The Excitable Heart

Part IV: Ventricular Tachycardia and Fibrillation

By Dr. Charles Antzelevitch, Executive Director
Masonic Medical Research Laboratory

Like the beating of distant drums, your heart modulates its pace, adjusting to environmental and physical demands by slowing down and speeding up. Occasionally, it goes into a frenzy, beating out of control, racing against time for no good reason. As discussed in part III of this series, this type of cardiac arrhythmia is referred to as a ventricular tachycardia (VT). It is most frequently observed after a heart attack, in otherwise diseased or scarred hearts, and occasionally in apparently normal and healthy hearts. In most cases, VT is due to a short-circuiting of electrical activity within the ventricles of the heart, thus giving rise to a circular movement of the electrical wave. This mechanism, known as reentry, continuously re-excites the heart, causing it to beat at rapid rates. In some individuals, VT is caused by a "focal" mechanism involving rapid and repeated firing of a small group of abnormal cells within the ventricles of the heart. In the latter case, the arrhythmias are often very sensitive to the sympathetic nervous system activity and to various stimulants.

Ventricular tachycardia, when relatively slow and regular, may occur without symptoms. At more rapid and/or irregular rates, VT usually produces symptoms in the form of palpitations, pre-syncope (dizziness) and syncope (fainting spells). The dizziness and fainting spells occur because the pumping chambers do not have sufficient time to fill with blood and as a consequence are inefficient in pumping blood to the brain and other organs of the body. The ECG will alert your physician as to how dangerous the arrhythmia may be. If the ECG signals attending each beat of the tachycardia are similar in size and shape, the tachycardia is said to be monomorphic. In contrast, when the signals are of varying amplitude and shape, the arrhythmia is said to be polymorphic. Generally speaking, the latter is more likely to be life-threatening. The danger of a rapid polymorphic tachycardia is that it can degenerate into ventricular fibrillation (VF), which is the principal cause of sudden death. Although a heart in VF beats at an extremely rapid rate, it is useless as a pump because the contractions are uncoordinated.

Treatment of VT depends on the cause. When secondary to a focal or discrete reentry mechanism, ablation therapy may be able to prevent the arrhythmia, using radiofrequency energy to burn the abnormal pacemaker or the troublesome tissue that allows reentry to develop. In some cases, antiarrhythmic drugs, such as amiodarone, beta-adrenergic blockers (such as propranolol), potassium and sodium channel blockers, may be helpful. In the case of life-threatening arrhythmias, the first line treatment is an Implantable Cardioverter Defibrillator (ICD). This is a device that senses when the heart goes into ventricular fibrillation and automatically delivers a shock to restore normal rhythm. These marvelous devices have dramatically changed the treatment of arrhythmias and have extended the lives of hundreds of thousands of people. In some cases, an ICD may be used in conjunction with antiarrhythmic drugs to limit the number of times that the device is activated.

VT/VF occurring in apparently normal hearts has been the subject of intense study in recent years. These studies have demonstrated the existence of primary electrical disease caused by defects in specific ion channels. Patients with these "channelopathies" generally have a structurally normal heart. One form of channelopathy is called the long QT syndrome (LQTS), because the QT interval in the ECG is prolonged in patients afflicted with this disease. It is hereditary and has now been linked to a genetic defect in one of twelve different genes that affect the function of ion channel that carry potassium, sodium or calcium channels. The ion channel defects lead to the development of a polymorphic tachycardia known as Torsade de Pointe's, which can degenerate to ventricular fibrillation. The syndrome tragically takes the lives of teenagers and young adults. The genetic definition of the disease has made possible the development of gene-specific therapy. While many patients are protected by use of beta-blockers, others require ICDs. Studies currently underway are examining the therapeutic value of sodium channel blockers such as ranolazine, based in part on reports from the Masonic Medical Research Laboratory.

Another type of primary electrical disease is known as the Brugada Syndrome. The Brugada syndrome has been linked to a defect in seven different genes encoding sodium, potassium and calcium channels. A very rapid polymorphic tachycardia develops in these patients, which may cause them to faint. In some cases sudden death is the first symptom. This too is a hereditary disease whose incidence is highest in individuals of Southeast Asian origin. For reasons that physicians and scientists do not as yet understand, the disease often lies dormant for three to four decades before emerging to rear its ugly head. The average age of death of Brugada patients is 40. ICDs are indicated in patients who have previously experienced syncope or who have been resuscitated from sudden death. Recent work from the Masonic Medical Research Laboratory has suggested a new pharmacological approach to therapy using "transient outward current" blockers, such a quinidine. This pharmacologic alternative may be critically important in many parts of the world where ICDs are not affordable.

Short QT syndrome (SQTS) is another inherited channelopathy characterized by abnormally short QT intervals on the ECG and an increased propensity to develop atrial and ventricular tachyarrhythmias. It was first described as a new clinical entity in 2000 and like LQTS and Brugada syndrome is responsible for sudden cardiac death (SCD) in individuals with structurally normal hearts. Cases of SQTS have been reported with presentation as early as in the first year of life, suggesting that it could be one of the etiologies underlying sudden infant death syndrome. The implantation of an ICD is first line therapy in symptomatic individuals. Genetic defects in five different genes encoding potassium and calcium channels have been associated with SQTS.

The knowledge that has made these diagnostic procedures and therapeutic measures available emanated from decades of painstaking research conducted at medical research laboratories throughout the world. Among the laboratories contributing fundamentally to our present day knowledge of cardiac electrophysiology and cardiac arrhythmias is the Masonic Medical Research Laboratory. For over fifty years, scientists at the MMRL have contributed to our understanding of the function of the heart in both health and disease. On-going research continues to focus on cardiac arrhythmias, the single largest

mechanism of death of Americans. In coming segments of this series, I will expand on other arrhythmias, their causes, treatments and cures.

The Masonic Medical Research Laboratory (MMRL) is a 501(c)3 not-for-profit corporation founded and sponsored by Freemasonry. Recognized as a one of the finest biomedical research centers in the world, the MMRL has contributed importantly to the modern day practice of cardiology. Over the past five decades MMRL investigators have been credited with either discovering or unraveling the mechanisms of a majority of known cardiac arrhythmias and is currently one of a handful of medical research institutes worldwide capable of studying the genetic causes of the lethal cardiac arrhythmias responsible for sudden death in young adults, children and infants. The MMRL is leading the way in the development of innovative safe and effective pharmacological treatment for atrial fibrillation, one of the greatest unmet medical needs facing our society.

The Masonic Medical Research Laboratory is the Flagship Charity of the Grand Lodge of Florida, Free and Accepted Masons. The institute is also supported by Grand Chapter of Florida, Royal Arch Masons and the general public as well as through corporate, foundation, National Institutes of Health and American Heart Association grants. On average, 84 cents of every dollar donated goes to cardiac research.

The Excitable Heart Series is provided as a public service through the MMRL. Please visit www.mmrl.edu or www.glflamason.org to learn more or make a donation.