type followed by vagal, permanent and adrenergic.

Afib Frequency

All 193 respondents had provided information about their episode frequency. The distribution was as follows:

Afib Frequency*	Male	Female	Total
Permanent	18%	13%	17%
Daily	23%	25%	23%
Twice weekly	27%	23%	26%
Weekly	10%	11%	10%
Twice a month	10%	15%	11%
Monthly	4%	4%	4%
Every 2 months	1%	0	1%
Every 3 months	5%	9%	6%
Every 6 months	1%	0	1%
Once a year	0	0	0
Less than once a year	1%	0	1%

* prior to first procedure

The majority of respondents (76%) experienced episodes at least once a week and 40% had daily ones (including permanent afibbers). Only 9% 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 8.5 hours with a wide range of from a few minutes to 120 hours. There was no statistically significant difference in episode duration between paroxysmal afibbers taking antiarrhythmics or blockers and those taking no medications on a continuous basis. Nor was there any significant difference in the effectiveness of the various medications.

Use of Antiarrhythmics and Blockers

The majority of respondents (88%) 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 168 afibbers who had provided information about AF type and drug use is presented below.

Drug	Adrenergic	Mixed	Vagal	Permanent	Total
Beta-blockers	7%	13%	9%	25%	13%
Calcium channel blockers	0	4%	4%	17%	5%
Flecainide	13%	21%	13%	8%	16%
Propafenone	7%	12%	13%	4%	11%
Disopyramide	13%	1%	2%	4%	3%
Amiodarone	0	11%	11%	13%	10%
Sotalol	27%	15%	15%	4%	14%
Dofetilide	0	5%	0	0	2%
Digoxin	0	1%	2%	8%	2%
Other (incl. combinations)	20%	9%	10%	9%	11%
No drugs	13%	8%	21%	8%	13%
TOTAL	**100%**	**100%**	**100%**	**100%**	**100%**

Flecainide (Tambocor) was the most prescribed antiarrhythmic and was used on a continuous basis by 16% of respondents. Sotalol (Betapace) was the second most popular drug followed by beta-blockers, propafenone and amiodarone. Over 40% of permanent afibbers were, as would be expected, on beta-blockers or calcium channel blockers. However, a rather astounding 33% were on antiarrhythmics which would not be expected to benefit permanent afibbers. It is encouraging to see the low usage of digoxin (Lanoxin) which should never be used by lone afibbers.

Almost 40% of vagal afibbers (paroxysmal or persistent) were on digoxin (2%) or drugs with beta-blocking properties (beta-blockers, propafenone and sotalol) on a continuous basis. These drugs are generally contraindicated for vagally-mediated AF. Sotalol was actually the most prescribed drug for vagal afibbers followed by flecainide, propafenone and amiodarone. Sotalol was also the most popular drugs for adrenergic afibbers, while flecainide was the most prescribed drug for mixed afibbers.

A table comparing drug usage with episode frequency for 128 paroxysmal afibbers is presented below.

	Episode Frequency				
Drug	A	B	C	D	Total
Beta-blockers	40%	33%	20%	7%	100%
Calcium channel blockers	20%	20%	40%	20%	100%
Flecainide	38%	33%	25%	4%	100%
Propafenone	13%	75%	12%	0	100%
Disopyramide	0	50%	50%	0	100%
Amiodarone	33%	33%	33%	0	100%
Sotalol	18%	68%	5%	9%	100%
Dofetilide	50%	50%	0	0	100%
Other (incl. combinations)	50%	50%	0	0	100%
No drugs	32%	37%	26%	5%	100%
TOTAL	**30%**	**47%**	**18%**	**5%**	**100%**

A = Daily
B = Weekly or twice-weekly
C = Monthly or twice-monthly
D = Less than once a month

It is clear that none of the drugs are effective in keeping this particular group of paroxysmal afibbers out of afib for prolonged periods. Thus the decision to undergo an ablation or maze procedure is further justified.

Twenty-six of 136 paroxysmal afibbers (19%) were using an on-demand (pill-in-the-pocket) approach to shorten their episodes. Median episode length was 5.5 hours with flecainide (range of 2-24 hours), 8.5 hours with propafenone (range of 1-90 hours), and 30 hours with other drugs (beta-blockers, calcium channel blockers and quinidine). One afibber could terminate episodes in an average time of 10 hours by using *Emergen-C* and low-sodium V8 juice. These episode durations compare with an average (median) of 9 hours for paroxysmal afibbers not using the on-demand approach (range of 0.1 – 96 hours).

RF Ablation for Atrial Fibrillation

One hundred and fifty-six respondents had undergone radiofrequency (RF) ablation as their initial procedure, 65 (42%) had undergone a second procedure, and 13 (8%) had undergone a third procedure.

Demographics

The majority of the 156 respondents (84%) had the paroxysmal or persistent form of AF, while 16% were in permanent afib. The most common type among the 108 paroxysmal afibbers who were aware of

their type was the mixed variety at 56%, followed by vagal at 32%, and adrenergic at 12%.

The median age of respondents was 57 years with a range of 29 to 86 years. The median age at diagnosis was 46 years with a range of 8 to 79 years and the median number of years that AF had been present was 7 years with a range of 1 to 50 years.

These numbers are not significantly different from the numbers obtained by considering all the entries in our main database, so there is no reason to believe that respondents to the ablation part of the survey were either younger or older than the general population of afibbers.

Twenty-six per cent of respondents were female, slightly higher than the proportion in the main database. The median age at which the ablation was performed was 55 years with a range of 27 to 85 years.

Most respondents (93%) had no underlying heart disease, but 6% had been diagnosed with mitral valve prolapse (MVP) and 14% with minor mitral valve regurgitation.

Initial Procedure Results

Only afibbers who had undergone their first ablation prior to March 2005 were considered in this part of the survey in order to avoid making premature conclusions as to success. Thus, 127 afibbers who knew the outcome of their ablation were included. A total of 49 out of the 127 afibbers (39%) went on to have a second AF ablation procedure, while 7 (6%) required an additional flutter or SVT procedure. One afibber had a mini-maze as his second procedure. The success rates for the 127 afibbers are given in the table below. Please note that anyone needing an additional procedure whether for AF or flutter was counted as a failure in this particular tabulation.

Results of Initial RF Procedure

Parameter	Complete Success	Partial Success	Failure	Average
% in group	**29**	**10**	**61**	**-**
Adrenergic %	11	0	4	6
Mixed %	41	42	47	45
Vagal %	27	25	23	24
Paroxysmal %*	78	67	74	75
Permanent %	16	25	13	15
Not sure %	6	8	13	10
Present age, median	59	51	59	58
Age at diagnosis, median	50	43	46	46
Age at ablation, median	58	49	57	56
Age at ablation, range	29-81	44-71	27-85	27-85
Years of AF	7	5	8	7
Females in group	24%	33%	31%	29%
Underlying heart disease	3%	17%	10%	9%
Mitral valve prolapse	3%	0%	9%	6%
Minor MV regurgitation	22%	42%	9%	16%
Adverse event rate %	22%	50%	54%	44%

* including persistent AF

None of the observed differences in the above table were statistically significant except for the adverse event rate between complete successes (22%) and failures (54%). This difference is extremely significant (p=0.005) indicating that a failed ablation is far more likely to be accompanied by an adverse event than is a successful one. There is no evidence that age at ablation, gender, years of afib, heart or mitral valve disease or type of afib has any bearing on the outcome of left atrium RF ablation.

It should be noted that the results of this survey are based on the patient's point of view. As far as the patient is concerned, a RF ablation procedure is successful only if the patient experiences no more afib episodes and requires no follow-up procedures be they another RF ablation, an ablation for right or left atrial flutter, tachycardia, etc. However, the EP and institution will deem a RF ablation successful if it stops the afib regardless of whether follow-up procedures may be required to correct problems often resulting from the first procedure.

In other words, my definition of success and partial success is more restrictive than the one used by the institution performing the procedure. A comparison of the two measures (for the total 189 procedures considered) is presented in the table below.

	Patient's View	Institutional View
Complete success	29%	31%
Partial success	10%	13%
Failure	61%	56%

The success rate uncovered by this survey is clearly disappointing, as is the high rate of adverse events. It is indeed difficult to think of another elective medical procedure with a success rate below 30% and a complication rate in excess of 40%. However, as we shall no doubt see as the evaluation progresses, both the success and complication rates are highly dependent on when and by whom the ablation was performed.

Six afibbers underwent their ablation at the age of 70 years or older. The rate of complete success was 29%, partial success was 14%, and the failure rate was 57%. Thus, based on this very small sample, RF ablations in elderly afibbers are not significantly less successful than those in younger ones

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). The data presented in the table below revealed no statistically significant correlations between episode frequency or duration and the success and failure rates.

Success Rate vs. Afib Severity

Parameters	Complete Success	Partial Success	Failure	Total
Episode frequency				
Permanent	28%	17%	56%	100%
Daily	22%	11%	67%	100%
Weekly or twice-weekly	32%	4%	64%	100%
Monthly or twice-monthly	25%	17%	58%	100%
Less than once a month	50%	0%	50%	100%
Episode duration, hrs				
Permanent	28%	16%	56%	100%
Less than 10 hrs	36%	9%	55%	100%
10 - 24 hrs	24%	3%	73%	100%
Longer than 24 hrs	31%	13%	56%	100%

Year of Ablation

The use of RF ablation to cure AF only began in earnest in 1997 and it would be expected that technological advances and skills progression would have improved outcomes substantially over the years.

Success Rate by Year of First Ablation

Year of Procedure	# of Procedures	Complete Success	Partial Success	Failure
1997-2000	6	17%	0%	83%
2001	7	0%	0%	100%
2002	13	23%	8%	69%
2003	37	35%	3%	62%
2004	52	29%	15%	56%
2005	12	42%	17%	42%
Average 1997-2005	**127**	**29%**	**10%**	**61%**

Although there has been some improvement in success rates and some reduction in failure rates, these changes are far from impressive. Limiting the evaluation to the 64 procedures performed in the years 2004 and 2005 yields a complete success rate of 31%, a partial success rate of 16%, and a failure rate of 53%. Still not very impressive!

Popularity of Procedures

There has been a steady development of new procedures since 1998 when Professor Haissaguerre discovered that 80-90% of all aberrant impulses causing AF originated in the pulmonary veins (PV). These new procedures focus on isolating the pulmonary veins from the left atrium using either electrophysiological or anatomical mapping and employs a variety of RF catheters. The following approaches were used in initial procedures:

Popularity of Procedures by Year (% use in year*)

Procedure	1997-2000	2001	2002	2003	2004	2005	Average
Focal ablation	43	25	20	8	6	9	11
PV ablation	14	75	40	26	32	20	30
Segmental PVI	14	0	0	16	9	20	12
Circumferential PVI	0	0	7	8	19	14	12
Antrum PVI	0	0	7	26	30	26	23
Unspecified	29	0	26	16	4	11	12
Total	**100%**	**100%**	**100%**	**100%**	**100%**	**100%**	**100**
Total, number	7	8	15	38	53	35	156

* including 29 procedures for which the outcome was uncertain

It is clear that focal ablation has declined in popularity over the years in the group surveyed. The various procedures aimed at isolating the pulmonary veins have, on the other hand, increased in popularity. The generic pulmonary vein ablation, which likely includes elements of the Haissaguerre, Natale and Pappone methods, is the most popular procedure at a 30% use rate over the period 1997-2005. It is followed by

the Natale method (PV antrum isolation) at 23%, and then the Haissaguerre (segmental PVI) and Pappone methods (circumferential PVI) at 12% each.

Considering just the last 2 years (2004 and 2005) the Natale method becomes the most popular at 28%, followed by the generic PVA at 27% and then the Pappone method at 17% and the Haissaguerre method at 14%. Of course, this distribution may be quite different if another group of afibbers was surveyed, especially if they resided in France or Italy.

The success rates associated with the various procedures are presented in the table below for the periods 1997-2003 and the period 2004-2005.

Success Rates by Procedure, %

	1997-2003			2004-2005		
Procedure	Complete Success	Partial Success	Failure	Complete Success	Partial Success	Failure
Focal ablation	18	9	73	33	0	67
PV ablation	19	0	81	16	21	63
Segmental PVI	17	0	83	33	0	67
Circumferential PVI	50	0	50	45	10	45
Antrum PVI	73	9	18	40	25	35
Unspecified	0	0	100	0	0	100
Total, number	17	2	44	20	10	34
Total, %	**27**	**3**	**70**	**31**	**16**	**53**

The pulmonary vein antrum isolation technique and the circumferential PVI are clearly the most successful with complete success rates of 40% and 45% respectively for the first procedure if performed in the period 2004-2005. It is interesting to note that the success rate of the antrum PVI procedure has dropped from 73% in 1997-2003 to 40% in 2004-2005. The failure rate for the antrum PVI procedure was clearly the lowest at 18% in 1997-2003 and 35% in 2004-2005. Thus, when the combined total of full success (no afib, no drugs) and partial success (no afib, but on drugs) is considered, then antrum PVI clearly comes out on top with a combined success rate of 82% in 1997-2003 and 65% in 2004-2005. Corresponding numbers for the circumferential PVI are 50% and 55% respectively.

Facility and Electrophysiologist

Although the procedure used is clearly important in determining success, it is likely that the facility and electrophysiologist actually performing the procedure is equally, if not more, important. Almost half of the ***successful*** procedures (46%) were carried out at the Cleveland Clinic. Most (75%) done by Dr. Andrea Natale and the remainder by Drs. Saliba, Schweikert and Tchou. Dr. Natale also carried out 4 successful first procedures at

Marin County General Hospital in California. Dr. Pierre Jais at the Hopital Cardiologique in Bordeaux accounted for 2 successful first procedures, as did Dr. Marcus Wharton at the Medical University of South Carolina.

Five of the 12 partially successful procedures were done at the Cleveland Clinic (4 by Dr. Natale, 1 by Dr. Saliba). Dr. Natale also carried out 1 partially successful procedure at Marin County General Hospital.

Of course, the fact that an EP carried out one or more successful procedures does not mean that he did not experience failures. It also does not mean that he did not correct these failures in a second ablation. These considerations, as well as considerations concerning adverse effects as a factor in the overall judgment of success, will be covered in a separate section – "Performance Rating".

Results of Follow-Up (Second) Procedure

Only afibbers who had undergone a second RF ablation prior to March 2005 were considered in this part of the survey in order to avoid making premature conclusions as to success. Thus, 57 afibbers who knew the outcome of their second ablation were included. The 57 respondents included 11 afibbers who had a right atrial flutter ablation, 2 who had a cryoablation, and 1 who had a left atrial flutter ablation as their first procedure, and then had the RF ablation as their second (follow-up) procedure.

A total of 12 out of the 57 afibbers (21%) went on to have a third RF ablation, while 4 (7%) required additional flutter, SVT or other procedures.

The success rates of the 57 afibbers who underwent a second RF ablation are shown in the table below.

	Results of Follow-up Procedure			
Parameter	Complete Success	Partial Success	Failure	Average
% in group	**28**	**11**	**61**	**-**
Paroxysmal %*	69	67	74	72
Permanent %	6	33	14	14
Not sure %	25	0	11	14
Females in group, %	19	0	26	21
Adverse event rate %	25	100	40	42

* including persistent AF

The above results do not differ significantly from those obtained for a first ablation procedure except for the adverse event rate for partial success procedures, which is 100% (50% hematomas). Again, the rate of complete success was astonishingly low at 28%. The partial success rate (no AF, but continued drug use) was 11%, and the failure rate was 61%. Only 2 afibbers over the age of 70 years had a follow-up procedure – 1 was fully successful and the other was a failure.

The finding that success and adverse event rates in the second procedure are almost identical to those experienced in the first procedure supports the conclusion that there is little difference in the technical difficulty in performing a first versus a second procedure.

The distribution of the procedures used in the follow-ups is presented in the table below.

Popularity of Procedures by Year
(% use in year)

Procedure	1997-2000	2001	2002	2003	2004	2005*	Average
Focal ablation	0	33	0	9	7	6	8
PV ablation	67	67	50	36	32	25	35
Segmental PVI	0	0	25	9	14	38	18
Circumferential PVI	0	0	0	18	7	13	9
Antrum PVI	0	0	0	0	25	13	14
Unspecified	33	0	25	28	15	5	16
Total, %	**100**	**100**	**100**	**100**	**100**	**100**	**100**
Total, number	3	3	4	11	28	16	65

* including 8 procedures for which the outcome was uncertain

For the second ablation the generic PVA is again the most popular procedure. It is followed by the segmental PVI, the antrum PVI, and the circumferential PVI. The segmental PVI (Haissaguerre method) seems to be used more frequently in the second ablation than in the initial one (12% vs 18%), while the circumferential PVI (Pappone method) is more popular for the initial procedure (12% vs. 9%).

The success rates associated with the various procedures are presented below for the period 1997-2003 and the period 2004-2005.

Success Rates by Procedure, %

	1997-2003			2004-2005		
Procedure	Complete Success	Partial Success	Failure	Complete Success	Partial Success	Failure
Focal ablation	0	0	100	50	0	50
PV ablation	30	0	70	8	42	50
Segmental PVI	0	0	100	38	0	62
Circumferential PVI	0	0	100	50	0	50
Antrum PVI	0	0	0	57	14	29
Unspecified	20	0	80	40	0	60
Total, number	4	0	17	12	6	18
Total, %	**19**	**0**	**81**	**33**	**17**	**50**

The chance of having undergone a successful second ablation before 2004 was clearly very low at 19% with an accompanying failure rate of 81%. The situation improved somewhat for the period 2004-2005 when the chance of a second ablation being completely successful rose to 33% and the failure rate fell to 50%. The most successful procedure in the 2004-2005 period was the antrum PVI, followed by the circumferential PVI, and the segmental PVI. In interpreting these results it should be kept in mind that the antrum PVI procedures were all performed by Dr. Andrea Natale – a very experienced and successful EP.

Considering the total of complete and partial success for the period 2004-2005 the procedures stack up as follows:

	Success
Pulmonary vein ablation	50%
Segmental PVI	38%
Circumferential PVI	50%
Antrum PVI	71%
Average	**51%**

Facility and Electrophysiologist

A third of the successful second procedures were carried out by Dr. Andrea Natale at the Cleveland Clinic and the Marin County Hospital. Drs. Haissaguerre and Jais at the Hopital Cardiologique in Bordeaux accounted for 2 successful second procedures each.

Twenty-three per cent of second procedures were performed by EPs other than the ones who had done the initial procedure. Afibbers who changed to a presumably more experienced EP for the second procedure had a 50% complete success rate versus a 35% complete success rate for those who stayed with their original EP (after the first ablation).

Results of Third Procedure

Only the 5 afibbers who had undergone a third RF ablation prior to March 2005 and who knew their outcome were considered in this part of the survey.

The success rates for the 5 afibbers who underwent a third RF ablation are shown in the table below.

Results of Third Procedure

Parameter	Complete Success	Partial Success	Failure	Average
% in group	**20**	**20**	**60**	-
Females in group, %	0	0	0	0
Adverse event rate %	0	0	67	40

Only one of the third attempt procedures was a complete success (performed by Dr. David Callans at the University of Pennsylvania).

Overall Results for RF Ablation

Combining the data for the total 189 procedures (first, second and third attempt) produces the following results:

Overall Procedure Results

	Complete Success	Partial Success	Failure	Average
Ablation Success				
1997-2003	26%	2%	72%	-
2004-2005	31%	17%	52%	-
1997-2005	29%	10%	61%	-
Adverse Events				
1997-2003	24%	50%	40%	36%
2004-2005	19%	63%	55%	46%
1997-2005	23%	62%	47%	43%

These results are not significantly different from those obtained by just considering the first procedure. Thus, it can be stated with some confidence that the average rate of complete success for RF ablation procedures performed between 1997 and February 2005 in this particular group of afibbers is 29%. That of partial success is 10% and the remaining 61% of 189 procedures considered resulted in failure.

The average adverse event rate was 43%. The rate of adverse events in the group having a completely successful ablation (23%) is significantly

different from the average rate of 47% experienced during ablations that failed (p=0.01).

The distribution of the 189 ablation procedures used in the first, second and third procedures is presented in the table below.

Popularity of Procedures (% by period)

Procedure	1997-2003	2004-2005	Average
Focal ablation	15%	5%	10%
PV ablation	38%	30%	34%
Segmental PVI	9%	17%	13%
Circumferential PVI	7%	14%	11%
Antrum PVI	13%	27%	21%
Unspecified procedure	18%	7%	11%
Total	**100%**	**100%**	**100%**
Total, number	86	103	189

The overall success rates associated with the 189 ablations used in the first, second and third procedures are presented in the table below.

Success Rates of Procedures, %

	1997-2003			2004-2005			Total		
	Comp	Part		Comp	Part		Comp	Part	
Procedure	Succ.	Succ.	Failure	Succ.	Succ.	Failure	Succ.	Succ.	Failure
Focal ablation	15	8	77	40	0	60	22	6	72
PV ablation	24	0	76	13	29	58	19	14	67
Segmental PVI	13	0	87	35	0	65	28	0	72
Circumferential PVI	33	0	67	43	7	50	40	5	55
Antrum PVI	73	9	18	43	21	36	51	18	31
Unspecified	7	0	93	25	12	63	13	4	83
Total, %	**26**	**2**	**72**	**31**	**17**	**52**	**29**	**10**	**61**
Total, number	22	2	62	32	17	54	54	19	116

It is clear that the pulmonary vein antrum isolation procedure (Natale method) was the most successful procedure in the period 2004-2005 with a combined success and partial success rate of 64% - still a far cry from the generally quoted 85-90%. It is interesting that the success rate for the Natale procedure has actually declined since the 1997-2003 period when the combined success rate was 82%. The circumferential PVI (Pappone method) is the second most successful procedure with a combined success rate of 45% in 2004-2005 versus 33% in 1997-2003. In interpreting these results it should be kept in mind that over half of the antrum isolation procedures were carried out by Dr. Natale.

Adverse Events

The following adverse events occurred during or shortly after RF ablation procedures performed during the time periods 1997-2003 and 2004-2005. Please note that some afibbers experienced more than one adverse event and that this part of the survey includes procedures done after February 2005.

Adverse Events, %

	1997-2003			2004-2005			1997-2005		
Adverse Event	Comp Succ.	Part Succ.	Failure	Comp Succ.	Part Succ.	Failure	Comp Succ.	Part Succ.	Failure
Hematoma	4	50	16	9	17	18	7	20	17
TIA	0	0	0	0	0	0	0	0	0
Stroke	0	0	1	0	0	0	0	0	1
PV stenosis	0	0	4	0	1	2	0	1	3
Tamponade	0	0	1	0	0	1	0	0	1
Fistula	0	0	0	3	0	0	2	0	0
Left atrial tach/flutter	4	0	7	0	17	18	2	15	12
Right atrial flutter	0	0	7	0	17	7	0	15	7
Other: Reversible	14	0	3	6	11	11	9	10	6
Other: Life-threatening	0	0	7	0	0	4	0	0	6
Other: Permanent	0	0	1	3	0	0	2	0	1
TOTAL, %	**22**	**50**	**50**	**21**	**67**	**60**	**22**	**65**	**55**
No adverse effects	78	50	50	79	33	40	78	35	45
GRAND TOTAL	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

The most common adverse event was post-procedure hematomas in the groin or thigh area. This was reported by 15% of ablatees. Left atrial tachycardia/flutter was reported by 10% and right atrial flutter by 6%. NOTE: 26% of all ablation procedures included a right atrial flutter ablation as a precautionary measure.

Minor, reversible events were experienced by 8%, pulmonary vein stenosis by 4%, serious or life-threatening events by 4%, and permanent damage by 1%. There was one stroke, but no transient ischemic attacks (TIAs) reported; two afibbers experienced tamponade (penetration of the heart wall) and another experienced a non-lethal atrial-esophageal fistula.

About two-thirds of all adverse events reported were fully resolved at the time the survey was completed.

Right Atrial Flutter Ablation

Twenty-six per cent of all RF ablation procedures included a right atrial flutter ablation, while 46% did not. Twenty-four per cent were uncertain

whether their procedure included a right atrial flutter ablation and 4% had undergone one earlier. There was no indication that having a right atrial flutter ablation procedure as part of the left atrium ablation resulted in a more favourable final outcome.

Stenosis Check

During the 3 months following the procedure 45% of all ablatees were checked for pulmonary vein stenosis, 37% were not checked, and 18% were uncertain. Pulmonary vein stenosis was diagnosed in 7 respondents corresponding to 4% of the total radiofrequency ablation population.

Inflammation

The majority (91%) of afibbers did not know their level of the inflammation marker, C-reactive protein, immediately after their procedures. However, 3% reported a level above 5.0 mg/L indicating inflammation, 3% reported a level between 1.0 and 5.0 mg/L (normal range), and 2% reported a level below 1.0 mg/L.

Forty-six per cent took anti-inflammatory drugs or supplements after their procedure(s), while 54% did not. The most popular anti-inflammatories were the following:

Aspirin	used after 20% of all procedures
Statin drugs	used after 15% of all procedures
Fish oil	used after 18% of all procedures
Prednisone	used after 1% of all procedures
Other (NSAIDs and herbs)	used after 6% of all procedures

NOTE: Some afibbers used more than one anti-inflammatory

There was no indication that taking anti-inflammatories after the procedure improved the rate of success.

Potassium Level

The majority (88%) of afibbers did not know their level of serum potassium after the procedure. This, however, is unlikely to be of major importance in view of the fact that of the 12% who did know their level, 86% were within the normal range (3.6-5.0 mmol/L) and only 14% were below 3.5 mmol/L. No measurements were above 5.0 mmol/L. Twenty per cent of all ablatees supplemented with potassium or consumed a high

potassium diet after their procedure, while 80% did not. There was no indication that supplementing with potassium after the procedure improved the success rate.

Vitamin Supplementation

About half (52%) supplemented with vitamins, minerals or antioxidants after their procedure(s). There was no indication that this improved the outcome of the procedure.

Ectopics After Procedure(s)

The percentage of procedures, which were followed by increased ectopic activity (PACs or PVCs), is presented in the table below.

Ectopics After Procedure(s)

	Complete Success	Partial Success	Failure	Total
No increased activity	36%	44%	14%	23%
Less than one month	4%	17%	17%	13%
One month	5%	0	2%	3%
Two months	5%	22%	6%	7%
Three months	18%	0	7%	10%
More than 3 months	22%	11%	43%	34%
Uncertain	10%	6%	11%	13%
TOTAL	**100%**	**100%**	**100%**	**100%**

Complete success was associated with a 36% prevalence of no increased ectopic activity after the procedure. The corresponding number for partial success was 44%. Failure, on the other hand, was associated with only a 14% prevalence of no increased ectopic activity. The differences between success and failure and partial success and failure are statistically significant (p=0.03) and clearly show that no increased ectopic activity is associated with a better chance of a successful or partially successful procedure. Increased ectopic activity for more than 3 months after the procedure is, on the other hand, associated with a significantly worse prognosis (p=less than 0.0001). There was no indication that supplementing with potassium or consuming a potassium-rich diet reduced the time period during which increased ectopic activity was observed.

Afib Episodes After Procedure(s)

The length of time after the procedure that ablatees continued to experience afib episodes is detailed in the table below.

Episodes After Procedure(s)

	Complete Success	Partial Success	Failure	Average
No afib episodes	63%	32%	9%	27%
Less than one month	22%	16%	19%	20%
One month	7%	11%	2%	4%
Two months	2%	21%	4%	5%
Three months	6%	0	3%	4%
More than 3 months	0	20%	56%	37%
Uncertain	0	0	7%	3%
TOTAL	**100%**	**100%**	**100%**	**100%**

It is clear that there is a very strong association between being afib-free immediately after the procedure and ultimate complete success. It is also clear that the chance of a successful outcome is substantially diminished if episodes continue beyond the first month. As a matter of fact, 85% of afibbers with a successful outcome experienced occasional episodes for less than 1 month after their procedure. Only 28% of those eventually classified as having a failed ablation experienced episodes for less than 1 month, while the majority of failed ablatees (56%) experienced them for more than 3 months. There was no indication that supplementing with potassium or multivitamins or taking anti-inflammatories after the procedure prevented post-procedure episodes.

Warfarin (Coumadin) Usage

The percentage of ablatees who were taking warfarin after their procedure is presented in the table below.

Warfarin (Coumadin) Usage

	Complete Success	Partial Success	Failure	Average
No warfarin after procedure	9%	5%	15%	12%
Less than one month	4%	0	5%	4%
One month	13%	5%	8%	9%
Two months	22%	16%	7%	12%
Three months	37%	32%	16%	24%
More than 3 months	9%	21%	19%	16%
Still on warfarin	6%	21%	30%	23%
TOTAL	**100%**	**100%**	**100%**	**100%**

A surprising 12% of all ablatees were not on warfarin at all after the procedure. Most (24%) were on it for 3 months, but almost 50% of those with a failed ablation were on it for more than 3 months.

Use of Antiarrhythmics and Blockers

The percentage of ablatees who were taking antiarrhythmics or blockers after their procedure is shown in the table below.

Use of Medications

	Complete Success	Partial Success	Failure	Average
No drugs after procedure	34%	0	22%	23%
Less than one month	4%	0	5%	4%
One month	15%	0	3%	6%
Two months	21%	0	5%	9%
Three months	17%	0	12%	12%
More than 3 months	9%	0	14%	11%
Still on medication	0	100%	39%	35%
TOTAL	**100%**	**100%**	**100%**	**100%**

Types of Medications Used After Procedures

	Complete Success	Partial Success	Failure	Average
No medications	29%	0	16%	18%
Flecainide	24%	23%	21%	22%
Propafenone	6%	23%	10%	10%
Disopyramide	2%	0	2%	2%
Amiodarone	0	0	8%	5%
Dofetilide	0	5%	5%	4%
Sotalol	15%	0	11%	11%
Beta-blocker	18%	44%	21%	22%
Calcium channel blocker	6%	5%	6%	6%
TOTAL	**100%**	**100%**	**100%**	**100%**

NOTE: Some respondents used more than one medication

The most popular post-procedure drugs were flecainide and beta-blockers. Beta-blockers were particularly popular among partial success respondents, but were usually taken in combination with flecainide or propafenone.

Total Recovery Time

The time it took to recover fully from a procedure is presented in the table below.

	Recovery Time			
	Complete Success	Partial Success	Failure	Average
Less than 1 month	41%	21%	34%	35%
1 - 2 months	17%	37%	28%	26%
2 - 3 months	24%	16%	8%	13%
More than 3 months	15%	26%	28%	24%
Uncertain	3%	0	2%	2%
TOTAL	**100%**	**100%**	**100%**	**100%**

The majority (61%) of respondents recovered fully in less than 2 months. About a quarter took more than 3 months to recover, and some never did. Age at ablation was not correlated with recovery time and neither was there any correlation between having more than one procedure and recovery time.

Final Outcome of Procedures

The final outcome of the 189 procedures undergone by the 127 respondents whose first procedure was a RF ablation and whose last procedure was performed prior to March 2005 is discussed below.

Fifty-eight of the 127 afibbers were no longer having episodes and were no longer on antiarrhythmics or blockers (complete success). Twenty-four were also afib free, but only with the aid of antiarrhythmics and blockers (partial success). The remaining 45 were still experiencing episodes with or without the use of antiarrhythmics or blockers (failures).

Thus, overall success rate after an average 1.5 procedures per afibber was as follows:

	Objective Judgment	Subjective Judgment
Complete success	46%	62%
Partial success	19%	23%
Failure	35%	15%
TOTAL	100%	100%

The subjectively judged success rate is clearly substantially higher than the success rate obtained through the use of objective criteria –

- Complete success = no afib – no drugs
- Partial success = no afib – controlled with drugs
- Failure = continued afib episodes

Obviously 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 their feeling of success.

Stroke Prevention

Warfarin and natural stroke prevention remedies were used by the following percentage of afibbers:

	Warfarin	Natural Remedies
Complete success	5%	62%
Partial success	29%	14%
Failure	40%	24%
TOTAL	22%	23%

Not surprisingly, afibbers whose procedures had been completely successful were far more likely to use natural remedies for stroke prevention than were those whose outcome had been unsuccessful. Ten per cent of afibbers took a daily aspirin for stroke prevention. The most commonly used natural supplements used for stroke prevention were fish oils (used by 55% of those who had specified their supplements), vitamin E (20%), nattokinase (11%), garlic (7%), and other supplements (7%).

Trigger Avoidance

While 84% of successful ablatees no longer needed to avoid previous triggers, only 20% 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.

	Trigger Avoidance			
	Complete Success	Partial Success	Failure	Average
No longer need to avoid	84%	58%	20%	57%
Still need to avoid	3%	4%	40%	17%
Much less sensitive	7%	29%	27%	18%
Not sure	6%	9%	13%	8%
TOTAL	100%	100%	100%	100%

Continuing Afib Episodes

Thirty-six respondents had kept track of their episode frequency prior to and after their procedures. The median number of episodes prior to the first procedure was 12 (over a 3-month period) compared to 3 after the procedures (range of 0-90). Thus, there was a general reduction in episode frequency after the ablation. However, this reduction was by no means uniform. While 67% saw a reduction in episodes, 24% experienced more episodes, and the remaining 9% stayed the same. Four out of 5 ablatees converted from permanent to paroxysmal AF. The median duration of the episodes decreased from 10 hours to 4 hours (range of minutes to 120 hrs) and this change was statistically significant. Again, the reduction in episode duration was not uniform across the board. The majority (70%) experienced shorter episodes, but 15% had longer ones and for 15% there was no change in episode duration.

Use of Pill-in-the-Pocket Approach

Twenty-three per cent of afibbers still experiencing episodes used the on-demand approach to shorten their duration.

Changes in Heart Rate

Changes in heart rate after the procedures were quite common as indicated in the table below.

Changes in Heart Rate

	Complete Success	Partial Success	Failure	Average
Increase in heart rate	58%	59%	20%	44%
No change in rate	34%	27%	52%	40%
Decrease in rate	8%	14%	27%	16%
TOTAL	**100%**	**100%**	**100%**	**100%**

The most frequent change was an increase in heart rate (experienced by 44%). This change was most common among afibbers who had undergone successful procedure(s) (58%) and least common among those whose procedures had failed to cure the afib (20%). Statistically, the difference was very significant (p=0.0015).

The reason for the increase in heart rate after an ablation is that a significant portion of vagal nerve endings are 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.

The increase in heart rate is usually temporary and abates as the vagal nerve endings heal.

Summary

- The overall objectively-rated complete success rate (no afib, no drugs) for 127 afibbers after an average of 1.5 RF ablations was 46%; partial success was achieved in 19% 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 62% feeling that the end results were total success, 23% claiming partial success, and 15% judging their procedures as a failure.

- The average objectively-rated complete success rate for a single RF ablation procedure was 29%, that of partial success 10%, and that of failure 61%.

  It should be noted that the results of this survey are based on the patient's point of view. As far as the patient is concerned, RF ablation procedure is successful only if the patient experiences no more afib episodes and requires no follow-up procedures be they another RF ablation, an ablation for right or left atrial flutter, tachycardia, etc. However, the EP and institution will deem a RF ablation successful if it stops the afib regardless of whether follow-up procedures may be required to correct problems often resulting from the first procedure.

  In other words, my definition of success and partial success is more restrictive than the one used by the institution performing the procedure. A comparison of the two measures (for the total 189 procedures considered) is presented below.

	Patient's View	Institutional View
Complete success	29%	31%
Partial success	10%	13%
Failure	61%	56%

- The adverse event rate averaged 47% for all procedures with the majority of the events being hematomas or the development of right atrial flutter or left atrial flutter/tachycardia. One stroke was reported, but no TIAs.

- There were no significant differences in success and adverse event rates between a first and second RF ablation perhaps indicating that the technical difficulty in performing them is pretty much the same.

- The majority (76%) of respondents experienced AF episodes at least weekly prior to their ablation.

- There was no evidence that age at ablation, gender, years of afib, heart or mitral valve disease, type of afib, or episode severity has any bearing on the outcome of left atrium RF ablation.

- The most successful procedure for the period 2004-2005 was the pulmonary vein antrum isolation procedure (Natale method) with a combined complete and partial success rate of 64%. The circumferential PVI (Pappone method) was the second most successful procedure with a combined success rate of 45% in 2004-2005 versus 33% in 1997-2003.

- About half (45%) of all ablatees were checked for pulmonary vein stenosis and the condition was diagnosed in 7 respondents corresponding to a 4% rate in the total RF ablation population.

- There was no indication that anti-inflammatories, potassium or vitamin supplementation affected the outcome of the procedure and no evidence that potassium supplementation reduced the incidence of increased post-procedure ectopic activity or episodes of AF.

- No increase in ectopic activity during the first month post-ablation was associated with a greater chance of a successful outcome, while increased ectopic activity

continuing beyond 3 months post-ablation was associated with an increased incidence of failure.

- A significant majority (63%) of afibbers who had a completely successful ablation experienced no AF episodes at all after the procedure. Only 9% of those "doomed to failure" experienced no episodes at all after their procedure. No completely successful ablatees experienced episodes for more than 3 months after the procedure, while 56% of unsuccessful ablatees did so. Thus, if increased ectopic activity and 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 almost certain to be a complete success.

- The majority (61%) of respondents recovered fully in less than 2 months. About a quarter took more than 3 months to recover, and some never did. Age at ablation was not correlated with recovery time and neither was there any correlation between having more than one procedure and recovery time.

- The majority (62%) of successfully ablated respondents used natural remedies for stroke prevention, while 40% of those whose ablation failed used warfarin. Ten per cent of all respondents took a daily aspirin for stroke prevention.

- While 84% of successful ablatees no longer needed to avoid previous triggers, only 20% 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 was generally associated with a reduced frequency and duration of AF episodes. However, some afibbers experienced increased severity after a failed ablation.

- A post-ablation increase in heart rate occurred among 44% of ablated afibbers. This phenomenon was far more prevalent among successfully ablated afibbers (58%) than among those whose ablation had failed (20%). This may indicate that a more aggressive approach (increased destruction of vagal nerve endings) is associated with a better outcome.

Performance Rating for RF Ablation

Our previous ablation survey (LAFS-8) concluded that the average complete success rate for a first ablation was 47% and the failure rate was 40%. However, it was very clear that the top half of experienced, skilled EPs had a substantially better first-procedure complete success rate (68%) than did the bottom half of less skilled EPs (average success rate of 21%). There is no reason to assume that a similar stratification would not exist in this survey.

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 and adverse event rates reported by afibbers treated at specific institutions. The outcome 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

Adverse Events Score

- No adverse events — score = 0
- Hematoma — score = -2
- Minor reversible events — score = -2
- Right atrial flutter — score = -5
- Left atrial flutter — score = -5
- Supraventricular tachycardia — score = -5
- Moderate PV stenosis — score = -5
- TIA — score = -5
- Phrenic nerve damage — score = -10
- Severe PV stenosis — score = -10
- Tamponade — score = -10
- Atrial/esophageal fistula — score = -10
- Other life-threatening events — score = -10
- Minor stroke — score = -10
- Events causing permanent disability — score = -20

The outcome factor adds the scores (for successes and adverse events) for each RF ablation and the Performance Rating then averages these outcome factors for each individual institution. For example, if a procedure is fully successful with no adverse events, than the outcome factor is +10. If a procedure is a failure and accompanied by the creation

of left atrial flutter or tachycardia, then the outcome factor is –5. The primary performance rating does not take into account that a large number of adverse events are resolved within a few months after the procedure. To acknowledge this, an adjusted performance rating is also shown in which the effect of resolved adverse events has been taken into account.

Please note that in this particular evaluation a RF ablation 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 which had reports from four or more patients participating in the survey. Based on the Adjusted Performance Rating the various institutions stack up as follows:

Procedural Performance Rating
(4 or more procedures)

Rank	# of Procedures	Institution
1	8	Marin County General Hospital, CA**
2	39	Cleveland Clinic, OH
3	12	Hopital Cardiologique du Haut Leveque, Bordeaux
4	4	Loyola University Medical Center, Chicago
5	4	University of California at San Diego
6	8	Medical University of South Carolina
7	6	University of Pennsylvania
8	5	Royal Jubilee Hospital, Victoria, Canada
9	6	Good Samaritan Hospital, Los Angeles
10	5	New York University Medical Center
11	6	Brigham & Women's Hospital, Boston
12	4	Johns Hopkins, Baltimore
13	5	Centinella Hospital (Pacific Rim Electrophysiology), Inglewood, CA
14	5	University of Michigan

** All ablations were performed by Dr. Andrea Natale

The first nine institutions in the above table accounts for 50% of all ablation procedures performed; their performance is evaluated in detail below.

Procedural Success
Top-Rated Institutions

Institution	Performance Rating		Success Rate,%			Adverse
	Adjusted	Primary	Complete	Partial	Failure	Event Rate
Marin County	6.6	6.1	63	13	24	38
Cleveland Clinic	5.7	5.0	56	18	26	41
Bordeaux	5.4	4.6	58	0	42	25
Loyola	5.0	5.0	50	0	50	0
USC, San Diego	5.0	2.0	50	0	50	75
MUSC	4.4	2.9	38	12	50	29
U Penn	4.2	3.5	34	33	33	50
Royal Jubilee	4.0	4.0	40	0	60	0
Good Samaritan, LA	3.3	3.0	33	0	67	20
Average			**51**	**12**	**37**	**34**

The electrophysiologists performing the procedures in the above 9 institutions are as follows:

Institution	Electrophysiologists
Marin County	Dr. Andrea Natale
Cleveland	Drs. Natale, Saliba, Schweikert, Tchou
Bordeaux	Drs. Haissaguerre, Jais
Loyola	Dr. David Wilber
San Diego	Dr. Gregory Feld
MUSC	Dr. Marcus Wharton
U Penn	Drs. David Callans, Marchlinski
Royal Jubilee	Drs. Richard Leather, Larry Sterns
Good Samaritan	Drs. Anil Bhandari, Neala Hunter

The average procedural success and adverse event rates for the remaining centers are given in the following table.

Procedural Success
Bottom-Half of Rankings

Institution	Performance Rating		Success Rate, %			Adverse Event Rate
	Adjusted	Primary	Complete	Partial	Failure	
Group 1	1	-1	12	16	72	63
Group 2	0.3	0.2	13	0	87	29
Group 3	1	0.02	12	17	71	50
Average	**0.6**	**-0.2**	**12**	**14**	**74**	**50**

Group 1 contains 5 institutions for which reports of 4 or more ablations were available.
Group 2 contains 5 institutions for which reports of 3 ablations were available.
Group 3 contains 44 institutions for which reports of less than 3 ablations were available.

The above statistics are indeed sobering. Undergoing an ablation procedure at an institution other than the 9 top-ranked ones is associated with an **average** complete success rate of 12%, a partial success rate of 14%, and a failure rate of 74%. This is accompanied by an **average** adverse event rate of 50%. I fully realize that averages can be deceiving, but quite frankly, I saw no convincing evidence that there were any "gems" hidden among the 54 institutions constituting the bottom-half of the ranking scheme.

Combined Procedural Success Rate

Combining the 9 top-ranked institutions with the 54 bottom-ranked ones gives the following results:

Combined Procedural Success

Institution	Complete Success	Partial Success	Failure	Adverse Event Rate
Top-rated	51%	12%	37%	34%
Bottom-rated	12%	14%	74%	50%
Average	**31%**	**13%**	**56%**	**43%**

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 whether it takes one or five individual procedures. About one third of all initial procedures were followed by one or more RF ablations. Overall finals results for the top 9 institutions are presented in the table below.

Final Performance Rating
Top-Rated Institutions

		Final Success Rate, %		
Institution	Repeat Rate, %	Complete Success	Partial Success	Failure
Marin County	14	72	14	14
Cleveland Clinic	8	62	19	19
Bordeaux	33	78	0	22
Loyola	33	67	0	33
San Diego	0	50	0	50
MUSC	60	60	20	20
U Penn	25	50	50	0
Royal Jubilee	20	50	0	50
Good Samaritan	50	50	0	50
Average	**20**	**62**	**14**	**24**

Comparative data for the bottom-rated institutions is given in the table below.

Final Performance Rating
Bottom-Ranked Institutions

		Final Success Rate, %		
Institution	Repeat Rate, %	Complete Success	Partial Success	Failure
Bottom-ranked	46	18	19	63

A total of 31 repeat ablations were performed in the bottom-ranked group with a complete success rate of 10%, a partial success rate of 18%, and a failure rate of 72%.

Combining the results for both groups produces the following final outcome (after repeat ablations).

Overall Final Outcome

		Final Success Rate, %		
Institution	Repeat Rate, %	Complete Success	Partial Success	Failure
Top-ranked	20	62	14	24
Bottom-ranked	46	18	19	63
TOTAL	**30**	**41**	**17**	**42**

Maze Surgery and Other Procedures

Forty-five afibbers reported that they had undergone procedures other than RF ablation to deal with problems (left or right atrial flutter) arising from a pulmonary vein isolation procedure, or to achieve a cure for their afib.

The distribution of the procedures covered in this part of the survey is as follows:

	Number of Procedures		
Procedure	Initial	Follow-up*	Total
Maze procedure	5	1	6
Mini-maze procedure	7	1	8
Cryoablation	3	0	3
AV node ablation + pacemaker	2	0	2
Right atrial flutter ablation	16	4	20
Left atrial flutter ablation	2	3	5
Other procedures	0	1	1
TOTAL	35	10	45

* F/U procedures are those done after an initial procedure of any kind (PVI, flutter ablation, etc.)

A total of 15 (33%) of the procedures covered in this part of the survey (mostly right atrial flutter ablations) were followed by standard pulmonary vein ablations.

Demographics

Most of the afibbers (51%) undergoing the procedures covered in this section had the mixed (random) variety of AF. The next largest grouping was permanent afibbers at 27%, vagal afibbers at 16%, and adrenergic at 6%. Women constituted 26% of the group and the median age at diagnosis was 49 years with a range of 20-68 years. The median age at which the procedure was performed was 58 years with a range of 39-69 years.

AF Frequency and Duration

The majority of respondents (79%) experienced episodes at least once a week and 42% had daily ones (including permanent afibbers). Only 7% of

those seeking a cure through the procedures covered here had episodes less frequently than once a month. This indicates that the vast majority in this group only opted for a procedure when the frequency of episodes became intolerable or permanent AF became a reality. The median duration of paroxysmal episodes was 9 hours with a range of 2-60 hours.

Maze Procedure

The maze procedure involves open-heart surgery and the use of a heart/lung machine since the heart needs to be stopped during the procedure. After making a 10-12 inch long incision and cracking open the ribs, scar tissue is surgically created (by cutting and sewing) on the surface of the heart to make pathways connecting the sinus node and the AV node and to eliminate the possibility of aberrant impulses initiating atrial fibrillation.

Five afibbers (4 males and 1 female) had undergone the maze procedure as their first (and only) procedure, while 1 male afibber had his after previously having undergone two failed RF ablations. One procedure used laparoscopic cryo surgery and involved the use of a heart/lung machine. It was performed in April 2005, so far it looks promising, but the side effects of edema and infections in the leg and groin were fairly severe.

Of the other 5 maze procedures three (60%) were fully successful, one (20%) was partially successful, and one (20%) was a failure. These rates are comparable to those obtained at top-ranked RF ablation facilities after one or more procedures.

The three successful procedures were performed by the following surgeons:

- Dr. Patrick McCarthy – Cleveland Clinic, OH
- Dr. Dale M. Geiss – St. Francis Medical Center, Peoria, IL (2 procedures)

Three of the 5 procedures, for which the outcome is known, were not accompanied by any adverse effects, but 2 afibbers incurred a transient ischemic attack (TIA), one of which is still causing problems.

Four out of 5 patients did not experience an increase in ectopics after the procedure, but the one partially successful case did.

Two out of the 3 successful cases experienced no post-procedural AF episodes, but one did so for a month and both the partial success and the failure also did so.

None of the 3 successes were on warfarin, but both the partial success and the failure were.

Neither the complete nor the partial success needed continuing avoidance of triggers and both the complete and partially successful cases subjectively judged their surgery to have been successful, while the failure deemed it a failure.

The successful cases took between 1 and 3 months to recover their stamina, while the partially successful and failure cases took more than 3 months to fully recover.

Conclusion
Based on this rather small sample of 6 afibbers it would appear that the success rate of a single maze procedure is comparable to that of an ablation (with repeat procedure if necessary) performed at a top-ranked RF ablation center. Considering that the full maze procedure involves stoppage of the heart and the use of a heart/lung machine (with its associated potential problems), that adverse events may be more serious, and that recovery times are longer, there would seem to be little benefit in choosing a full maze procedure over a RF ablation carried out by a top EP at a top-ranked center.

Mini-Maze Procedure

This procedure is similar to the maze in that scar tissue is created on the outside of the heart rather than on the inside as is done in ablation procedures. Access to the heart is through two or more small incisions between the ribs and it is not necessary to stop the heart during the procedure. Lesions are created with a standard RF ablation catheter rather than by cutting and sewing. The left atrial appendage, a small pouch where blood clots tend to form, is also removed during the procedure.

Seven afibbers (2 females and 5 males) had undergone the mini-maze procedure as their first (and only) procedure, while one male afibber had his after two failed RF ablations. One of the procedures used microwaves for ablating, but as it was only done in May 2005 it has not been included in the evaluation of overall success rate.

Of the 7 remaining, 6 (86%) were fully successful and the remaining 1 (14%) was a failure. The success rate of 86% with just one procedure is superior to that obtained at top-ranked RF ablation centers using one or

more procedures. I believe only the very best EPs would be able to equal it.

The 6 successful procedures were performed at the following institutions:

- Ohio State University - Dr. James Cox
- University of Cincinnati - Dr. Randal Wolf (2 procedures)
- Medical City Hospital, Dallas, TX - Dr. Michael Mack
- Holy Cross Hospital, Fort Lauderdale, FL
- James Cook University Hospital, UK - Dr. Steve Hunter

Five of the 7 procedures were free of adverse events, while 1 was accompanied by a major accumulation of blood in the chest cavity and 1 resulted in a shingles-like nerve pain. Neither of these adverse effects were fully resolved 7 months post-procedure.

Six out of 8 patients did not experience any increased ectopic activity after their procedure, while 2 did experience some for less than a month post-procedure. Three of the successful cases experienced no post-procedure AF episodes, 2 experienced them for less than a month, and 1 experienced them for more than three months.

All the successful cases were off warfarin, while the unsuccessful case was still on warfarin. Most successful cases (4 out of 6) no longer needed to avoid previous triggers, while the remaining 2 were not sure. The unsuccessful case still needed to avoid known triggers.

The recovery time varied considerably. Among successful cases one recovered after 1-2 months, two recovered after 2-3 months, one recovered after 3 months, and two needed more than 3 months to recover.

Conclusion

Based on this rather small sample of just 8 afibbers, it is evident that the mini-maze is a highly successful procedure when carried out by a skilled cardiac surgeon. Recovery times are somewhat longer than for RF ablation and side effects can be more serious, but radiation exposure is likely to be negligible to nil. Overall, the mini-maze will no doubt soon emerge as a worthy competitor to RF procedures done at top-ranked institutions. However, not many cardiac surgeons have extensive experience with the procedure, so it is important to either wait a while or choose a surgeon who has already performed a hundred or more.

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 themselves.

Three male afibbers reported having undergone cryoablation as their first procedure. Two had the mixed variety of AF and one was vagal. One procedure was performed in the early days of cryoablation (April 2000) and was not successful. It was followed by two segmental pulmonary veins ablations which were also unsuccessful. One procedure, carried out by Dr. Gregory Feld at the University of California at San Diego, was successful with no adverse effects. The remaining procedure was done in connection with an aortic valve replacement procedure and the patient remains on amiodarone one year post-procedure. Both left and right atrial flutter was introduced by the procedure.

Conclusion

It is clearly not possible to conclude anything about the success rate of cryoablation based on just 3 cases.

AV Node Ablation + Pacemaker

Another approach to eliminating the effects of the fibrillation of the atrium on ventricular beats is to isolate the AV node (the ventricular beat controller) from any extraneous impulses and feed it its marching orders from an implanted pacemaker. This procedure has three major drawbacks:

- It does nothing to stop the fibrillation of the atria, which in itself can be quite uncomfortable, and necessitates continuing anticoagulation (warfarin) therapy.
- It makes the patient entirely dependent on the pacemaker. If it malfunctions or the batteries run out the patient dies.
- It does nothing to remedy the fatigue and reduced exercise capacity caused by the fibrillation of the atria.

AV node ablation is performed in much the same way as a RF ablation except that it is the area around the node that is ablated. A recent study found the procedure to be relatively safe for patients with lone AF, but another more recent study concluded that the procedural mortality rate is about 2.1%. Although AV node ablation and pacemaker implantation

does improve the quality of life, it is still considered a last resort approach, especially for lone afibbers.

Two male afibbers (1 permanent, 1 vagal and both with no underlying heart disease) had undergone AV node ablation and pacemaker installation with no adverse events. They are both on warfarin (permanently), but are not taking antiarrhythmics or blockers and are not experiencing symptomatic AF episodes. They no longer need to avoid previous triggers. Thus, within the above-mentioned limitations, these two procedures were successful.

Right Atrial Flutter Ablation

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 flutter 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. Despite the 1998 discovery by Prof. Haissaguerre that 80-90% of all AF episodes are initiated in the

pulmonary veins (left atrium), right atrial flutter ablations are still carried out today in an attempt to cure AF. They are also performed in cases where the patient suffers from right atrial flutter or a combination of AF and atrial flutter.

Sixteen (13 males and 3 females) had undergone a right atrial flutter ablation as their first procedure. Of these one (female) had a successful right atrial flutter ablation and an ablation for PVCs and now has no further problems. One (female) had a successful right atrial flutter ablation which also cured AF. The remaining 14 had both AF and flutter and the flutter ablation, while in most cases (85%) curing the flutter, did not cure the AF. Eleven of the 14 went on to have RF ablation for AF, while one had a repeat atrial flutter ablation.

The majority (75%) experienced no adverse events related to the flutter ablation. Three patients (19%) experienced hematomas in the groin and thigh area, while one developed left atrial flutter/tachycardia.

Four afibbers developed atrial flutter after their PVI procedure and were successfully ablated for right atrial flutter. It is interesting to note that only one of the 20 right atrial flutter ablation procedures was carried out at a top-ranked institution.

Conclusion
Right atrial flutter ablations are generally successful in curing the flutter, but only very rarely (1 in 15) cures coexisting AF as well.

Left Atrial Flutter Ablation

Left atrial flutter is considerably less common than right atrial flutter, but can also occur as a result of a PVI procedure. The PVI-related left atrial flutter may disappear on it own over a 6-month period or so, but some cases require a repeat ablation to fix the flutter.

Two respondents had left atrial flutter as their primary condition and were successfully ablated for this. One of them also had AF and was successfully ablated for this as well.

Three of the respondents who developed left atrial flutter as a sequel to their AF procedure had a successful follow-up procedure to eliminate it.

Conclusion
Left atrial flutter can occur as a sequel to an AF ablation. In many cases it disappears on its own, but in some cases a repeat ablation is necessary

to correct the flutter. This procedure (based on a very small sample size) is usually successful.

Other Procedures

One successfully ablated afibber had a follow-up ablation (successful) for supraventricular tachycardia.

Summary

A total of 45 procedures other than RF ablation was carried out in order to eliminate AF or conditions arising from a PVI procedure. The following observations were made:

- Based on a very small sample (6 procedures) it would appear that the success rate of a full maze procedure is comparable to that of a RF ablation (with repeat procedure as necessary) performed at a top-ranked institution.

- Based on a small sample (8 procedures) it would appear that the mini-maze is a highly successful procedure when carried out by a skilled cardiac surgeon.

- There were only 3 responses from afibbers who had undergone cryoablation, so it is not possible to draw conclusions regarding the success rate and safety of this procedure.

- Two responses were received from afibbers who had undergone AV node ablation and pacemaker implantation. Both procedures were successful and eliminated symptomatic AF. Nevertheless, this procedure remains the procedure of last resort.

- Twenty respondents had undergone a right atrial flutter ablation either as a follow-up to a PVI procedure, in an attempt to cure associated AF, or to eliminate atrial flutter on its own. Procedures were generally successful as far as eliminating flutter is concerned, but very rarely cured coexistent AF.

- Five respondents were successfully ablated for left atrial flutter either precipitated by a PVI procedure or present as a primary condition.

- One successfully ablated afibber had a successful follow-up ablation for supraventricular tachycardia.

Update to Performance Ratings

Since the publication of the original LAF Survey-9 results in September I have received additional responses relating to procedures performed prior to August 2005. Data is now available covering the outcome of 215 RF (radiofrequency) ablation procedures performed on 165 individual afibbers. The success rates for the individual procedures are given below:

Success Rates – Individual Procedures

Procedure	# of patients	Complete success(1)	Partial success(2)	Failure(3)
First procedure	165	34%	14%	52%
Second procedure	45	36%	9%	55%
Third procedure	5	20%	20%	60%
Average	215	33%	13%	54%

(1) No afib episodes, no antiarrhythmics or blockers
(2) No afib episodes, but still on antiarrhythmics or blockers
(3) Recurring afib episodes

It is clear that only about one third of all RF ablation procedures covered in the survey have a fully successful outcome, while just over 50% do not result in the elimination of afib episodes even with the continued use of medications. About 30% of survey respondents underwent a second or third procedure.

Of course, the most important aspect for an afibber undergoing RF ablation is whether or not they will ultimately be cured – no matter how many procedures it takes. The overall outcome for the 165 survey participants is given below:

Overall Outcome

# of patients	Complete success	Partial success	Failure
165	44%	16%	40%

The actual, objectively determined, complete success rate of 44% is disappointing and is lower than the percentage of afibbers who subjectively felt that their ablation has been a success (56%).

Whichever success rate one looks at, it is clearly much lower than the success rates claimed by top institutions such as the Cleveland Clinic and the Hopital Cardiologique du Haut Leveque in Bordeaux.

Thus, it would be of interest to analyze the data a bit closer to account for the influence on success of the electrophysiologist performing the ablation and the institution where it is done.

Procedural Performance Rating

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 and adverse event rates reported by afibbers treated at specific institutions. The outcome 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

Adverse Events Score

- No adverse events — score = 0
- Hematoma — score = -2
- Minor reversible events — score = -2
- Right atrial flutter — score = -5
- Left atrial flutter — score = -5
- Supraventricular tachycardia — score = -5
- Moderate PV stenosis — score = -5
- TIA — score = -5
- Phrenic nerve damage — score = -10
- Severe PV stenosis — score = -10
- Tamponade — score = -10
- Atrial/esophageal fistula — score = -10
- Other life-threatening events — score = -10
- Minor stroke — score = -10
- Events causing permanent disability — score = -20

The **outcome factor** adds the scores (for successes and adverse events) for each RF ablation and the **performance rating** then averages these outcome factors for each individual institution. For example, if a procedure is fully successful with no adverse events, than the outcome factor is +10. If a procedure is a failure and accompanied by the creation of left atrial flutter or tachycardia, then the outcome factor is –5. The primary performance rating does not take into account that a large number of adverse events are resolved within a few months after the procedure. To acknowledge this, an **adjusted performance rating** is also shown in which the effect of resolved adverse events has been taken into account.

Please note that in this particular evaluation a RF ablation 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 where results for 4 or more procedures were available. Based on the adjusted performance rating the various institutions stack up as follows:

Procedural Performance Rating
(4 or more procedures)

Rank	# of Procedures	Institution
1	9	Marin County General Hospital, CA*
2	45	Cleveland Clinic, OH
3	15	Hopital Cardiologique du Haut Leveque, Bordeaux
4	4	Loyola University Medical Center, Chicago
5	4	Royal Jubilee Hospital, Victoria, Canada
6	8	Medical University of South Carolina
7	5	University of California at San Diego
8	7	University of Pennsylvania
9	6	Good Samaritan Hospital, Los Angeles
10	7	New York University Medical Center
11	6	Centinella Hospital (Pacific Rim Electrophysiology), Inglewood, CA
12	4	St. Paul's Hospital, Vancouver, Canada
13	6	Brigham & Women's Hospital, Boston
14	4	Johns Hopkins, Baltimore
15	5	University of Michigan

* All procedures performed by Dr. Andrea Natale

The first 9 institutions (Group A) in the above table account for close to 50% of all ablation procedures performed; their performance is evaluated in detail below:

Procedural Performance Ratings – Group A

Institution	Adjusted Rating	Complete Success	Partial Success	Failure	Adverse Event Rate (1)
Marin County	7.0	67%	11%	22%	44%
Cleveland Clinic	6.1	58%	20%	22%	38%
Bordeaux	5.7	60%	0	40%	20%
Loyola	5.0	50%	0	50%	0
Royal Jubilee	5.0	50%	0	50%	0
MUSC	4.4	38%	12%	50%	38%
USC, San Diego	4.0	40%	0	60%	20%
U Penn	3.6	29%	29%	42%	57%
Good Samaritan, LA	3.3	33%	0	67%	20%
Average	**-**	**52%**	**13%**	**35%**	**32%**

(1) Please note that the major category of adverse events were hematomas in the groin or thigh area. The majority of adverse events (57%) were resolved within a couple of months of the procedure.

The electrophysiologists performing the procedures in the above 9 institutions are as follows:

Institution	Electrophysiologists
Marin County	Dr. Andrea Natale
Cleveland	Drs. Natale, Saliba, Schweikert, Tchou
Bordeaux	Drs. Haissaguerre, Jais
Loyola	Dr. David Wilber
Royal Jubilee	Drs. Richard Leather, Larry Stern
MUSC	Dr. Marcus Wharton
USC, San Diego	Dr. Gregory Feld
U Penn	Drs. David Callans, Marchlinski
Good Samaritan	Drs. Anil Bhandari, Neala Hunter

The average procedural success and adverse event rates for the remaining centers are given in the following table.

Procedural Performance Ratings – Other Institutions

Institution	Proced. in Group	Adjust Rating	Complet Success	Part Succ.	Failure	Adverse Event Rate
Group B	32	0.5	13%	16%	71%	35%
Group C	15	- 0.1	13%	0	87%	50%
Group D	65	1.7	18%	15%	67%	38%
Average	**-**	**1.1**	**16%**	**13%**	**71%**	**38%**

Group B contains 6 institutions for which reports of 4 or more ablations are available.
Group C contains 5 institutions for which reports of 3 ablations are available.
Group D contains 48 institutions for which reports of 1 or 2 ablations are available.

Combining the 9 top-ranked institutions with the 59 other ones yields the following results:

Combined Procedural Performance Ratings

Institution	Complete Success	Partial Success	Failure	Adverse Event Rate
Group A	52%	13%	35%	32%
Group B, C and D	16%	13%	71%	38%
Average	**33%**	**13%**	**54%**	**35%**

The above statistics are indeed sobering and do no support the popular "myth" that a RF ablation is "a piece of cake". Undergoing an ablation at an institution other than one of the 9 top-ranked ones is associated with an **average** complete success rate of 16%, a partial success rate of 13%, and a failure rate of 71%. This is accompanied by an average adverse event rate of 38%.

While it is fairly clear that an institution where 3 out of 4 procedures were failures belongs in the bottom-half, it is much more difficult to rate institutions where data for only one or two procedures are available. Thus, the following information may be of interest.

Institutions performing two procedures of which one was a complete success at first attempt are:

- Beaumont Hospital, Detroit, MI – Dr. David E. Haines
- Deaconess Medical Center, Spokane, WA – Dr. Gerhard Mulheims
- Mayo Clinic, Rochester, MN – Dr. Douglas L. Packer
- Riverside Methodist Hospital, Columbus, OH – Dr. John Hummel

Institutions performing one procedure with a 100% complete success rate at first attempt are:

- Lahey Clinic Medical Center, Burlington, MA – Dr. Roy M. John
- Prince of Wales Hospital, Sydney, Australia – Dr. R.M. Allen
- Utah Valley Regional Medical Center, Provo, UT – Dr. Chun Hwang
- St. Vincent's Hospital, Portland, OR – Dr. Blair Halperin
- Tulane University, New Orleans, LA – Dr. McKinnie
- Valley Hospital, Ridgewood, NJ – Dr. Jonathan Steinberg

The scarcity of data clearly means that nothing can be concluded about the general success rate of the above institutions or EPs. However, it may provide comfort to someone considering an ablation there, that they have had at least one success at first attempt.

Success Rate on First Attempt

The success rates of the initial procedure were as follows for institutions in Group A.

Performance Rating – First Attempt

	# of	Final Success Rate		
Institution	Patients	Complete	Partial	Failure
Marin County	8	63%	13%	24%
Cleveland Clinic	38	58%	21%	21%
Bordeaux	10	50%	0	50%
Loyola	3	67%	0	33%
Royal Jubilee	4	50%	0	50%
MUSC	5	40%	0	60%
USC, San Diego	5	40%	0	60%
U Penn	4	0	50%	50%
Good Samaritan	4	25%	0	75%
Combined	**81**	**51%**	**13%**	**36%**

Initial success rates for institutions in Groups B, C, and D are presented below.

Performance Rating – First Attempt

	# of	Final Success Rate		
Institution	Patients	Complete	Partial	Failure
Group B	21	10%	14%	76%
Group C	11	18%	0	82%
Group D	52	21%	17%	62%
Combined	**84**	**18%**	**14%**	**68%**

It is clear from the above that the best chance of being cured of afib with just one procedure can be found at Marin County Hospital (Dr. Natale), the Cleveland Clinic or Loyola University Medical Center (Dr. David Wilber)

Ultimate Success Rate

The ultimate measure of success for the individual afib patient is, of course, whether or not they are cured of afib irrespective of whether it takes 1 or 5 separate procedures. About one third of all initial procedures were followed by one or more additional RF ablations. Overall final results for the top 9 institutions (Group A) are presented in the table below.

Final Performance Rating

	# of	Repeat	Final Success Rate		
Institution	Patients	Rate(3)	Complete	Partial	Failure
Marin County	8	13%	75%	13%	12%
Cleveland Clinic	42(1)	8%	62%	21%	17%
Bordeaux	11(2)	40%	82%	0	18%
Loyola	3	33%	67%	0	33%
Royal Jubilee	3	0	67%	0	33%
MUSC	4	75%	75%	25%	0
USC, San Diego	5	0	40%	0	60%
U Penn	5	60%	40%	40%	20%
Good Samaritan	4	50%	50%	0	50%
Combined	**85**	**21%**	**64%**	**15%**	**21%**

(1) 4 of the 7 patients having repeat ablations did not have their initial procedure at Cleveland Clinic. NOTE: No significant differences in success rates were observed for the 4 EPs doing PVAIs at the CC (Drs. Natale, Saliba, Schweikert, and Tchou)
(2) 1 of the 5 patients having repeat ablations did not have their initial procedure at the Hopital Cardiologique du Haut Leveque.
(3) The repeat rate applied to the number of patients having their initial procedure at the institution.

The average repeat rate was 21%. However, if Marin County Hospital and the Cleveland Clinic, which both have very low repeat rates, are omitted then the repeat rates rise to 36% indicating that even EPs at the top institutions often need to perform two procedures to achieve a cure.

Comparative data for the institutions in Groups B, C, and D is given below.

Final Performance Rating

Institution	# of Patients	Repeat Rate(3)	Final Success Rate		
			Complete	Partial	Failure
Group B	22	45%	18%	18%	64%
Group C	10	30%	20%	0	80%
Group D	48	25%	25%	21%	54%
Combined	**80**	**34%**	**22%**	**18%**	**60%**

Combining the results for all groups produces the following final outcome (after repeat ablations).

Overall Final Outcome

Institution	# of Patients	Repeat Rate(3)	Final Success Rate		
			Complete	Partial	Failure
Group A	85	21%	64%	15%	21%
Group B, C and D	80	34%	23%	17%	60%
Combined	**165**	**27%**	**44%**	**16%**	**40%**

A recently published worldwide survey involving 8745 patients treated at 90 different institutions concluded that the overall complete success rate (no afib – no drugs) was 52% - including 27% who needed a touch-up procedure[1]. Institutions having performed more than 300 ablation procedures had an overall complete success rate of 63.8% - not substantially different from the 64% complete success rate observed for the 9 top-ranked institutions in this survey.

The overall repeat rate observed in our survey is identical to the one observed in the published survey (27%).

The success rate among institutions having performed less than 30 ablation procedures was 30% - somewhat higher than the 23% complete success rate observed for other than the 9 top-ranked institutions. I believe the reasons for this difference is the recent enormous increase in the number of ablations conducted and the fact that many of these ablations are performed by electrophysiologists operating during the very early stages of the learning curve.

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 average rate of complete success for top-ranked institutions found in this survey (64%) is identical to the one reported in the *Circulation* study (63.8%). Similarly, the repeat (touch-up) rates found in the two surveys are identical at 27%.

The LAF Survey-9 results (including follow-up data) are based on a total of 215 procedures involving 185 individual patients, not an overly large number, but enough to draw reasonably valid conclusions in general terms. Where the survey results become somewhat less "solid" is in the evaluation of the success rates of individual institutions. A sample of just 4 or 5 procedures is clearly not very significant in a statistical sense and it is quite possible that a larger sample 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 9 top-rated institutions presented in this survey. There may well be other institutions and individual EPs that deserve top ranking, but I have no compelling evidence that this is indeed the case.

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, is likely to lead to disappointment.

[1] Cappato, R, et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circulation, Vol. 111, March 8, 2005, pp. 1100-05

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.

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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