Atrial Fibrillation: A Historical Perspective

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We shall not cease from exploring and the end of all our exploring will be to arrive where we started and know the place for the first time.

—T.S. Eliot

The foregoing quotation is particularly a propos as we review the historical developments in atrial fibrillation (AF). This is exemplified by the fact that one of the first mechanisms proposed for initiation of AF invoked a focal trigger. For much of the twentieth century, a focal trigger was discounted until the landmark observation by Haissaguerre described pulmonary vein (PV) foci, and thus ushered in the ablation era. Although we engage in this ''circus movement'' in an attempt to understand AF better, we someday hope to eliminate the ''excitable gap'' in our knowledge, leading to the ''cure'' of AF.

AF has undoubtedly become one of the most well-studied arrhythmias today in terms of pathophysiology and diagnostic and therapeutic (interventional) electrophysiology. Although it lends itself to an apparently easy diagnosis on the surface electrocardiography (ECG), myriad electromechanical mechanisms underlie its origin. We have now reached an era of technology that makes AF not only ''treatable'' but potentially ''curable.'' This article aims at walking through the historical ''corridors'' and ''mazes'' that led to the present day understanding of this common yet complex arrhythmia.

EARLIEST CLINICAL SIGHTINGS

The earliest record of AF seems to be in the Yellow Emperor's Classic of Internal Medicine in the seventeenth century.[1] William Harvey is credited with the first description of ''auricular fibrillation'' in animals, however, in 1628. After Harvey's description, the misunderstanding that the pulse was independent of the heartbeat continued to prevail, likely because of the dissociation that frequently exists between the irregular heart contractions and the palpable radial pulse in AF. This is now well recognized as the ''pulse deficit,'' which can be a valuable clue to the bedside diagnosis of AF. In 1863, Chauveau and Marey[2] conducted various studies on cardiac physiology utilizing the ''sphygmograph,'' an instrument used to record the pulse graphically, and thereby described a pulse tracing from a patient with AF.[1] Various descriptions of the irregular pulse as ''intermission of the pulsation of the heart'' (Laennec), ''ataxia of the pulse'' (Bouilland), delirium cordis (Nothnagel), and, finally, ''pulsus irregularis perpetuus'' (Hering) later ensued.[3] In 1907, Arthur Cushny at University College of London published the first case report of AF in his patient after surgery for an ''ovarian fibroid'' recorded with a ''Jacques sphygmochronograph.''[4] This was the first correlative clinical report on the electrical record and palpated irregularity of the pulse in AF. The development of the string galvanometer in 1909 opened the door on the electrical nature of AF, allowing further correlation with the physical examination.

AF is most commonly associated with mitral valve disease. Jean Baptiste Senac connected AF (which he called ''rebellious palpitation'') and mitral stenosis (MS) in 1783.[5] Robert Adams[6] reported irregular pulses associated with MS in 1827. In 1897, James Mackenzie[7] first noted that the jugular ''A wave'' was lost in a patient who

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had MS and that the presystolic murmur of MS disappeared in a patient who went from a normal to irregular rhythm. In more recent literature, AF has been reported to occur in 29% of patients who had isolated MS, in 16% who had isolated mitral regurgitation, and in 52% who had combined MS and regurgitation of rheumatic etiology.[8]

In the years that followed, the pure clinical face of AF was accompanied by further electromechanical insight facilitated by ECG and, over the years, newer recording and imaging modalities.

ELECTROCARDIOGRAPHY: REVEALING THE ELECTRICAL FACE OF ATRIAL FIBRILLATION

The development of ECG by Willem Einthoven (**Fig. 1**)[9] in 1902 provided a simple means for recording the electrical events that represent AF. His device consisted of a string galvanometer (with various complex attachments) and required transmission of electrical signals over telephone wires to his laboratory (**Fig. 2**). He recorded 26 single-lead ECG strips of various cardiac rhythm disturbances, one of which depicted AF (he called this electrical pattern pulsus inequalis and irregularis). In 1909, Thomas Lewis[10] described the classic ''absence of P waves'' and ''irregularity of the F waves'' that define AF (**Fig. 3**). In 1928, technical advances were made to amplify ECG recordings.[11] Frank Sanborn developed the first portable ECG machine the same year.[12] This was a significant development in the miniaturization of ECG recording. Further research started focusing on finer points of ECG that can help to glean more useful and corroborative information regarding mechanisms and cardiac activity during AF. The atrial cycle length has been studied as a predictor of paroxysmal AF and of recurrence after cardioversion. This is done using frequency analysis of fibrillatory ECG.[13] Further studies have led to elucidation of initiating mechanisms for AF. In 1998, the PVs assumed an important role as the triggers driving paroxysmal AF. Ablation in the region of the PVs also rewardingly treated AF, leading to an exciting chase to identify the anatomic and electrical characteristics of these veins better. Certain ECG morphologies of the P waves can predict paroxysmal AF and identify the culprit PV.[14,15] Newer technologies, such as the 65-lead ECG mapping system (Resolution Medical, Inc., Pleasanton, CA), can facilitate noninvasive localization of AF trigger sites by matching the P wave integral map morphology of a premature atrial contraction with the reference database of 34 mean paced P wave integral map patterns.[16] AF

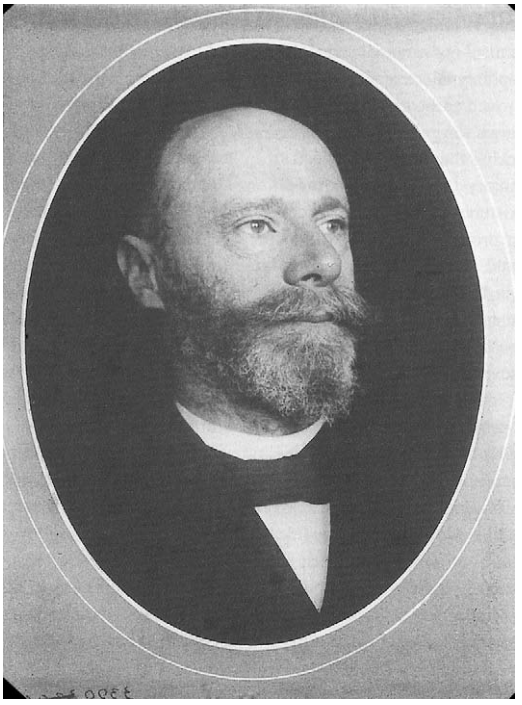

Fig. 1. Willem Einthoven when rector of the senate of the university in 1906. (*Courtesy of* The Einthoven Foundation, Leiden, The Netherlands; with permission.)

Fig. 2. Patient sitting in the university hospital while his telecardiogram is recorded in the physiology laboratory. His hands are immersed in strong salt (NaCl) solution. (*Courtesy of* The Einthoven Foundation, Leiden, The Netherlands; with permission.)

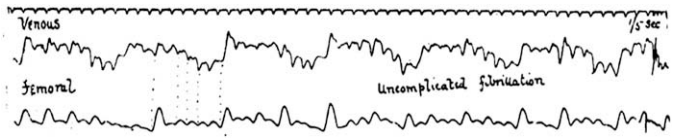

Fig. 3. Venous and femoral artery tracings from a dog during AF show a completely irregular pulse. (*From* Lewis T. The reaction of the heart to digitalis when the auricle is fibrillating. BMJ 1910;2:1670; with permission.)

was also later appreciated on intracardiac ECG.[17,18] Algorithms have been developed that can help to localize PV activity using intracardiac recordings during spontaneous and paced PV activity.[19] Time-frequency analysis of surface ECG has been reported to aid noninvasive monitoring of effects of antiarrhythmic drugs on fibrillatory rate and waveform.[20] We have come a long way since Einthoven but still use the same basic principles of ECG diagnosis of AF. Many more advances are likely to occur in understanding AF, but ECG is always likely to remain a trusted, economic, and noninvasive source of invaluable information that assists in clinical decision making.

PATHOPHYSIOLOGY: WHAT CAUSES ATRIAL FIBRILLATION?

The understanding of mechanisms underlying the initiation and maintenance of AF has evolved over the past decades. The earliest concept of re-entry proposed by Winterberg in 1906[21] and by Lewis and Schleiter[22] in 1912 advocated that rapid focal activity from one or more centers accounted for AF. In 1913, Mines[23] showed that the mechanism of re-entry was an impulse circling a large anatomic obstacle. In 1947, Scherf[24] revived the theory of focal trigger in AF. In the 1960s, Moe and colleagues[25] supported the theory of randomly propagating multiple wavelets as the main mechanism underlying AF. The re-entrant wavelet hypothesis required that the concept of ''wavelength'' of the arrhythmia circuit be introduced. In the 1970s, Allessie and colleagues[26] introduced the concept of ''leading circle re-entry.'' In a goat model of AF, they demonstrated that the average circuit diameter was 20 to 30 mm and that a minimum of five to eight random wavelets was required to sustain AF. All these theories of random re-entry wavelets explained the sustenance of AF, but how it was initiated was also warranted. Allessie and colleagues[27] offered several possible explanations: a ''stable background circuit'' capable of initiating new AF when the earlier episode dies out, abnormal focal trigger sites in the atria, and the possibility of an echo beat from the AV node or from an accessory pathway. The present understanding is that AF requires a ''critical atrial mass'' needed to maintain the arrhythmia and that there is a critical rate greater than which organized atrial activity cannot continue. Thus, at a certain rate, organized atrial activity can disintegrate into AF provided that the critical tissue mass is available to sustain it. Recent studies in isolated human atrial preparations showed that a single meandering functional re-entrant wavefront produced AF.[28] Recent work by Jalife and colleagues[29] questions the randomness of atrial activity in AF. Their study suggests the presence of a possible ''mother circuit'' that serves as a periodic background focus; the presence of anatomic obstacles (eg, scar, orifices) serves to break up the wavefront from the mother circuit into multiple wavelets that spread in various directions. Wu and colleagues[30] have proposed the role of pectinate muscles as obstacles that break the activation wave, thus promoting re-entry. They may also serve as an anchoring site for the wave, leading to rotor-like activity. The likelihood that focal activation plays some role in AF is now well accepted. In 1966, in an anatomic study of the left atrium–PV junction in human hearts, Nathan and Eliakim[31] reported that the proximal portion of the PV has a sleeve of myocardium that is a direct extension from the adjacent atrial tissue and is electrically coupled to the atrium. Haissaguerre and colleagues[32] reported arrhythmogenicity of the PVs as possible focal triggers in some cases of AF. The myocardial sleeves that extend from the left atrium onto the PVs seem to be the pathologic correlate of the arrhythmogenic focus. Since then, multiple other foci of AF have been discovered in the thoracic venous structures connected to the atria, including the superior vena cava,[33] coronary sinus,[34] and vein of Marshall.[35] The autonomic basis of AF was also explored by Coumel,[36] who classified AF as adrenergic or vagally mediated. There has also been research implicating genes that predispose to AF.

GENETICS OF ATRIAL FIBRILLATION: BORN WITH IT?

Genetics has excitingly permeated every domain of medicine, and cardiac electrophysiology is no exception. Interest in the genetic basis of AF was driven by the occurrence of AF in families and its association with other arrhythmic conditions with genetic bases, such as Wolff-Parkinson-White (WPW) syndrome[37] and hypertrophic

cardiomyopathy.[38] Familial AF was first reported in 1943.[39] Recent studies show that routinely encountered AF may have a genetic basis more commonly than previously considered.[40] In 1997, Brugada and colleagues[41] reported the first monogenic basis for familial AF implicating a gene on chromosome 10. Ellinor and colleagues[42] mapped a gene for familial AF to chromosome 6. Genes coding for potassium channels have been discovered to date that are held responsible for AF.[43] More genes are likely to be discovered, and, although remote at this time, genetic therapy may someday be a means to cure or prevent AF in those predisposed.

MAPPING ATRIAL FIBRILLATION: LOCALIZING THE ORIGIN OF ATRIAL FIBRILLATION

The development of mapping techniques[44] is central to appreciating the success we have today in treating AF with ablation. Mapping AF has helped to clarify its mechanism and localize possible anatomic sites for effective radiofrequency (RF) ablation. Conventionally, this has been done by correlation of 12-lead surface ECG with intracardiac data. Three-dimensional imaging of the triggering foci and correlation with the activation sequence can better localize therapy. Electroanatomic or CARTO mapping is a nonfluoroscopic mapping system that uses magnetic technology to determine the location and orientation of the mapping and ablation catheter accurately while simultaneously recording local electrograms from the catheter tip. Noncontact mapping is performed using the EnSite3000 (Endocardial Solutions, St. Paul, Minnesota) mapping system, consisting of a balloon or multielectrode array that detects endocardial activation recorded by noncontact intracavitary electrodes. The activation points are displayed as computed electrograms or isopotential maps.[45] Other techniques used include the basket (EPT; Boston Scientific, Natick, MA) and amplification technique. The electrodes are coupled to achieve bipolar recordings, and each electrode couple is then amplified and filtered separately for every channel (CardioLab System; Prucka Engineering, Houston, Texas). Intracardiac echocardiography can be a valuable tool in localizing anatomic areas for ablation. It allows for assessment of wall contact of ablation catheters for creation of long linear lesions for catheter ablative treatment of AF.[46] Inverse ECG images the activation time map on the entire surface of the heart from ECG mapping data, enabling reconstruction of unifocal, multifocal, and more distributed activation patterns.[47,48] MRI has also shown promise in demonstrating pulmonary venous anatomy, which is central to the technique of RF ablation of focal AF.[49] Since the focus on PVs as triggers for AF, there is an increasing need to identify their anatomy and electrical functionality correctly. Ablation in the region of the PVs is fraught with risks,[50] mandating that this procedure be made as successful yet safe as possible. Newer technology aims at precisely doing this. One of the most logically developed technologies seems to be superimposition of a three-dimensional anatomic image with the image of the ablating catheter while correlating it with the electrical activation maps. This has been successfully achieved using multislice multidetector CT combined with three-dimensional electroanatomic mapping.[51] The PV anatomy has also been studied using high-frequency intravascular ultrasound.[52] The other recent advances have been the use of remote navigation combined with electroanatomic mapping[53] and the use of robotic surgery.[54] Mapping technology should continue to evolve, making ablation techniques safer and more successful. These should also become more noninvasive, allowing ablations to become technically easier and analytically simpler, thus reducing procedure times.

DRUGS FOR ATRIAL FIBRILLATION: FROM DIGITALIS TO DRONEDARONE

Medical therapy for AF is still the primary modality of treatment, although ablation may become a first-line therapy in well-chosen patients in the future. Digitalis was probably the first drug available to treat AF. Digitalis was discovered in 1785 by William Withering (**Fig. 4**),[55] who described its various qualities and uses. Quinidine was likely the next antiarrhythmic medication; it was used in 1951 to treat AF.[56] Amiodarone and disopyramide were explored in the 1970s to treat AF. Multiple studies regarding the efficacy of amiodarone in AF showed that it is useful and effective.[57,58] Disopyramide was reported to be as effective as quinidine in double-blind trials conducted in 1980.[59] Vaughan Williams[60] first classified antiarrhythmic drugs into four classes based on their pharmacologic actions in 1984. The class IC agent encainide was tried for treatment of AF in 1988 and was noted to have a 27% incidence of proarrhythmia.[61] After data from the Cardiac Arrhythmia Suppression Trial (CAST)[62] were reported, the class IA and IC agents were relegated to treatment of AF in patients exclusively without structural heart disease. Flecainide and propafenone recently made a comeback as effective medications for a ''pill-in-the-pocket'' approach to treating AF.[63] Sotalol was a class III drug that has received much approval for use in AF. It was known that sotalol

Fig. 4. William Withering, discoverer of the medicinal use of digitalis, in 1775.

had electrophysiologic properties in addition to beta-receptor blockade.[64] Intravenous infusion of sotalol was initially reported as ineffective in restoration of sinus rhythm but as effective in rate control in AF;[65] later, its antiarrhythmic efficacy was also proved. Dofetilide and ibutilide are the newer class III agents that were studied in 1992 to 1993 as options in treating AF.[66,67] The toxicity of long-term amiodarone use has led to the discovery of a congener drug, dronedarone. Dronedarone, azimilide, tedisamal, and trecetilide (class III agents) are still awaiting US Food and Drug Administration approval pending long-term safety data regarding their clinical use. Future drug development and use are likely to be guided by a better molecular understanding of the electrical basis of AF. The long-standing battle of rate versus rhythm control strategy has been subdued, although not put to rest, after the results of the recent Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM)[68] and Rate Control Versus Electrical Cardioversion (RACE)[69] trials were published. These trials showed the noninferiority of rate control to rhythm control, but this division is not so clear when it involves patients with heart failure or symptomatic AF. AF portends a considerable risk for thromboembolism; this was reported as early as 1958 in a patient with paroxysmal AF and a normal heart.[70] Fisher[71] reported using anticoagulants for cerebral thrombosis in the same year. Today, it is considered standard of care to treat high-risk patients with anticoagulants and low-risk patients with antiplatelet therapy. This is facilitated by the $CHADS_2$ (Congestive Heart Failure, Hypertension, Age > 75 years, Diabetes mellitus and previous Stroke) score.[72] The inflammatory nature of AF (as evinced by elevated C-reactive protein levels) is another pathophysiologic aspect of AF that is being explored because it may have significant clinical and therapeutic implications.

CARDIOVERSION: BEATING ELECTRICITY WITH ELECTRICITY

Cardioversion is the process of restoration of normal sinus rhythm by application of a synchronized external or internal current to the heart. It can be considered as an interim measure in the management of AF because it is more likely to be successful early in the course of AF and may ward off the need for more invasive therapy in some patients if normal sinus rhythm can be maintained on or off pharmacotherapy. In 1962, Lown and colleagues[73] described the first known device for application of electrical energy to the heart for correction of rhythm disturbances. The term *cardioversion* was first used in the next year for electrical correction of AF.[74] In 1963, Lown and colleagues also showed that cardioversion was safer and more effective than quinidine. In 1968, diazepam was the first agent reported as an effective sedative for cardioversion.[75] It was also realized that cardioversion did not obviate the need for anticoagulation if AF was present for more than a week.[76] The next step was to evaluate the long-term success of cardioversion in the management of AF. Within the next few years, longer duration of AF,[77] increased left atrial size,[78,79] and presence of congestive heart failure[80] came to be predictors of lower success rates with cardioversion. Cardioversion was also recognized to be dangerous in the setting of digitalis toxicity.[81] The recognition of atrial stunning for 3 weeks after cardioversion was next recognized by pulsed Doppler studies.[82] These studies underscore the need for optimal anticoagulation that is recommended today in the pericardioversion period. The exact positioning of the external electrodes for successful cardioversion was initially considered as unimportant as long as the current traveled along the long axis of the heart;[83] this has been shown in recent studies as well.[84] If external cardioversion works, so should internal cardioversion. This was the logic behind developing the ''atrial cardioverter-atrioverter,''[85] the atrial rhythm control device counterpart of the implantable defibrillator that works so well for ventricular arrhythmias. The atrial

cardioverter is still being evaluated as useful therapy for AF because of problems with patient discomfort associated with delivery of the shock. Studies have shown that it is accurate in targeting AF for cardioversion not associated with ventricular proarrhythmias. Today, cardioversion is widely used and works for selected patients, especially when used in combination with or under the cover of antiarrhythmic medications, when attempting conversion to and maintenance of normal sinus rhythm.

ABLATING ATRIAL FIBRILLATION: LEARNING WHILE BURNING

In 1982, Scheinman and colleagues[86] used direct current (DC) energy to treat supraventricular tachycardia. RF energy has since replaced DC energy as a source of energy for catheter ablation of arrhythmias. Once again, the PVs assumed center stage as the target for ablation therapy in AF. Other sites of ablation include the left atrium and the thoracic veins, which have now been identified as sustaining AF after PV ablation. In 1994, Haissaguerre and colleagues[87] reported successful treatment of AF by ablation of the PVs. Since then, multiple techniques have been developed at various leading centers globally, with varying success in curing AF ablation. The use of RF energy has been concerning because it can be thrombogenic and cause complications from damage to underlying structures depending on the site of ablation. Other sources of energy that have been successfully used include cryoenergy (using a freeze-thaw cycle), microwave energy (by generation of frictional heat), ultrasound energy (using oscillation for heat generation), and laser energy (generates heat by harmonic oscillation in water molecules).[88] These energy modalities have been used during surgery utilizing the Maze procedure for successful creation of endocardial lesions, thus interrupting AF. RF energy is still the most commonly used energy source, and the other sources are used only at specific centers that are experienced in their use. Although ablation is not first-line therapy for paroxysmal AF at this time, trials are underway to discuss this further.[89] RF ablation also does not have pristine outcomes at this time; however, improved success rates are being reported. Like any other condition, optimal success rates are only likely to be achieved by correct patient selection; the criteria for selection can only be born out of large randomized controlled trials. Until then, we have to be content with attempting drug therapy first and considering ablation for failed drug therapy. Surgical intervention is only likely to be used in patients undergoing cardiac valve repair or other intracardiac procedures. Catheter technology also continues to advance, permitting better energy delivery systems that ensure interruption of the AF circuits. When the only available ablation technology was RF energy applied through tip deflectable ablation catheters with a single electrode, long linear atrial lesions could only be made by a ''drag'' technique.[90] Multielectrode catheters were developed to surmount this problem so that a linear atrial lesion can be produced by placing it against the atrial wall and delivering energy.[91] Lesh and colleagues[92] developed a catheter design integrating a cylindric ultrasound transducer within a water-filled balloon to produce narrow circumferential zones of hyperthermic tissue death at the PV ostia. Newer catheters have been developed that permit the delivery of other energy modalities, leading to better success rates of AF ablation.

THROMBOEMBOLISM IN ATRIAL FIBRILLATION: IS CLOT GOING TO STAY HOME OR NOT?

The thromboembolic risk for AF is now well appreciated, and its prevention is one of the prime goals of therapy, especially in patients in whom achieving sinus rhythm is difficult or not possible. The earliest studies on thromboembolic complications from AF were in patients who had mitral valve disease. The incidence of thrombosis reported was as high as 84% in MS and 9% in mitral insufficiency.[93] In 1958, the National Institute of Neurology and Blindness listed AF as a cause of cerebral infarction of cardiac etiology.[94] At a symposium on thrombosis and anticoagulants in 1960, AF as a risk factor for thrombosis in patients who have rheumatic heart disease and the importance of anticoagulation in this situation were emphasized.[95] In recent years, the presence of a local hypercoagulable state in the left atrium in the setting of AF has been recognized, adding another dimension to the pathogenesis of thromboembolism in AF. This hypercoagulable state has been found to be related to the hematocrit, fibrinogen concentration, left atrial size,[96] various hematologic abnormalities, and endothelial dysfunction.[97,98] Differences in thrombus composition (abundance of fibrin in in situ atrial thrombi versus tissue factor and platelet-leukocyte clusters in embolized clots) have now been revealed using immunohistochemistry. These inherent differences likely decide which thrombus persists in the atrium and which one travels far and wide.[99] Inflammation has been proposed as a possible contributor to thrombogenesis in AF.[100] Paroxysmal AF carries the same risk as persistent or permanent AF.[101] Lone atrial flutter is now known to portend the same thromboembolic risk as that in patients

with lone AF (incidence of thrombi as high as 11%–21% and embolic risk ~7%),[102,103] especially in patients with a reduced ejection fraction, thus warranting anticoagulation.[104] Anticoagulation offers the best strategy to combat the stroke risk associated with AF. The management of a patient who had MS and AF with the successful use of quinidine and anticoagulation was reported in the early 1950s.[105] The presence of atrial thrombosis was verified soon thereafter at mitral valve surgery,[106] and multiple reports since then have noted the importance of diagnosing the presence of atrial thrombi and the importance of anticoagulation.[107–111] Historically, warfarin sodium, dicoumarol, and phenindione have been used as anticoagulants in various studies.[112–114] Today, warfarin sodium is the most commonly used anticoagulant in the United States. Its comparison to aspirin in stroke prevention was the subject of many trials; its superiority has been proved beyond doubt in patients at high risk for embolism. Aspirin is still the recommended treatment for low-risk patients with lone AF.[115,116] The issue of when to stop anticoagulation after cardioversion or after AF ablation procedures is currently a matter of debate, with concerns about silent AF recurrences. The details of management of thromboembolism in AF are the subject of a separate article in this issue. The discovery of an ideal alternative to warfarin continues to elude us to date. The hopes raised by such agents as ximelagatran have unfortunately been dashed because of complications of hepatotoxicity.[117] Mechanical devices (eg, Percutaneous Left Atrial Appendage Transcatheter Occlusion [PLAATO system; PLAATO Inc., Plymouth, MN],[118] WATCHMAN, [Atritech Inc., Plymouth, MN],[119] Amplatzer septal occluder)[120] have now been developed that attempt to seal the left atrial appendage, resulting in containment of the thrombus at its most common site of origin (responsible for 90% of left atrial thrombi). These devices are not standard therapy for AF at the current time. The search for an ideal agent with a wide therapeutic window, comparable or greater efficacy than warfarin, a reasonable safety profile, less frequent need for monitoring, yet affordable by the many individuals with AF is a formidable challenge that remains to be overcome.

SURGERY FOR ATRIAL FIBRILLATION: DOWN THE CORRIDOR AND INSIDE THE MAZE

The assumption that the electrophysiologic basis of AF is the multiple random circulating re-entrant wavelets led to the development of the Maze surgical procedure. In 1991, James Cox and colleagues[121] reported their success with the original Maze procedure. Multiple surgical procedures were devised and tested in dogs, which finally led to a surgical approach that effectively creates an electrical Maze in the atrium. The atrial incisions prevent re-entry and allow sinus impulses to activate the entire atrial myocardium in a channeled manner, thereby preserving atrial transport function after surgery. Thus, there is resolution of the electrical dysfunction and restoration of the atrial mechanical function. The procedure had been tried in 7 patients since 1987 (5 with paroxysmal AF and 2 with chronic AF), with cure from AF and freedom from postoperative antiarrhythmic medications. These researchers went on to present further data on 75 patients in 1992, with a 98% cure rate for AF at an average of 3 months of follow-up.[122] By 1995, it was claimed that the procedure had been standardized to the extent that a good outcome was likely independent of the surgeon and did not depend on mapping guidance.[123] In the same year, the Maze procedure was modified twice, resulting in the Maze III procedure. This was intended to overcome the problems of chronotropic incompetence and left atrial dysfunction seen to result in some patients after the original Maze procedure.[124] The Maze III procedure was then combined with mitral valve surgery, yielding a success rate of 79% for treatment of AF; fine fibrillatory waves and an enlarged left atrium were predictive of failure.[125] Cox and colleagues[125] emphasized that return of atrial mechanical function was key to the success of the Maze procedure. In 1997, Cox[126] reported return of right atrial contractile function in 99% of cases and return of left atrial contractile function in 93% of cases. These success rates were reported to persist 3 years later. In an attempt to restore left atrial function, modifications have been introduced to the Maze III procedure.[127] The Maze III procedure can now be performed through a minimally invasive approach, although there is skepticism about its success.[128] In 1997, Patwardhan and colleagues[129] reported success of the Maze procedure using RF bipolar coagulation in patients who had rheumatic heart disease and AF to produce atrial lesions, with a success rate of 80%. Pulsed wave Doppler evaluation at follow-up showed return of atrial transport function, and presence of ''A'' wave in all these patients in tricuspid valve flow and in 75% patients in mitral valve flow. Calkins and colleagues[130] performed a Maze-like procedure using the Guidant Heart Rhythm Technologies Linear Ablation System (St. Paul, MN) to create long transmural lesions. Bipolar RF ablation avoids the morbidity of cut-and-sew lesions, reduces procedural time, and increases the likelihood of transmurality and continuity of lesions

created compared with unipolar devices.[131] A combination of energy sources has also been used successfully for the Maze procedure.[132] The other surgical technique to treat AF has been the Corridor procedure. The procedure is a surgical open heart procedure designed to isolate a "corridor" from the right and left atrium consisting of the sinus node area, the atrioventricular nodal junction, and the connecting right atrial mass. The principle of this surgery is to channel the electrical impulse from the sinus to the AV node through an atrial area small enough to prevent AF. Between 1987 and 1990, 20 patients with severely disabling symptoms attributable to frequent paroxysmal AF underwent the Corridor operation, with permanent success in 16 patients.[133] The Corridor procedure has been used successfully in patients undergoing surgery for mitral valve disease, with results comparable to the Maze procedure (75% success rate).[134] The surgical options for AF seem to be evolving as well; the focus seems to fluctuate from trying to isolate the trigger to trying to modify the substrate. The other area of focus is to move to a "minimally invasive" mode for achieving successful interventional management of AF.[135,136] Surgical treatment of AF is still extremely rewarding when performed concomitant with surgery for associated surgically amenable cardiac disease.

BACK TO THE FUTURE: WHERE DO WE GO FROM HERE?

We have come a long way in the successful management (treatment for the most part and cure in some cases) of AF. It is only when we look back that we can appreciate how far we have come. Although technology continues to advance, we cannot help but admire the efforts of those who laid the foundation for clinical recognition, physical diagnosis, electrical documentation, drug therapy, and interventional and surgical management of this interesting disorder. The "grandfather arrhythmia" has come a long way; it continues to show us newer mechanisms and presents us with newer challenges in its management. The future holds a lot in store as regards pharmacologic and nonpharmacologic therapies as more advanced molecular biology, imaging, and mapping techniques evolve. Someday, we may finally be ideally equipped to deal with AF, and, eventually, the simple yet complete cure may be in sight.

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