INTRODUCTION

Heart is an organ whose study requires integration of the basic principles of physics, chemistry and biology. Most important perhaps is the application of the physical principles of electricity for the understanding as well as control of cardiac rhythm. In fact, two major events in the history of cardiology relate to this close relationship between electricity and the heart. The first event was the discovery of Electrocardiogram (ECG) by Einthoven in 1902 and the second one was the invention of pacing by Zoll in 1952. The 100th Anniversary of the first event and 50th Anniversary of the second were celebrated recently in 2002. The present article is a humble recollection of the works of all the great men who reshaped the world of cardiology by applying the principles of electricity.

Detecting the electrical activity of the heart:

A frog’s leg started it all! The readers may arch a collective eyebrow in suspicion at such a plebian origin of one of the glorious discoveries in medicine. But, believe it or not, Kolliker and Muller in 1856, contacted a frog’s leg (nerve-muscle preparation) to a beating frog’s heart to demonstrate the cardiac electrical activity for the first time.3 The twitching of the frog’s muscle corresponded to each ventricular contraction. Their work was probably inspired by John Walsh, a fellow of the Royal Society, who demonstrated a visible spark from an electric eel way back in 1774 and by the Italian anatomist Luigi Galvani who showed twitching of dissected frog’s leg by touching it with a metal scalpel in 1780.

After about another three decades, Henry Martin in 1883, recorded the first ECG of a living animal – a rabbit, with the help of a capillary electrometer, devised by the French physicist Gabriel Lippman.4 The first man to have his ECG done, must had weird, if not unpleasant experience, of having his two hands dipped into two dishes of salt solution, which were connected with the two sides of a capillary electrometer. That was indeed the technique employed by A.D. Waller in 1887 to record the first human ECG.4 Later on, Waller strapped the electrodes to the chest of his patients, thereby making the movement of the mercury column in the capillary electrometer, more evident. Two waves were recorded in this primitive ECG, which were named V₁ and V₂ by Waller to indicate the ventricular events.

Later on, Willhem Einthoven, using a more refined Lippman capillary electrometer, recorded an ECG with four deflections. He labelled them as ABCD: A indicating electrical activity of the atria; and B the first downward deflection, C the first upward deflection and D the last downward deflection, due to electrical activity of the ventricle. In 1895, Einthoven applied a mathematical correction for the inertia and friction of the mercury column in the capillary tube and showed five, instead of four, deflections.5 He named them as PQRST, probably under the influence of the labelling system of Descartes, the inventor of analytical geometry. But the real epoch making discovery came in 1902, when Einthoven used a modified string galvanometer to record the first accurate human ECG. This machine which weighed over 1/4th of a ton and required five people for its operation, was the forerunner of the modern ECG machine. The discovery of Einthoven, as rightly pointed out by Seymour Furman, was as important to the understanding of cardiac physiology and disease processes as invention of writing to the human civilization, and quite justifiably won him the Nobel Prize in 1924.*

Einthoven introduced three limb leads in 1902 and proposed the equilateral triangle hypothesis in 1912, which provided a mathematical correlation between the
direction and size of the deflections recorded with these leads.

The first commercially available ECG machine, devised by Cambridge Scientific Instrument Company, was used by Sir Thomas Lewis to study cardiac arrhythmias at University College Hospital in London. In 1912 he published a contemporary review on cardiac arrhythmias. In 1928, Fred Smith expanded the application of ECG beyond arrhythmias, by describing ECG changes in experimental coronary artery occlusion.5 Parkinson and Bedford first published the ECG changes in 28 cases of cardiac infarction in 1928. In 1932, Wolferth and Wood, introduced the concept of pericardial leads to describe ischaemic changes in the left anterior descending coronary artery territory.6 In 1931, Wilson first described unipolar leads – VR, VL and VF, which were further refined by Goldberger in 1942, to introduce augmented limb leads.7,8 In 1949, Sokolow and Lyon described the criteria for diagnosing left ventricular hypertrophy from ECG.9 Thus, the present day 12-lead ECG format and the diagnostic criteria for cardiac arrhythmias, cardiac ischemia and alterations in the geometry of the cardiac chambers evolved. The ECG interpretation gained considerable importance and in 1951 Wilson commented that – ‘most of the population was in greater danger of having their peace and happiness destroyed by an erroneous reading of an electrocardiogram than by a nuclear holocaust’.

Application of electricity for treating cardiac diseases:

Much before the first attempts were made to unravel the mystery of the electrical activity of the heart, man tried to harness electricity for management of cardiac ailments. As early as in1775, Peter Abildgaard, in a bid to find out the mode of death by electrocution, conducted a series of experiments on the effect of electrical shock on animals.10 He succeeded in first rendering a fowl lifeless by an electric shock on its head and then reviving it by a counter shock applied to the chest. After another 124 years, Prevost and Battelli, in 1889, described the fibrillating effects of a weak current on the heart and defibrillation by strong currents.11

In 1947, Beck reported the first successful human ventricular defibrillation. His patient was a 14 years old boy who underwent external resection for severe congenital funnel chest. During closure of the wound the patient developed cardiac standstill. After re-exposure and rhythmical massage of the heart for 35 minutes, a ventricular fibrillation was recorded. Following an injection of procaine hydrochloride into the right article and a brief period of cardiac massage, the heart was defibrillated by placing it between two electrodes and momentarily passing ordinary 110V AC current through it. Two series of shocks were required for the defibrillation.

Fifteen more years passed by before Lowne, in 1962, introduced synchronized direct current shock for cardioverting atrial fibrillation to sinus rhythm.12

In 1980, Mirowski and colleagues introduced implantable cardioverter – defibrillator (ICD) for treating the survivors of repeated attacks of malignant ventricular tachyarrhythmias non-responsive to anti-arrhythmic drug.13 Initially, the device was implanted abdominally and connected to a transvenous defibrillation electrode in the superior vena cava and a defibrillation patch positioned epicardially through a thoracotomy. Although the original device could only defibrillate, all devices had been able to cardiovert since 1982 and perform as well a variety of anti-tachycardia pacing modalities since late 1980s. In the early 1990s, the replacement of the monophasic defibrillation waveform by the more effective biphasic waveform allowed for the implantation of transvenous instead of epicardial defibrillation leads.14 This led to widespread use of ICDs.

During the period, electrical cardioversion was being developed to its present mature form, simultaneous efforts were on for more sustained application of electrical current to treat patients with Stokes – Adams attack. Various methods were tried viz. application of Galvanic and faradic current to the heart, electro-puncture, mechanical irritation by a fine needle and application of heat to the precordium. In early 1930, Albert S. Hyman, a cardiologist in New York City, invented an artificial pacemaker, in which, output voltage was generated by a magneto-generator driven by winding a hard rank.15 However, all these methods were proved to be ineffective.

The first real breakthrough in pacing was achieved by Paul M. Zoll in 1952. He attached the negative electrode of a borrowed physiologic stimulator to a needle in the subcutaneous tissue just outside the cardiac apex, and positive electrode to a chest electrode on the skin at the fourth intercostal space in the right mid-axillary line, of a patient of complete heart block with syncope. Electric shocks in incremental intensities were given at frequencies from 25 to 60 per minute until ventricular responses were observed and recorded electrocardiographically. Though this response was only brief and the patient died, Zoll subsequently attained success with his second patient, whom he paced for 5 days in a similar manner, before discharging him with a stable idioventricular rhythm. Zoll’s invention set the pace for the development of artificial cardiac stimulation.

However, another 5 years elapsed before this transcutaneous, closed chest, cardiac stimulation could be replaced. But this time, open heart surgery had began for repair of congenital heart lesions particularly ventricular septal defect, with complete heart block occurring frequently as its complication. In 1957, a cardiac surgeon from the University of Minnesota, Walton Lillehei, first tried external pacing via a
myocardial electrode applied either through a needle into the closed chest or placed in situ at the time of open heart surgery. This technique was used with the line current operated pacemakers available till then. Another significant event followed towards the end of the same year. On October 1957, a power-failure caused cessation of pacing in postoperative children and one of them died. This prompted Lillehei to request Earl Bakken, an electrical engineer, to develop a battery-powered pacemaker for his use. In December 1957, Bakken, developed world’s first battery-operated pacemaker, which made pacing independent of line current and eventually allowed ambulatory outpatient management of those with complete heart block.

Soon after the introduction of cardiac pacing with exteriorized myocardial electrodes, it became apparent that peri-electrode infections would preclude its long-term use. To avoid this complication, in 1958, Mauro introduced a totally implantable battery-powered pacemaker with an epicardial lead and a radio frequency stimulator inductively coupled through intact skin to induce the pacemaker to pace the heart. In the same year, Seymour Furman achieved successful pacing via a transvenous catheter electrode introduced through the basilic vein, under fluoroscopic guidance, into the right ventricular outflow tract in a patient with complete heart block undergoing colonic resection. After operation, the catheter was removed without complication and the patient resumed his original idioventricular rhythm. It was again in this year, that the first attempt at pacing implantable pacemaker was made by Senning at Sweden. The pacemaker which was small enough to be implanted subcutaneously in the epigastrium, was developed by Elmqvist. The first pacemaker was powered with a rechargeable nickel-cadmium cell. Unfortunately, the electrode, which was essentially an entwined stainless suture wire with polyethylene insulation was found unsuitable. The stimulation threshold increased after only a few weeks and the unit ceased to stimulate. In 1960, the first fully implantable cardiac pacemaker carrying its own power supply was put in a 77 years old man with complete heart block, by Chardac, Gage and Greatbatch, with good long-term result. After several years, the addition of a long-lasting lithium battery and the ability to externally program the pacing parameters favoured the use of a totally implantable cardiac pacemaker. In 1962, Lagergren first demonstrated transvenous pacemaker implantation, and in another three years this technique gained wide acceptance. In the same year, the first pacemakers capable of sensing cardiac activity to modify their own function were introduced. With transvenous implantation and the sensing of the heart to modify pacemaker and cardiac function, the modern era of cardiac pacing began.

In the 1940s and 1950s, when electrical cardioversion was taking its final shape and cardiac pacing was still in its infancy, the emergence of cardiac catheterization marked the event of yet another great event in the field of cardiology. With the evolution of catheterization techniques, it became apparent that these intravascular catheters could be safely placed at almost any region of the heart for a substantial period of time. This knowledge encouraged Girad, Puech and their co-workers, in 1960, to place a catheter at the His bundle of the heart to record the His bundle potential. However, the work of Scherlag and his associates on the His bundle activity of dogs and humans, in 1968, first defined the basic electrode catheter techniques, on which future developments in the field of electrophysiology were built up. At about the same time the team of Scherlag were detailing the catheter technique of recording His bundle activity, Durrer from Amsterdam and Coumel from Paris, independently formulated a method for programmed electrical stimulation of the heart. They showed for the very first time that arrhythmias could be initiated and terminated by critically timed premature beats. But the real quantum leap occurred in 1972, when Wellens, a student of Durrer, combined the technique of programmed stimulation with intracardiac recordings. The introduction of this technique led to a greater understanding of the functional components of the A-V specialized conducting system, including the refractory periods of the atrium, AV node, His bundle, Purkinje system and the ventricles. It also made possible the assessment of the effects of drug on these parameters and induction and termination of a variety of arrhythmias.

Enthused by a more clear understanding of the cardiac electrophysiology, efforts were now initiated to place multiple catheters for recording and stimulation of different locations within the heart, first in the atria and thereafter in the ventricle. This led to the development of endocardial catheter mapping techniques by Mark E. Josephson from University of Pennsylvania in 1978, to define the location of bypass tracts and the mechanisms of supraventricular tachyarrhythmias. Seminal publications soon followed on the substrate and mechanism for ventricular tachycardia in man. Working with his surgical colleagues, Josephson subsequently developed the map guided subendocardial resection to cure ventricular tachycardia. Time magazine referred to the procedure as the “Pennsylvania Peel” in honour of the success of this new intervention in arrhythmia management.

Till 1980s, direct dissection of the A-V junction during open heart surgery remained the sole anti-arrhythmic ablative procedure. Unfortunately, the surgical mortality was as high as 10%. In 1978, the ablative therapy ushered into a new era, with Fontaine and co-workers, reporting the first catheter ablation using a DC shock. It was a startling chance discovery, as while defibrillating a patient, one defibrillator electrode accidentally came in contact with a catheter electrode positioned at the
bundle of His, and produced complete A-V block, after the shock was discharged.36 In the early 80’s high voltage DC ablation was further developed by Gallagher and Scheinman and used as a therapeutic approach to treat supra-ventricular tachycardia. 37,38

This catheter ablation technique obviated the need for open heart surgery, was associated with low mortality with morbidity and had minimal recovery time. The tissue was destroyed probably by a combination of thermal, electrical and physical injury. However, the relatively uncontrolled nature of this energy was a matter of concern as it was likely to produce injury to the thin-walled structures like atrial free wall and coronary sinus in the heart. For this reason, alternative modalities of catheter ablation were pursued, including intracoronary ethanol infusion, laser irradiation, cryothermy, microwave, ultrasound and radiofrequency (RF) current. The ability of the RF current a low voltage high frequency alternating current, to produce precise small-sized lesions gained it favour over all other modalities. In 1987, Huang and co-workers experimented with the use of radiofrequency energy for catheter ablation, followed by the first A-V node ablation by Budde and his colleagues and the interruption of an accessory pathway by Borggreffe and his co-workers using this technique.39,40

Early efforts at this technique had variable results. But with the introduction of RF ablation catheters with large (4 mm) distal electrode tips, the procedure success rates improved dramatically. Success rates of 95% to 99% were typically reported by experienced operators for SVTs and VTs without structural heart disease.41

Indications for catheter ablation had now expanded routinely to include patients with atrial flutter and refractory re-entrant VT with structural heart disease.

CONCLUSION

The progress from electrocardiogram to electrophysiology had thus been a long journey spanning over a period of more than 100 years. But the way these 100 years changed the world of cardiology is similar to that of one geologic age to the evolution of man. In the present day practice, time and again, when we detect a lethal arrhythmia from an ECG or retrieve a way these 100 years changed the world of cardiology is spanning over a period of more than 100 years. But the electrophysiology had thus been a long journey

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**Book Review**

**Pharmacology and Pharmacotherapeutics Revised Nineteenth Edition**

**RS Satoskar, SD Bhandarkar, Nirmala N Rege**

The revised and updated 19th Edition of Pharmacology and Pharmacotherapeutics by Dr. RS Satoskar, Dr. SD Bhandarkar and Dr.(Smt) Nirmala N Rege features a reader-friendly format, logical arrangement of text material, and authoritative guidance on current therapy of diseases, especially tropical diseases, which has made it useful to the students and the practitioners alike.

The book not only gives information about various drugs but also provides guidelines for how to choose a drug for a given patient and then use it wisely.

It integrates pathophysiology of diseases with pharmacology, and correlates basic concepts with rational therapeutics. The information and recommendations are clear, concise, unambiguous and practical for the management of both inpatients and outpatients. Bold headings, plenty of summary tables and an extensive index allow easy access to the specific information one requires.

**Highlights of the 19th Edition**

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- Monoclonal antibodies in therapy
- Recent advances in the therapy of tuberculosis and AIDS
- New hypnotics and management of sleep disorders
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**Published by**

Popular Prakashan Private Ltd,
35-C, Pandit Madan Mohan Malaviya Marg,
Tardeo, Popular Press Bldg, Mumbai – 400 034

Indian Price: Rs. 595.00