

CLASS 1

Historical Summary of the Relevant Facts in Electrocardiography

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“The time is at hand, if not already come, when an examination of the heart is incomplete if this new method is neglected”.

Sir Thomas Lewis, Cardiff, Wales (Heart 1912;3:279)

INTRODUCTION

Electrocardiography has played an important role in our understanding of heart disease. It together with its offspring, electrophysiology, remain the final arbiter of the nature of rhythm disturbances. Moreover, it retains great value in managing patients with ischemic heart disease. It was among the first bits of technology to supplement physicians' clinical skills by providing objective data on the function and structure of the human body. Many researchers contributed to the development and refinement of electrocardiograph. We suggest that knowledge of the evolution of this most frequently used technology will assist in its interpretation.

The ECG is not only the oldest but, in fact, 117 years after its introduction, continues as the most commonly used cardiovascular laboratory procedure. It is interpreted by cardiologists, internists and to various extents by primary care physicians, specialized nurses and more and more by computers. It is noninvasive, simple to record, highly reproducible and can be applied serially. Electrocardiography serves as a gold standard for the clinical, noninvasive diagnosis of cardiac arrhythmias (Fisch 1989).

1761/1786

Giovanni Battista Morgagni (1761): Prof. from Padua, Italy, considered the father of anatomical pathology, provides the first data on “slow pulse and convulsive seizures.” (Figure 1).

Luigi Galvani (1786): Luigi Galvani and Volta, Italian physicians and physicists at the University of Bologna, first noted that electrical current could be recorded from skeletal muscles. He recorded electrical activity from dissected muscles (Kirby, Pinto et al. 1990). Later Galvani (Galvani LA, 1791) wrote a manuscript about “De viribus electricitatis in motu muscular: commentarius comment”.



Figure 1. GIOVANNI BATTISTA MORGAGNI (1682-1771)

Sir William Stokes (1827): he describes thoroughly in the book “Disease of the Heart and Aorta”, the symptoms of the syndrome called by his name currently, the eponym Stokes-Adams, “epileptic” seizures associated to intense bradycardia (Figure 2).

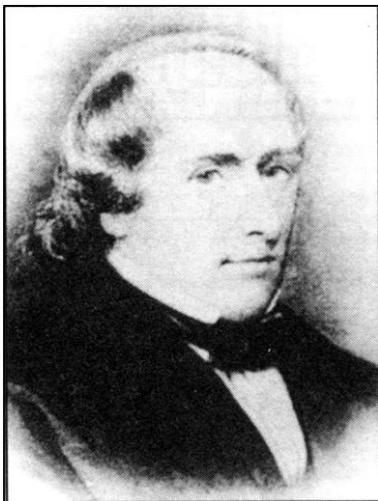


Figure 2. SIR WILLIAM STOKES (1804 – 1878)

Carlo Matteucci (1842): professor of physics at the University of Pisa, demonstrated that electrical current accompanies every heart beat in a frog (Matteucci C, 1842).

Robert Adams (1846): he associates “epileptic” seizures accompanied by slow pulse as having a cardiac source (Figure 3).

The full eponym is Stokes-Adams-Morgagni syndrome



Figure 3. ROBERT ADAMS (1791 – 1875)

1827

He acknowledges Atrial Fibrillation (AF) for the first time as a clinical sign of Mitral Valve Stenosis (MVS) (Adams R, 1827) ¹. AF is part of the natural history of MVS (Figure 4).

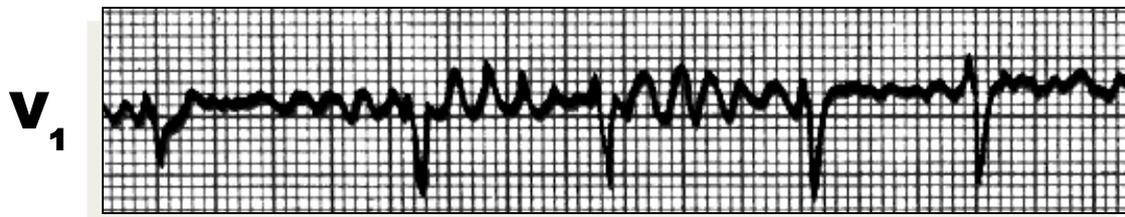


Figure 4. “f” waves of voltage > than 0.5 mm or 1 mm. Check the irregularity of the QRS complexes

HISTORY OF ATRIAL FIBRILLATION

Perhaps the earliest description of atrial fibrillation is in The Yellow Emperor's Classic of Internal Medicine (Huang Ti Nei Ching Su Wen). The legendary emperor physician is believed to have ruled China between 1696 and 2598 BC. The poor prognosis associated with chaotic irregularity of the pulse was clearly acknowledged by most of the ancient physicians, but in recorded history (Lip and Beevers 1995).

- **1628:** William Harvey was probably the first to describe "fibrillation of the auricles" in animals.
- **1927:** In clinical practice and with the aid of Laennec's recently invented stethoscope, Robert Adams reported the association of irregular pulses with mitral stenosis. Adams was the first to recognise the condition clinically but as a "sign of mitral stenosis"
- **1939:** Hoep Identified irregular pulse in association with mitral stenosis-exercise worsened the total irregularity, whereas it abolished an intermittent pulse
- **1863:** Etienne Marey published a pulse tracing from tracing of atrial fibrillation from a patient with mitral stenosis.
- **1874:** Vulpina Observed atrial fibrillation in vivo in dogs.
- **1894:** Engelman Reported atrial fibrillation caused by multiple foci in the atrial.
- **1900:** Einthoven Invented the electrocardiograph
- **1909:** Lewis Reocrde atrial fibrillaiton with electrocardiographñ sudied mecahninsms of tthe condition.
- **1909:** Rothemberg amd Winterberg Identified "arrhthymia perpetua " and " fibrillation of the auricules ".
- **1935:** Jean Baptiste Boulland, Found that digitalis reduced the ventricular rate dramatically even though irregularity of pulse persisted. He said that he considered digitalis to be "a sort of opium for the heart."The discovery of the therapeutic properties of digitalis leaf (*Digitalis purpurea*) in 1785 by William Withering brought some relief to patients with severe heart failure. It is interesting that Withering recorded a patient who had a weak, irregular pulse that became "more full and more regular" after five draughts containing Fol Digital Purp oz iv.

- **1969:** Lown Recommended cardioversion of atrial fibrillation

1856

In 1856 Köllicker and Müller discovered that the heart muscle could produce electric activity.

1860

May 21, 1860: Willem Einthoven is born in Semarang, capital of Central Java, in the Dutch East Indies (currently Indonesia). He is considered the father of electrocardiography (Figure 5).



Figure 5. Location of Semarang, in Indonesia, place of birth of the father of electrocardiography.

1869

Muirhead in London recorded the first electrocardiogram (ECG) in man in 1869 or 1870 with a siphon instrument.

1882

The French physiologist and physicist developed the capillary electrometer. The device consisted of a thin glass tube with a column of mercury located beneath sulfuric acid. The mercury surface moved with the electrical potential variations and was observed through a microscope.

The best recording device in the 19th century used in research labs was for a long time, Lippmann's capillary electrometer, created by him in his internship in Kirchoff's lab in Heidelberg, in 1873, and introduced to the scientific world in a publication by Gabriel Lippmann himself, in 1875 (Figure 6).

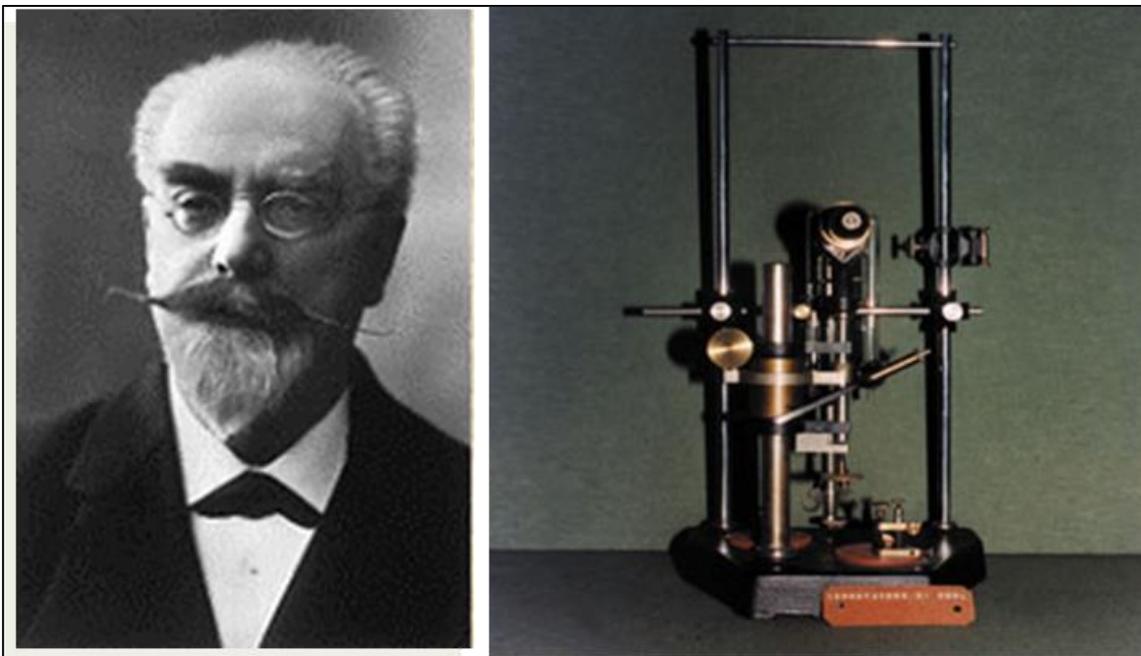


Figure 6. Gabriel Lippmann and the Lippmann's capillary electrometer.

This is Lippmann's capillary galvanometer, which used the same principle as the device used by Waller and later, by Einthoven, with mild differences in its configuration. A small drop of mercury located within a horizontal capillary tube moved under the influence of an electric field applied by two electrodes.

The device was supplied by a scale engraved in glass for projection (Figure 7).



Figure 7. Lippmann's capillary galvanometer.

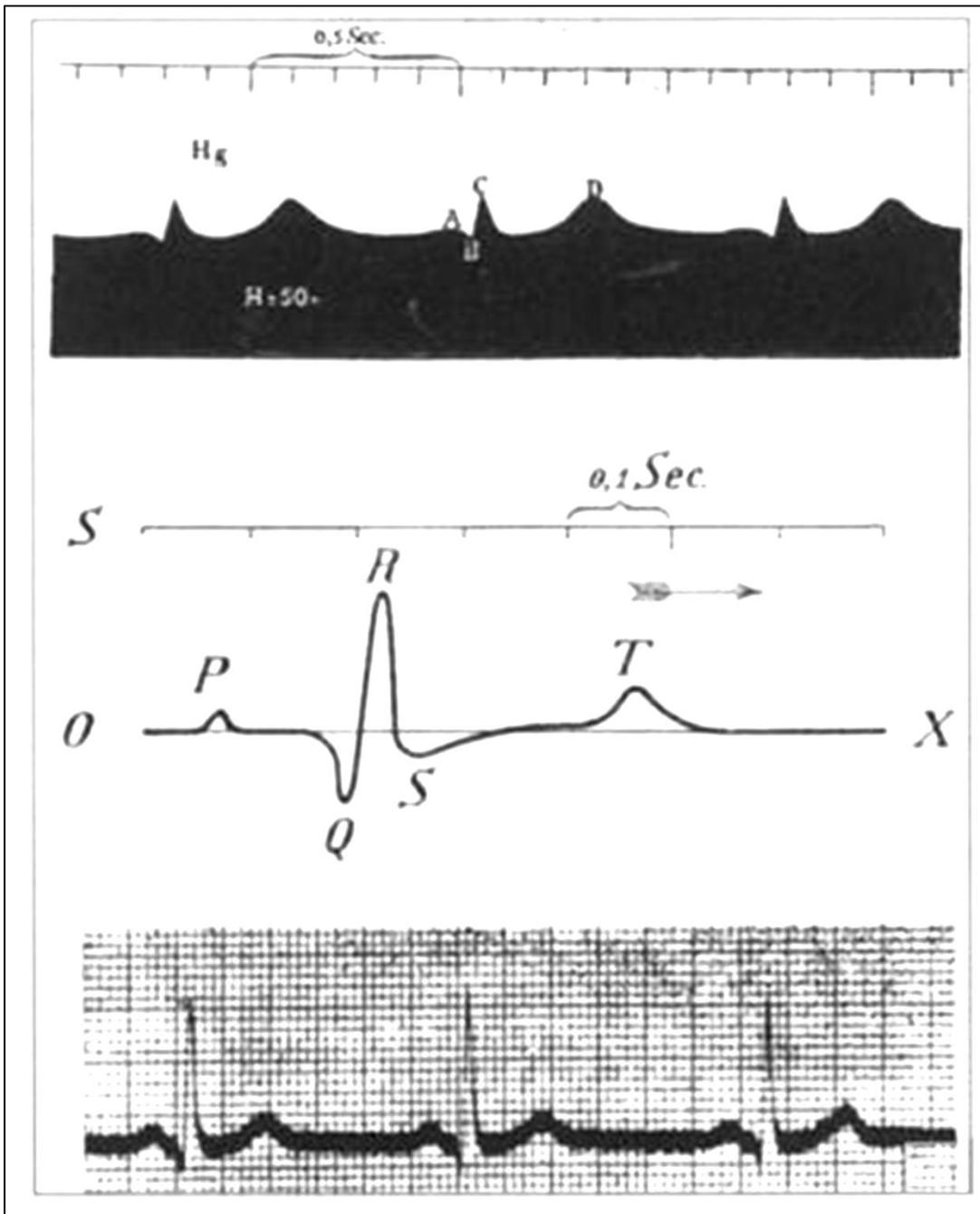


Figure 8. The upper recording was made using the capillary electrometer. The lower one, using a string galvanometer.

1876

The French physiologist Etienne-Jules Marey uses Lippmann's capillary electrometer to record the electrical activity of a batrachian's heart (a frog) exposed (Marey EJ et al, 1876). He develops the famous "Marey capsule" (Marey EJ et al, 1881). Marey, through chronophotography stood out as one of the precursors of cinema. Marey was a physiologist concerned with "observing the invisible." (Figure 9).



Figure 9. Etienne-Jules Marey (1830 – 1904)

1872

Augustus Waller (1872), a British physiologist of St Mary's Medical School in London, published the first human electrocardiogram using a capillary electrometer and electrodes placed on the chest and back of a human. He demonstrated that electrical activity preceded ventricular contraction (Waller AD, 1872) (Figure 10).

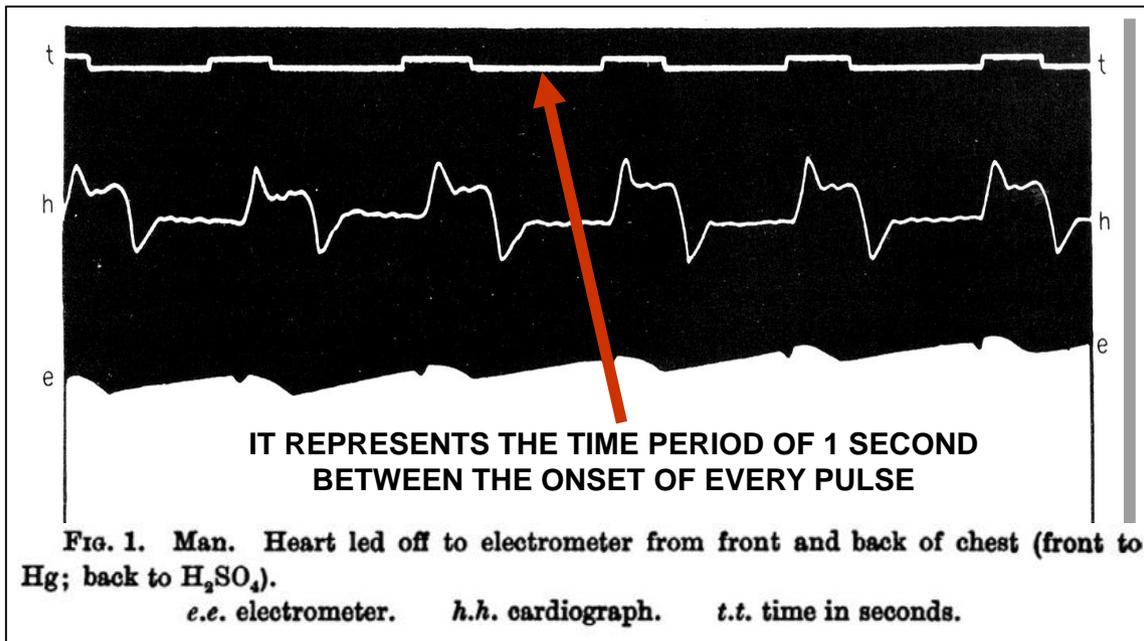


Figure 10. First human electrocardiogram recorded by Augustus D. Waller of St Mary's Medical School showing simultaneous electrometer and cardiograph tracings showing an electrical activity preceding every heartbeat.

1878 / 1884

The British physiologists John Scott Burdon-Sanderson (Figure 11). and Frederick Page record the electrical activity of the heart of batrachians using Lippmann's capillary electrometer. These investigators are the first to show the two phases in the electrical activity of the heart, later called QRS and T, corresponding to depolarization and repolarization (Burdon Sanderson J, 1878).

Eight years later, they show the graphic recording of the electrical excitatory phenomenon in the heart of turtles (Burdon Sanderson J, 1884).

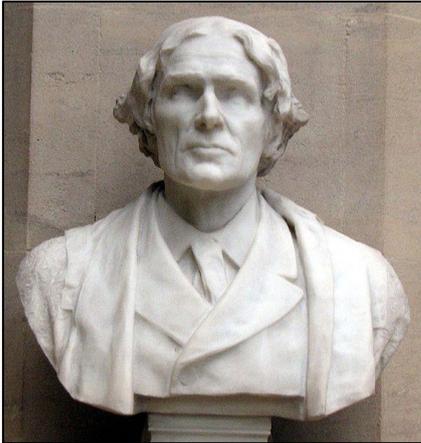


Figure 11. John Scott Burdon-Sanderson (1828 – 1905)

1887

The British physiologist Augustus Desiré Waller (Figure 12) from the St. Mary's Medical School of London, makes the first human ECG, using the mercury capillary electrometer, recorded in a patient called Thomas Goswell, a technician working at the lab (Waller AD, 1887). It was Waller who introduced the term ECG into science.

This author proposed the creation of ten leads. Later, Einthoven perceived that there were some favorable and other unfavorable ones.

An example of the former is the connection of the two hands, and of the latter, the connection between the feet.



Figure 12. Augustus Desiré Waller (1856-1922)

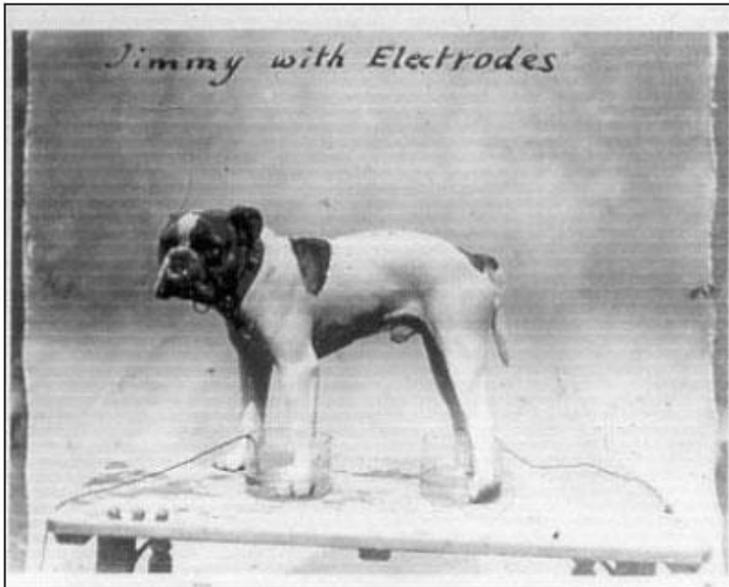


Figure 13. This picture shows Waller's dog, called Jimmy, connected to the electrocardiogram by his legs in a saline solution.

1889

ECG is a method developed into its current mode by the pioneer Dutch physiologist Einthoven (Figure 14), during the 1st International Congress of Physiology in Bali, at the end of the 19th C and the beginning of the 20th C.

Einthoven is considered the father of electrocardiography. His work was conducted at the Leiden University, the Netherlands.

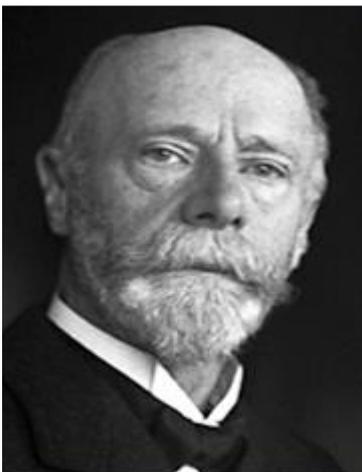


Figure 14. Willem Einthoven (1860-1927)

Dr. Willem Einthoven was a Dutch physiologist inspired by the work of Waller, refined the capillary electrometer even further and was able to demonstrate five deflections which he named ABCDE (Einthoven W, 1895). To adjust for inertia in the capillary system, he implemented a mathematical correction, which resulted in the curves that we see today.

Following the mathematical tradition established by Descartes (Henson 1971), he used the terminal part of alphabet series (PQRST) to name these deflections. The term ‘electrocardiogram’ used to describe these wave forms was first coined by Einthoven at the Dutch Medical Meeting of 1893 (Einthoven W, 1893). In 1901, he successfully developed a new string galvanometer with very high sensitivity, which he used in his electrocardiograph. His device weighed 600 pounds (Burnett 1985) (and Einthoven W, 1901).

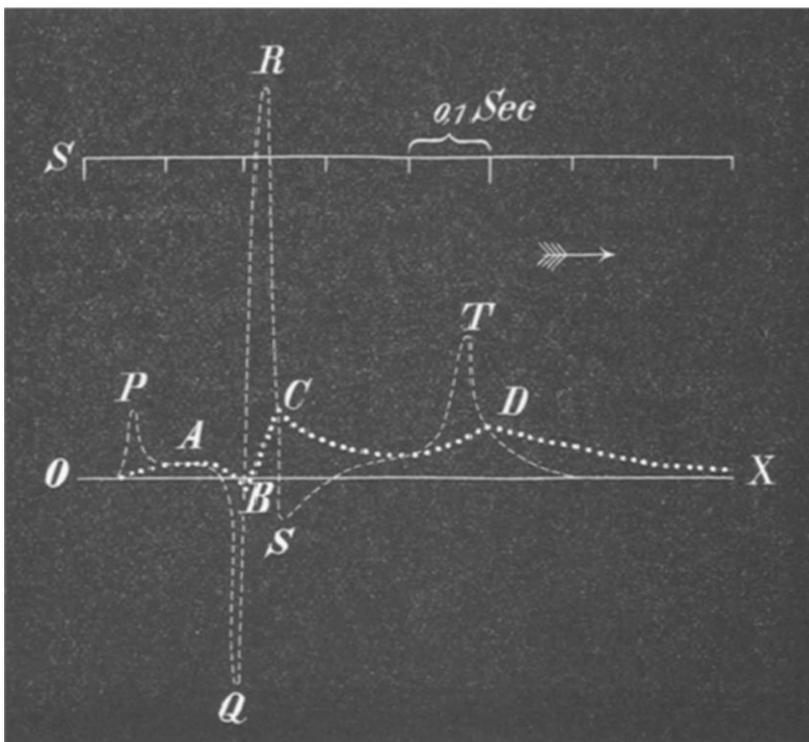


Figure 15. Two superimposed ECGs are shown. Uncorrected curve is labeled ABCD. This tracing was made with refined Lippmann capillary electrometer. The other curve was mathematically corrected by Einthoven to allow for inertia and friction in the capillary tube. He chose the letters PQRST for the corrected curve based on mathematical tradition of labeling successive point on a curve.



Figure 16. In this picture, we see young Professor Einthoven with his assistants in the laboratory at the Leiden University.

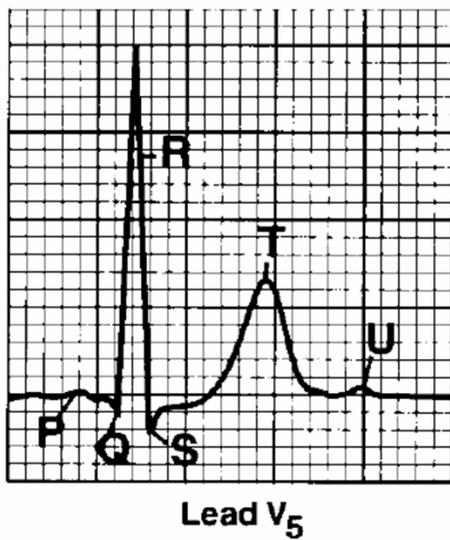
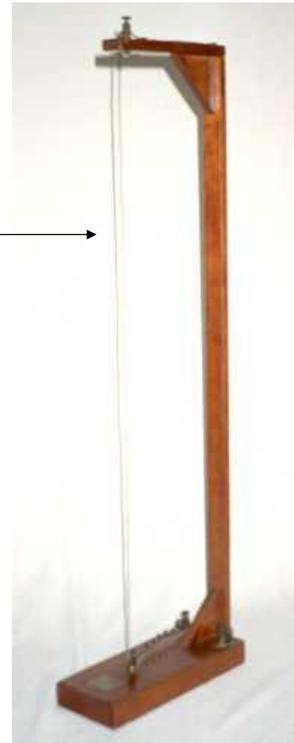
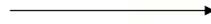


Figure 17. This ECG shows in lead V_5 the waves that Einthoven called P, QRS, T and U. Einthoven identified the U wave some years later (Snellen HA, 1994), just with the string galvanometer (Hurst JW, 1991).

Associated eponyms:

Galvanometer of Einthoven:

The string galvanometer invented in 1901.



Einthoven's Law:

In ECG, at any given moment, any wave of lead II is equal to the sum of the potentials of leads I and III.

Einthoven's Triangle:

Imaginary equilateral triangle, where the heart is hypothetically located at the center, representing the three bipolar or standard limb leads.

Figure 18.

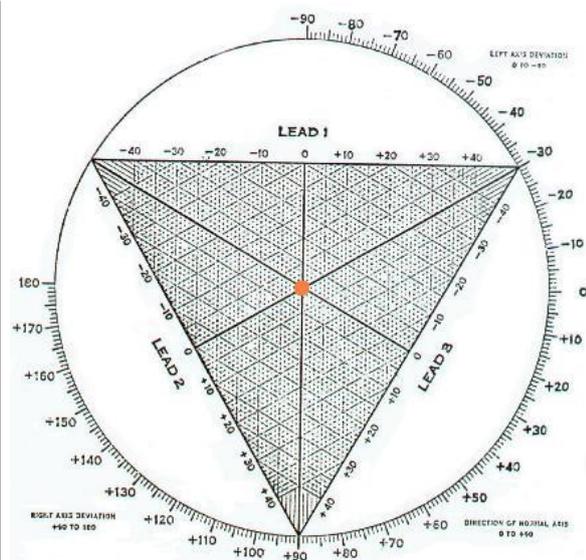
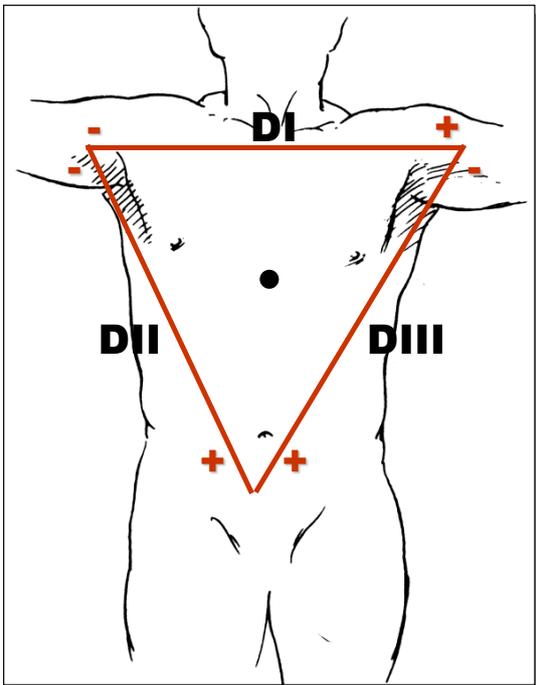


Figure 19. Imaginary equilateral triangle where the heart is hypothetically located in the center, representing the three bipolar or standard limb leads.

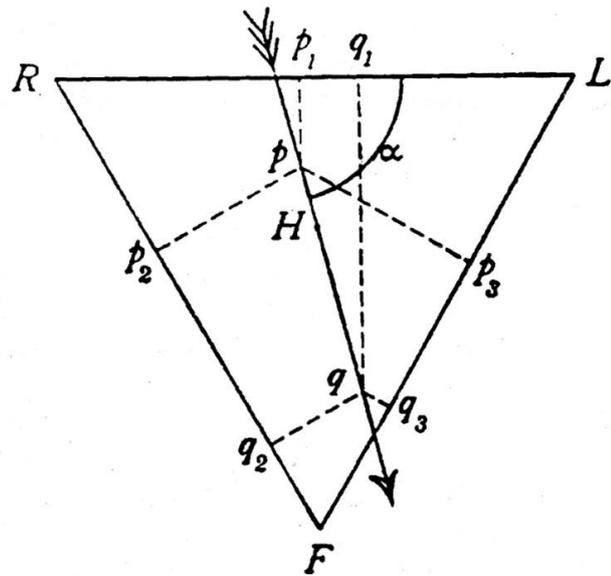


Figure 20. This is the original draft of Einthoven's triangle made by his own hand. Einthoven described the bipolar leads, imagining the heart at the center of a hypohetic triangle. The hands and one of the feet were submerged in a container with saline solution.

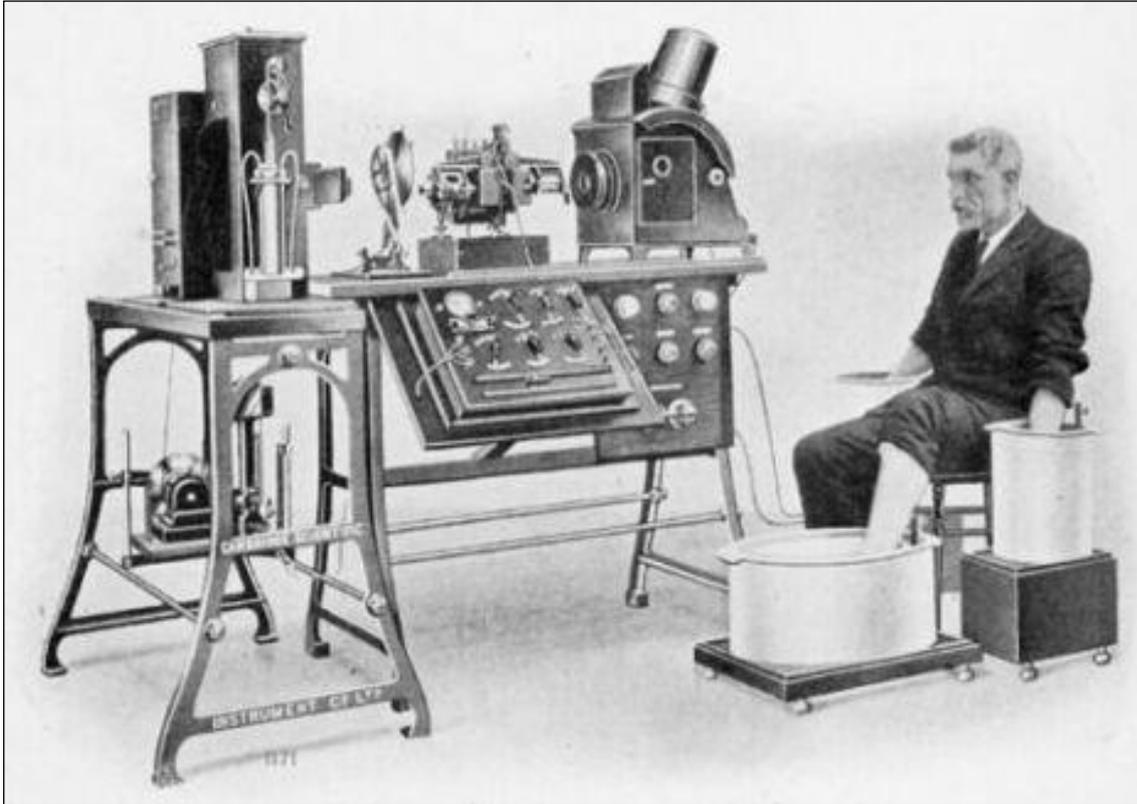


Figure 21. Picture of a complete electrocardiograph, where the way the electrodes were placed is shown. The hands and one foot were submerged in saline solution. Old string galvanometer electrocardiograph showing the big machine with the patient rinsing his extremities in the cylindrical electrodes filled with electrolyte solution.



Figure 22. Einthoven and his co-workers in Leiden, the Netherlands in 1916, during the 1st World War.

1893

Willem Einthoven, in a meeting of the German Medical Association, introduced the term electrocardiogram (Einthoven W, 1893). Later he clarified that it was Augustus Désire Waller who was the first to use such term.

His described the left His system as trifascicular (His W, 1893).

1895

In 1895 Einthoven published his classic article on the “Form of the Human Electrocardiogram”. Einthoven, using an improved electrometer and developing formulas of his own, identified five deflections he called P, Q, R, S and T (Einthoven W, 1895).

Why PQRST and not ABCDE?

The choice of P is a mathematical convention using the letters of the second half of the alphabet. N has a different meaning in mathematics and the letter is used to indicate the origin of cartesian coordinates. P is just the following letter. Einthoven used O....X to indicate the timeline.



Figure 23. Einthoven as a medicine student at the Utrecht University, 1878.

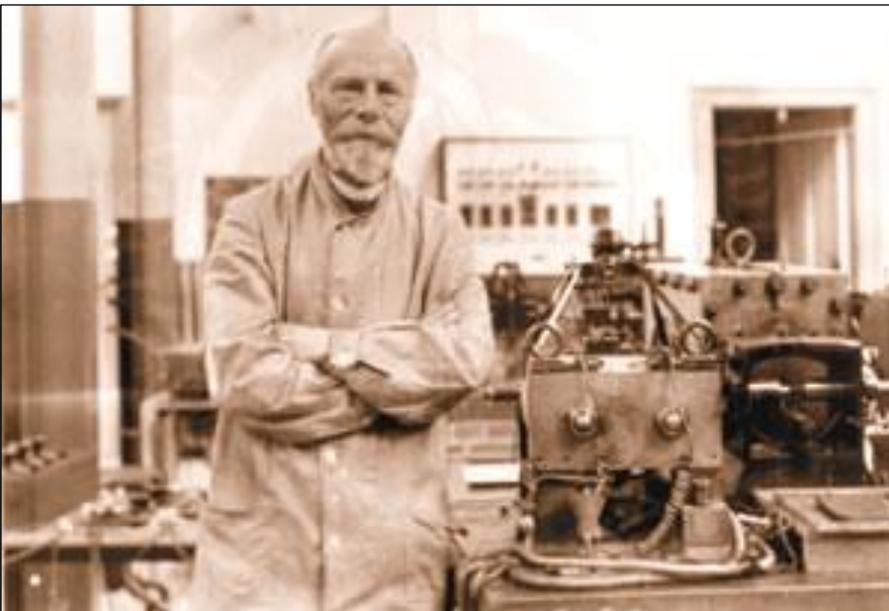


Figure 24. Einthoven and his laboratory in Leiden – the Netherlands

1897

The French electrical engineer Clement Ader, publishes a system of amplification called string galvanometer. The system was used for submarine telephone lines (Ader C, 1897).

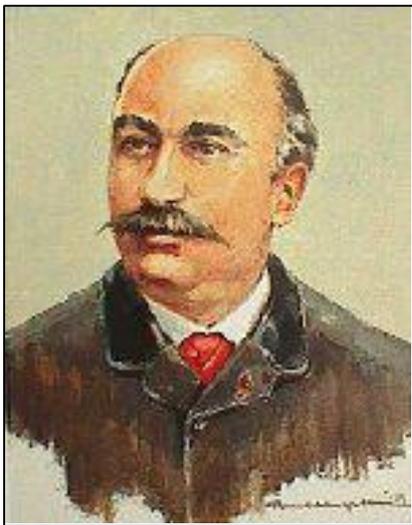


Figure 25. Clement Ader

1899

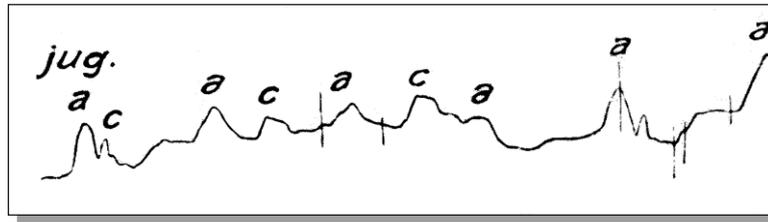
Karel Frederik Wenckebach publishes a paper analyzing the irregular pulse, describing the problem of AV conduction with progressive prolongation in toads.

Later, the Wenckebach-type block (Mobitz type I) would be known as “Wenckebach phenomenon. This is the original tracing of the jugular venous pulse made by Wenckebach. Check the progressive prolongation of the A-C interval (corresponding to the PR interval) until the wave is not followed by the C wave.

The brilliant Wenckebach described the arrhythmia before the discovery of ECG!!!



**KAREL FREDERIK
WENCKEBACH**



TRACING OF JUGULAR VENOUS PULSE

Figure 26.

1900

In 1900, Einthoven developed the string galvanometer, with a preliminary report in 1901. He showed that his mathematically predicted form of the electrocardiogram (ECG) derived from the capillary manometer agreed well with the one recorded with the string galvanometer (Einthoven W, 1895).

He published these results in 1904 in the Proceedings of the Royal Netherlands Academy of Arts and Sciences. The invention of the string galvanometer and, thus, the electrocardiograph by Einthoven has drastically and lastingly changed the practice of medicine (Krikler 1987). “It literally created a new branch of medicine, and even produced a new industry” (Burch EG et al, 1964).

1901

Einthoven modifies the string galvanometer to perform ECGs, initially developed by the French engineer Clement Ader. His galvanometer weighed 600 pounds (270 kg), it required 5 operators and hold 2 rooms (Einthoven W, 1901). From the lab, it was connected to the patients in the hospital through a 1.5 km long wire.

1902

Einthoven publishes the performance of the first ECG with a string galvanometer (Einthoven W, 1902; (Howell 1991) (Fye 1994). This new string galvanometer had very high sensitivity.

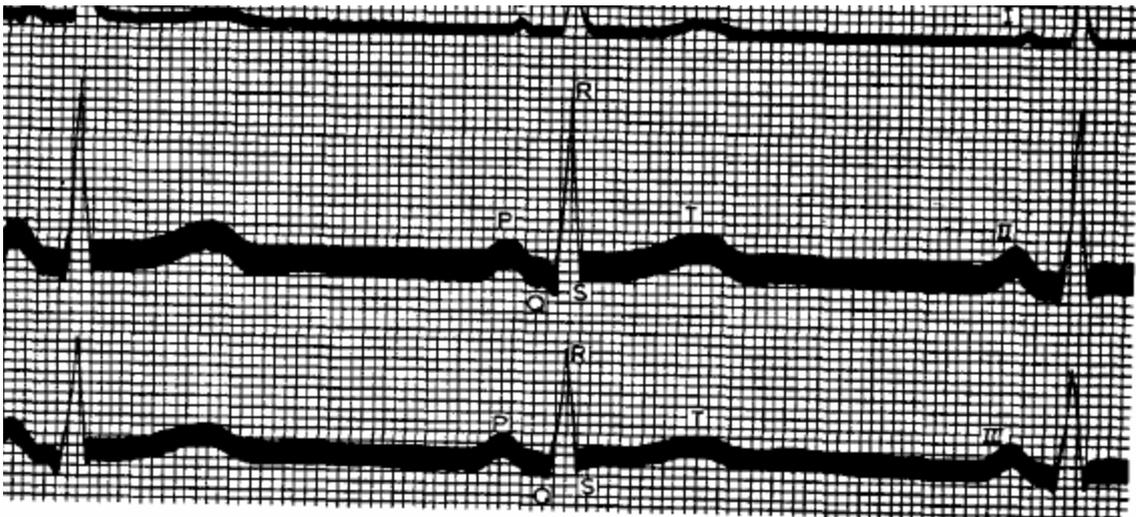


Figure 27.

As the string galvanometer electrocardiograph became available for clinical use, improvements were made to make it more practical. Earlier electrocardiograms recorded by Waller used five electrodes, one on each of the four extremities and the mouth, with 10 leads derived from the different combinations (Waller AD, 1889). Einthoven was able to reduce the number of electrodes to three by excluding those which he thought provided the lowest yield, the right leg and the mouth electrodes. The resulting three leads were used to construct Einthoven's triangle, an important concept to this day (Einthoven, Fahr et al. 1950).

The first electrodes were cylinders of electrolyte solution in which extremities were rinsed. The positive leads were placed on the left arm and leg to produce positive deflections on electrocardiogram tracing as the normal electrical activation of the heart

was noted to be from the right-upper quadrant to left-lower quadrant (Burch GE et al, 1964).

1903

Einthoven starts the commercial production of the string galvanometer associating to Max Edelmann from Munich, and a company of scientific instruments in London: the Cambridge Scientific Instruments Company.

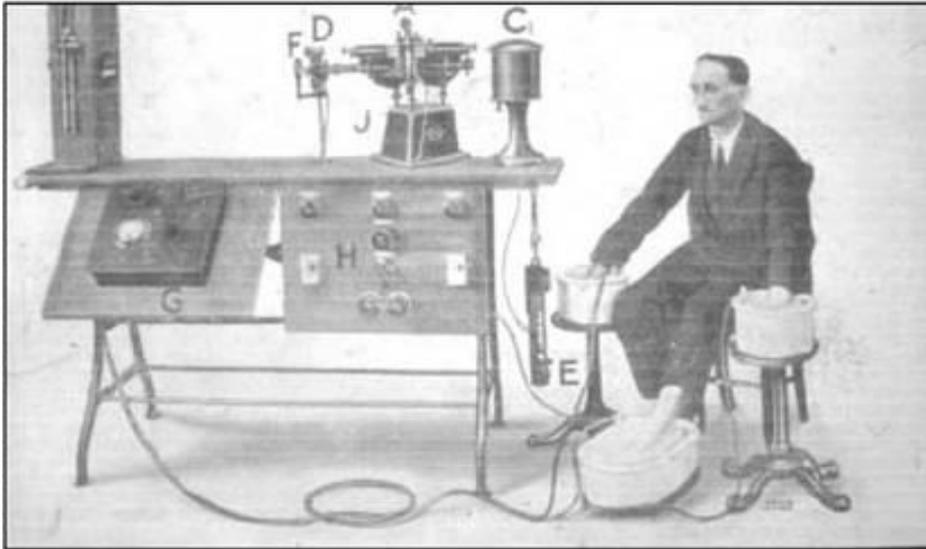


Figure 28. Old Cambridge ECG

1904

This is the cover of the first book on cardiac arrhythmias written by Wenckebach and titled: “Arhythmia of the Heart – A Physiological and Clinical Study”.

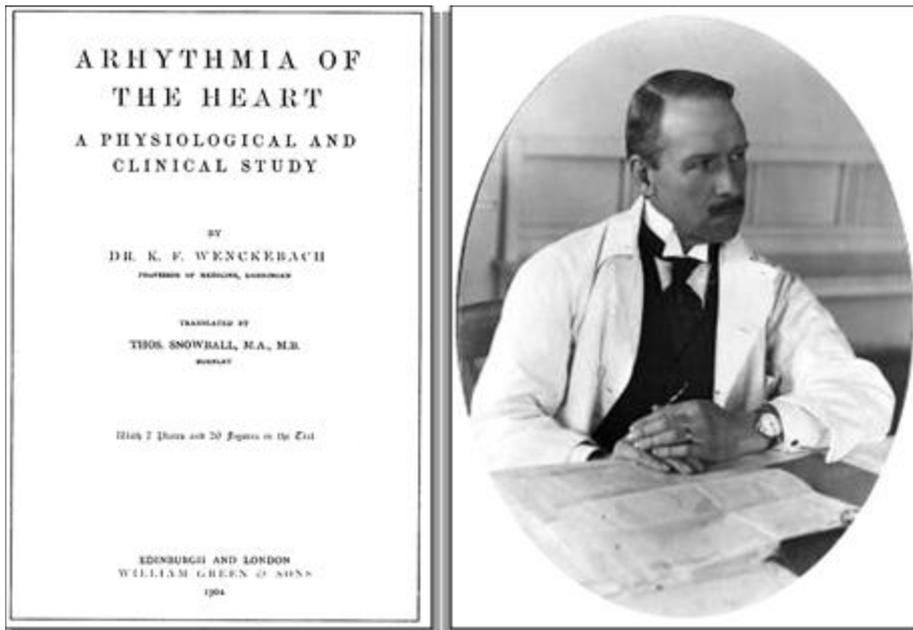


Figure 29. Old Cambridge ECG

1906

Einthoven publishes his first introduction of the normal and abnormal string electrocardiogram, describing atrial and ventricular enlargements, premature ventricular contractions, bigeminy, atrial flutter and complete AV block. Einthoven introduced "Le Télécardiogramme" in 1906 by which a cable connected his instrument to a hospital one and a half kilometres away. The string galvanometer produced precise ECG recordings but it was like the opera primadonnas of the time, voluminous and unpredictable (Johansson 2001).

In 1906, Einthoven identified the U wave for the first time (Einthoven W, 1957).

In that year, Tawara identified the atrioventricular node (Tawara S, 1906).

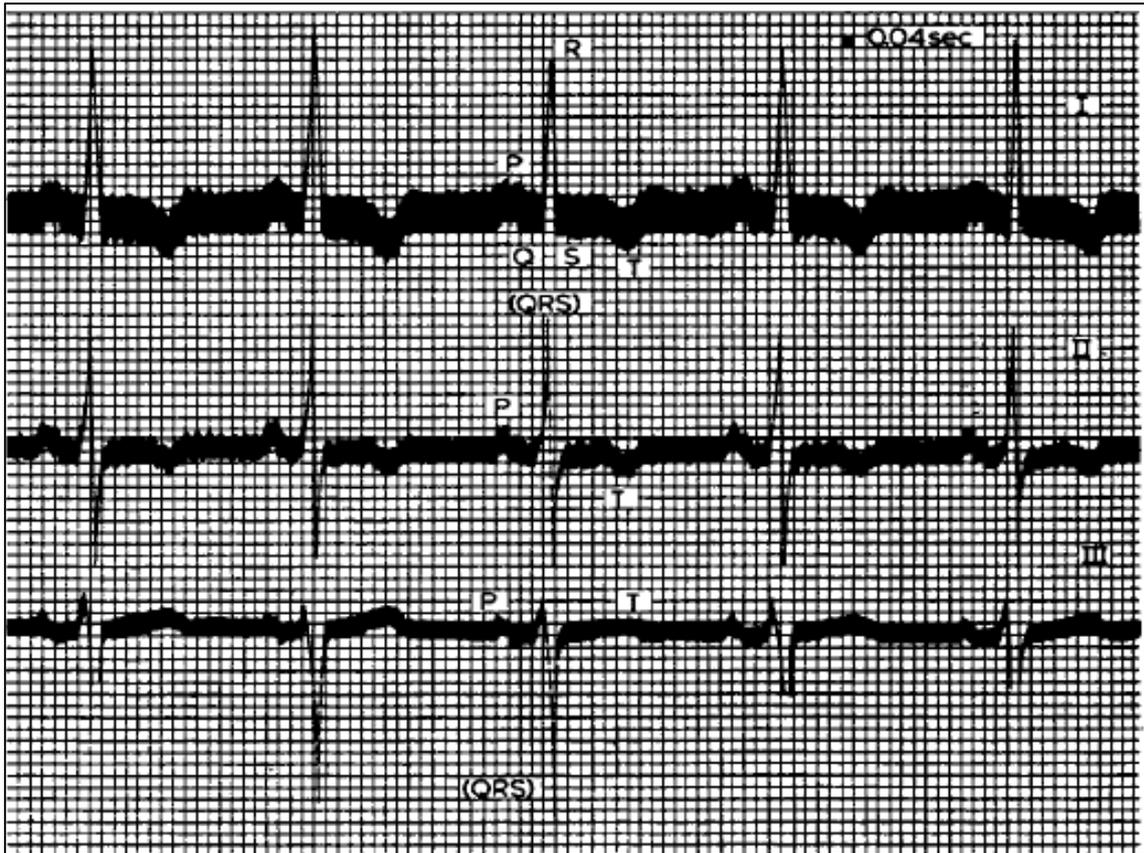


Figure 31. This is the original ECG of Einthoven, showing LVE pattern for the first time. S wave voltage very negative in III. The tracing was made simultaneously in the three leads (Einthoven W, 1957).

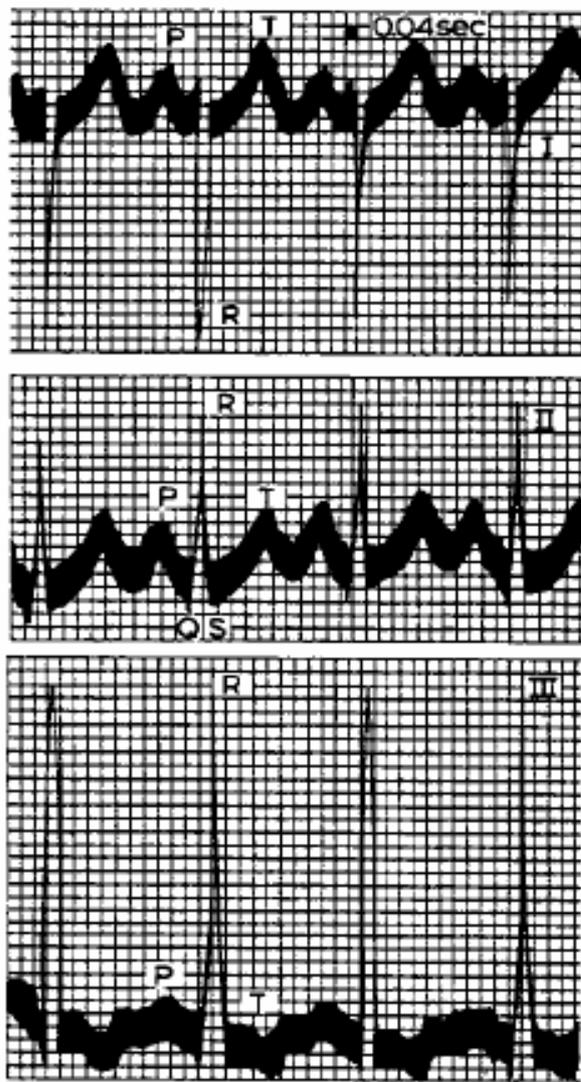


Figure 32. This is the original ECG by Einthoven, displaying RVE pattern for the first time: Negative QRS complex in I and very positive in III. Non-simultaneous leads (Einthoven W, 1957).

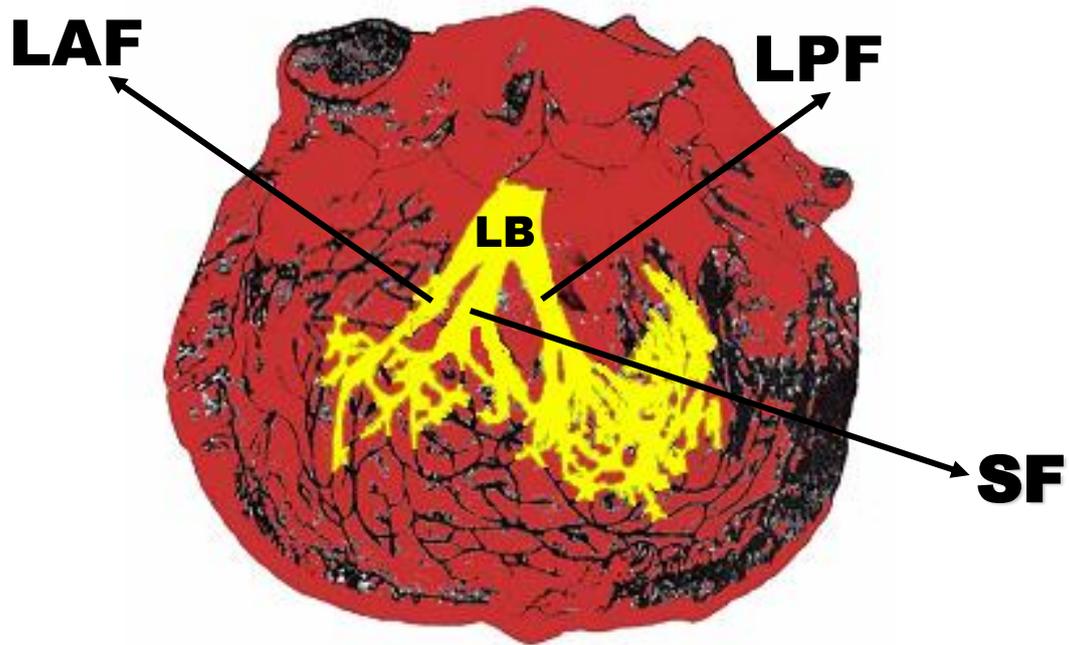


Figure 33. The anatomical description by Sunao Tawara from the onset of the 20th century (1906) shows that the left branch truncus of the His bundle (LB) splits into three fascicles and not into two: anterior fascicle (AF), posterior fascicle (PF) and septal fascicle (SF). “IF HEMIBLOCKS DO EXIST, THEY ARE ONLY TWO - IF A THIRD ONE IS POSTULATED, HEMIBLOCKS DO NOT EXIST!” (De Pádua F et al, 1976 and De Pádua F et al, 1977).

1907

Arthur Berridale Keith and his assistant Martin William Flack published the discovery of the sinoatrial node, the eponym of which holds their names: “Keith-Flack node”.

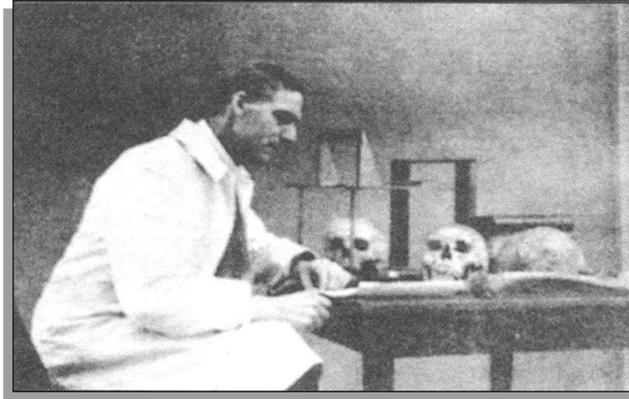
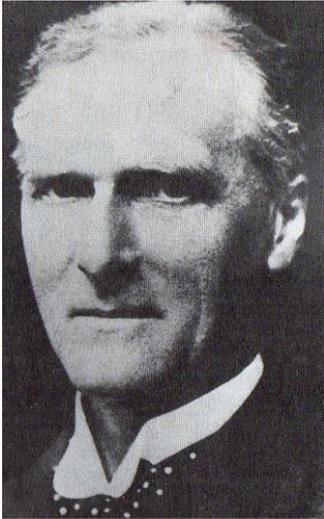


Figure 34. SIR ARTHUR BERRIDALE KEITH (1886-1955)

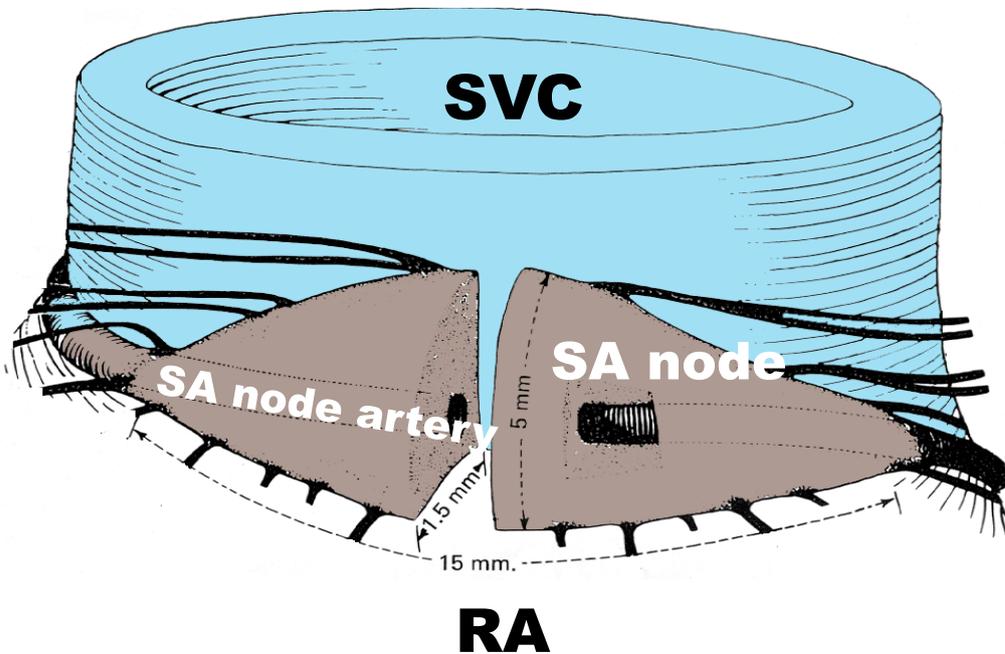


Figure 35. Sinotrial Node of Keith-Flack or SA node: The SA node holds P cells, responsible for cardiac automaticity. The name P comes from their characteristics: “Pale” (cytoplasm poor in glycogen), Pacemaker, Primitive (the oldest in phylogenesis) and the Principal or main ones in the organ.

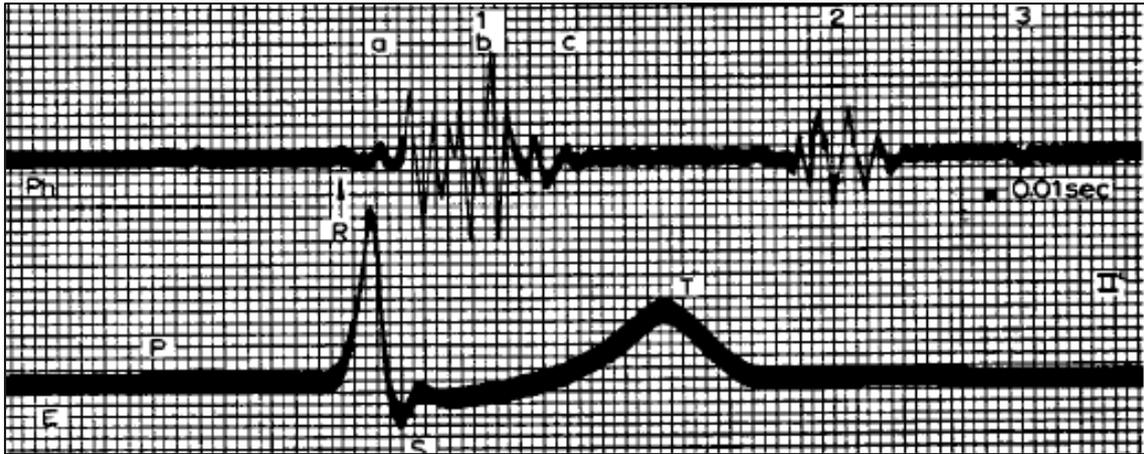
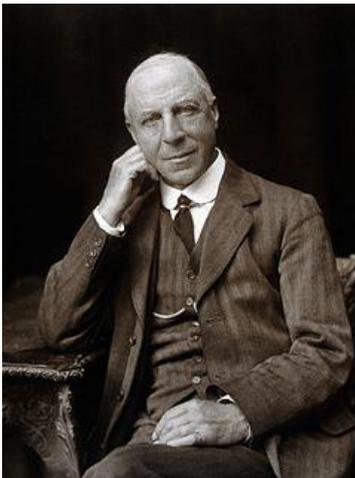


Figure 36. First ECG/Phonocardiogram correlation: original tracing made by Einthoven in 1907, where he correlates ECG waves in time with the cardiac sounds of the phonocardiogram (Einthoven W, 1907).

1908

Sir Edward Schafer (Figure 37) of the University of Edinburgh was the first to buy a string galvanometer electrograph for clinical use in 1908.



**EDWARD SCHAFER
1850 –1935)**

Figure 37. First ECG/Phonocardiogram correlation: original tracing made by Einthoven in 1907, where he correlates ECG waves in time with the cardiac sounds of the phonocardiogram (Einthoven W, 1907).

1909

The first electrocardiogram machine was introduced to the United States in 1909 by Dr. Alfred Cohn at Mt. Sinai Hospital, New York (Burnett 1985). In 1909, Alfred E. Cohn (1879-1957) brought one of these devices from London to New York—the first electrocardiograph in the United States. In studies at the Rockefeller Hospital, Cohn developed the use of the electrocardiograph to characterize the functioning of the heart in human diseases such as pneumonia and rheumatic fever.

His research also contributed to the basic understanding of electrical patterns produced by the heart, the anatomy of the heart, and the diagnosis of disease. Alfred E. Cohn, one of the first cardiologists in the United States, was born in New York City and received the MD from the College of Physicians and Surgeons at Columbia University in 1904. Between 1907 and 1909 he studied in Freiburg, Vienna, and London.

When he returned to the United States, Cohn joined the staff of Mount Sinai Hospital in New York. In 1911 he moved to the Rockefeller Hospital, bringing his electrocardiograph with him. He remained at Rockefeller for the rest of his career, retiring in 1944. Cohn took a leading role in organizations such as the New York Heart Association, New York Academy of Medicine, Veterans Administration, China Medical Board, Asia Institute, Sydenham Hospital, and the Committee for Displaced Foreign Scholars and Displaced Foreign Physicians. Cohn also published books of essays dealing with the philosophy of medicine and its role in society.

The first ECG where the presence of VT was shown in humans was made by Sir Thomas Lewis (Figure 38) as “single and successive extrasystoles” (Lewis T, 1909). Lewis reasoned by analyzing the phlebogram, that the event had a ventricular origin. He observed that VT could be caused by coronary artery ligation (Lewis T, 1909).



SIR THOMAS LEWIS

Figure 38. Sir Thomas Lewis Portrait.

In 1909, Sir Thomas Lewis of University College Hospital, London, discovered that ‘Delirium Cordis, a clinical diagnosis of irregular heartbeat, was a result of atrial fibrillation using the electrocardiogram (Lewis T, 1909) (Hering 1909).

Isolated T wave alternans, corresponding to phase 3 of action potential (AP) is described (Hering HE, 1909). Later, in 1928, Doctor Helen Brooke Taussig observed T-wave alternans in the papillary muscle of cats (Taussig HB, 1928).

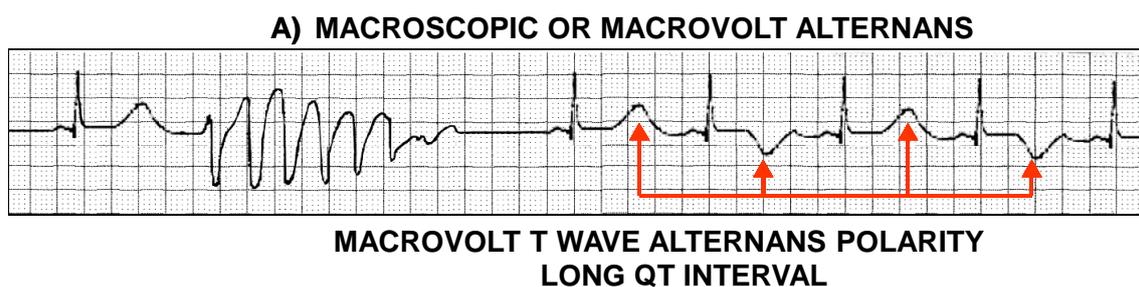


Figure 39. Isolated T wave alternans

1905/1907/1910/1913

In 1905, William Ritchie records the first Atrial Flutter in a patient with complete AV block (Ritchie W, 1905).

In 1907, Einthoven records 2:1 atrial flutter (Einthoven W, 1906).

In 1910 Jolly and Ritchie study the same patient using ECG (Jolly WA et al, 1910).

In 1913, Sir Thomas Lewis announces the Atrial Flutter criteria (Lewis T, 1913). (Cohn and Lewis 1913)

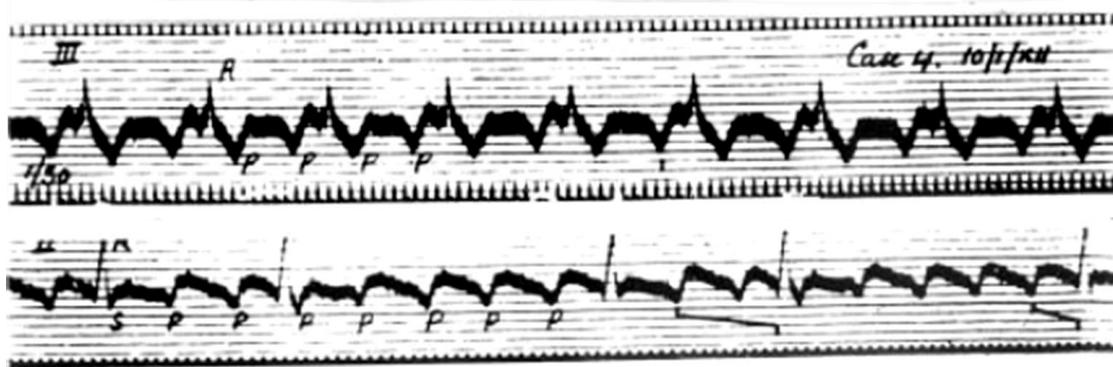


Figure 40. Electrocardiograph used by Lewis at the University College Hospital Medical School built by Cambridge Scientific Instrument Company of London in 1911. From left to right: camera and the falling glass camera, the galvanometer and light source. The ECG in the lower panel recorded with the above instrument. (Reprinted from: BMJ 1950;1:720, British Medical Association, London, with permission.)

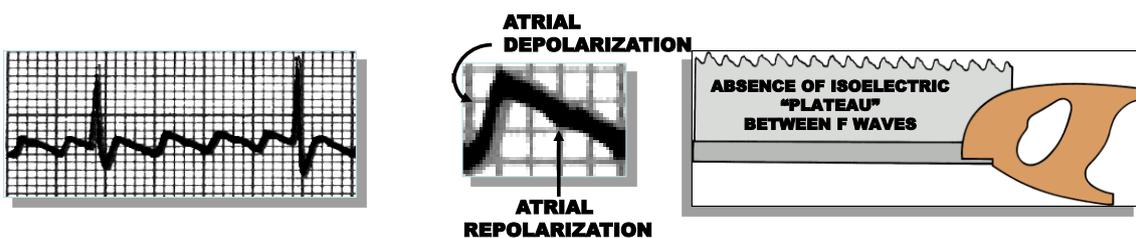


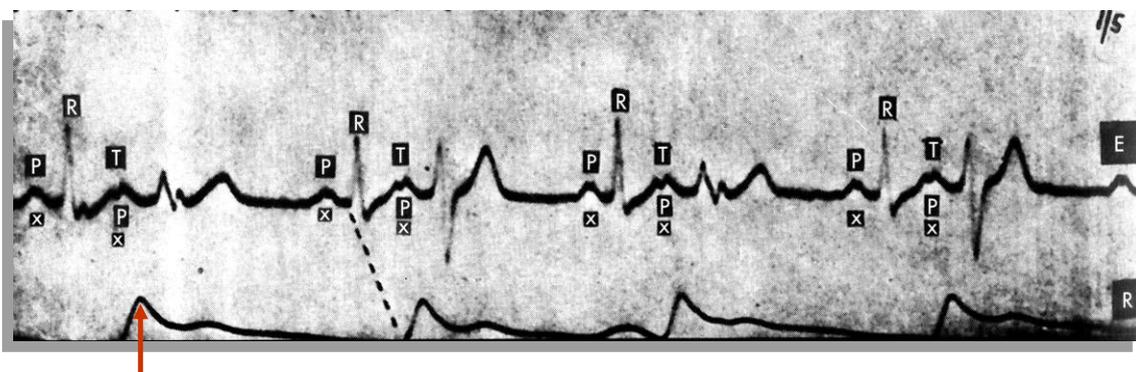
Figure 41.

1910

After the recognition of myocardial infarction as a clinical entity in 1910, attempts were made to recognize electrocardiogram patterns suggestive of ischemic heart disease.

Walter James from the Columbia University and Horatio Williams from the Cornell University published the first American review of ECG. In it, they describe ventricular enlargements, premature atrial and ventricular contractions, AF and FV (James WB et al, 1910).

This year, Lewis published the first example of aberrant ventricular conduction in a patient in sinus rhythm with atrial bigeminy. Every premature contraction is conducted aberrantly and the morphology of this aberration alters.



THE LOWER RECORDING REPRESENTS RADIAL PULSE

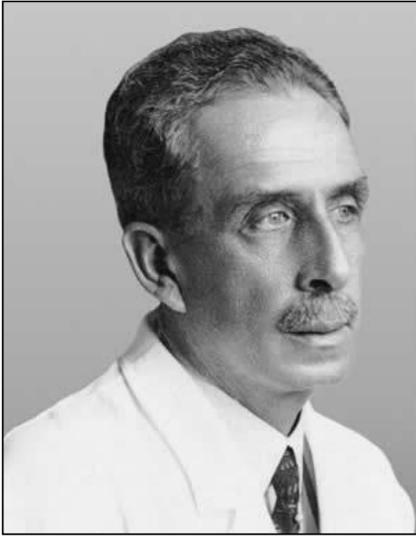
Figure 42.

1910/1912

Carlos Chagas, in 1910, in Brazil acquired for the Instituto de Maguinhos in Rio de Janeiro, the first electrocardiograph. In the same year, Duque Estrada was sent to France to study radiology and there he bought two devices of the string galvanometer type.

One of them was assembled at the old hospital of Praia Vermelha, presently the Rector's Office of the Universidade Federal do Rio de Janeiro, in the Service of Juliano Moreira, where Zacheu Esmeraldo, a psychiatrist in 1912, prepared his thesis on "Atrial Fibrillation".

“The second ECG device was assembled in Brasil, in the inner yard of the Santa Casa de Misericórdia in RJ and delivered to Dr. Miguel Couto, who prepared his PhD thesis on premature contractions (1912)”.



DR. CARLOS CHAGAS



DR. MIGUEL COUTO

Figure 43.

1911

Sir Thomas Lewis published the classical textbook called “The Mechanism of the Heartbeat” and dedicates it to Willem Einthoven.



Figure 43. Historical picture at the Boerhaave Museum of Leiden, the Netherlands. Einthoven and Lewis.

1919

The American Hubert Mann from the cardiology lab at the Mount Sinai Hospital, described a monocardium, which would later be called vectocardiogram (Brinberg 1958, Brinberg 1958) (Mann H, 1920).

The Newyorker Harold Pardee publishes the first ECG of an acute myocardial infarction in a human, and describes the T wave alterations that are known today as “Pardee Complex” (Pardee HEB, 1920), that resemble monophasic action potential.

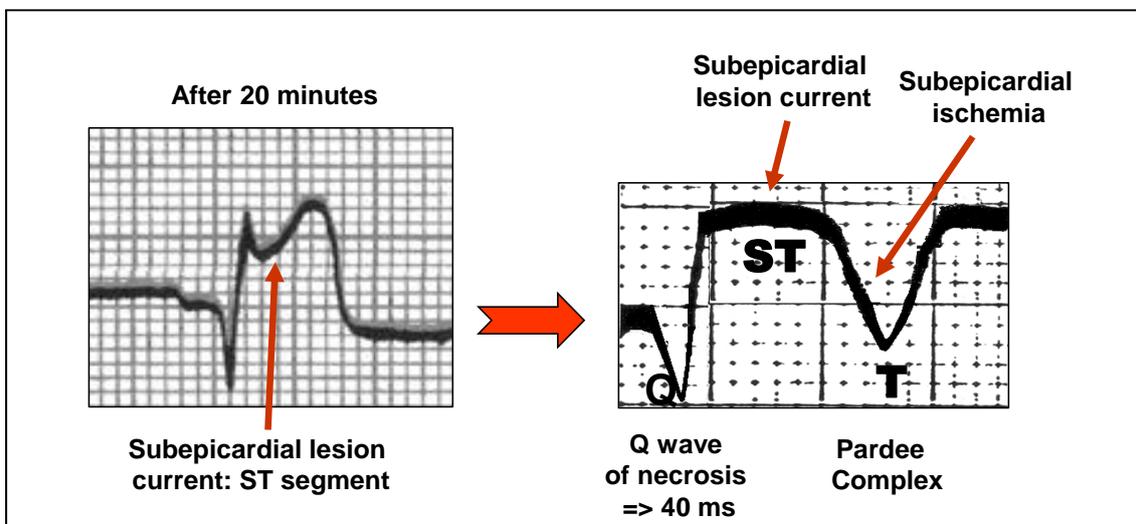


Figure 44.

1920



Figure 45. Cambridge Electrocardiograph, 1920

1921

Lewis points out that atrial flutter has a mechanism by circular movement (Lewis T, 1921).

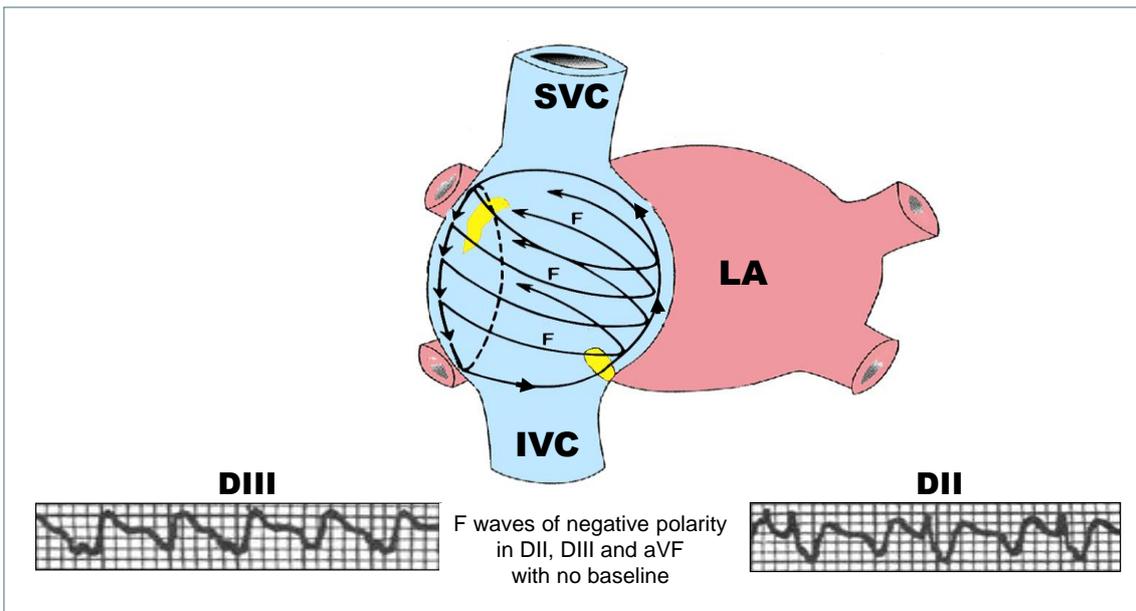


Figure 46.

1924

Willem Einthoven is awarded the Nobel Prize of Medicine and Physiology in 1924 “for his discoveries on the mechanism of the electrocardiogram, string galvanometer and measurement of the action potentials of the heart”.

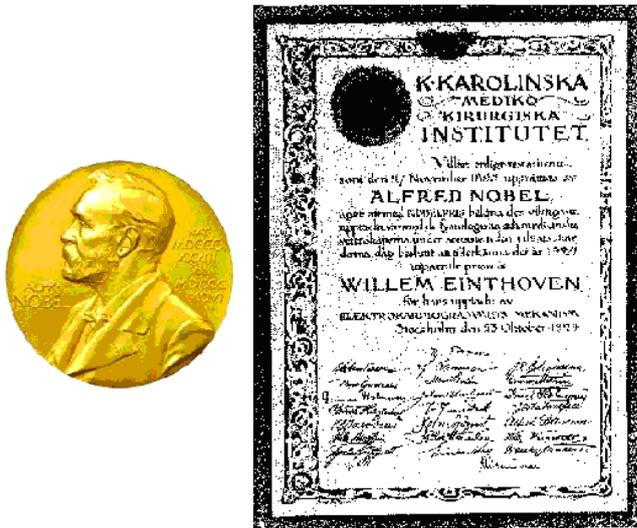


Figure 47. Gold medal and diploma given to Willem Einthoven by the Nobel Prize.



Figure 48. Willem Einthoven dressed to receive the Nobel Prize in Oslo - Sweden.



Figure 49. The first picture shows Willem Einthoven and his wife in 1924. Standing behind them, the sister of Mrs. Einthoven, Mrs. de Voogd. In the second picture, Willem in the same trip.

Woldemar Mobitz publishes his classification of second degree AV blocks (Mobitz type I and type II) based on the ECG and jugular pulse, the latter observed before the age of ECG by Wenckebach (**Mobitz W, 1924**). He mentions that type I was of a physiological character and type II caused by a severe infranodal disease of the His system.

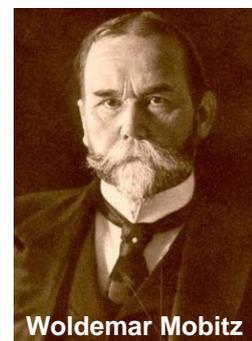
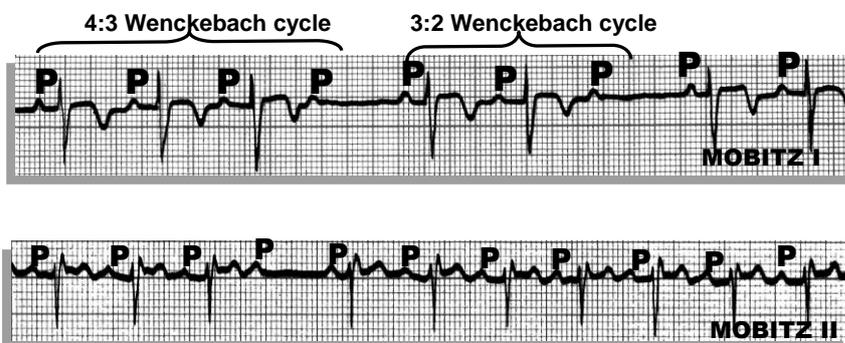


Figure 50.

1925

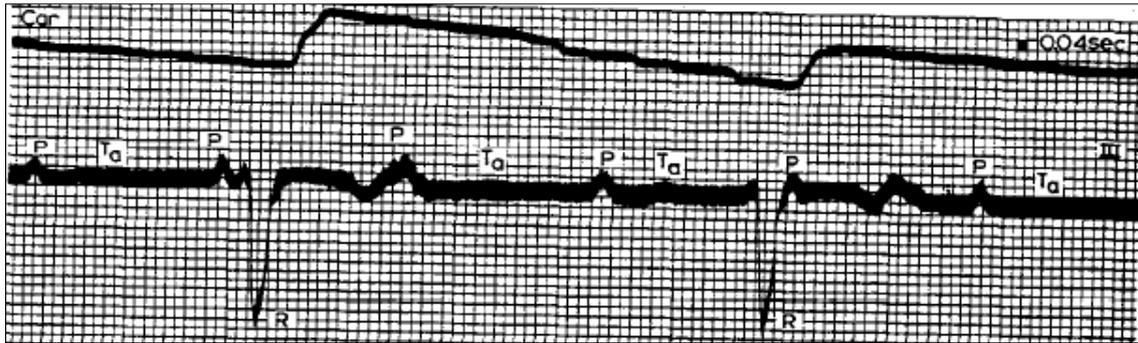


Figure 51. Original tracing performed by Einthoven and presented as “Nobel Lecture, December 11, 1925”. The tracing shows what he called “Stoke-Adams disease” with LV hypertrophy.

1927

Willem Einthoven dies of cancer after a long suffering, on September 28, 1927, at 67 years of age, in Leiden.

He was buried in a reformed church in Oegstgeest (Lama 2004).



Figure 52. In this picture, the tomb of Willem Einthoven, his wife and son in Oegstgeest, in the Netherlands.

1929/1930

In 1929, Levine described the coronary thrombosis and its various clinical features (Levine SA, 1929).

In 1930, it was recognized the importance of electrocardiogram in differentiating cardiac from non-cardiac chest pain; in fact, some patterns were considered so characteristic that the electrocardiogram alone could be used to confirm the diagnosis of myocardial infarction.

1930

Wolff, Parkinson and White publish an ECG (Figure 53) characterized by the association of the short PR interval, QRS prolongation and paroxysmal tachyarrhythmias (Wolff, Parkinson et al. 2006).

Fifteen years earlier, Frank Wilson had published a case in which the vagal action influenced the QRS morphology: “the patient presented 4 different rhythms and at least 3 types of ventricular complexes” (Wilson FN, 1915).

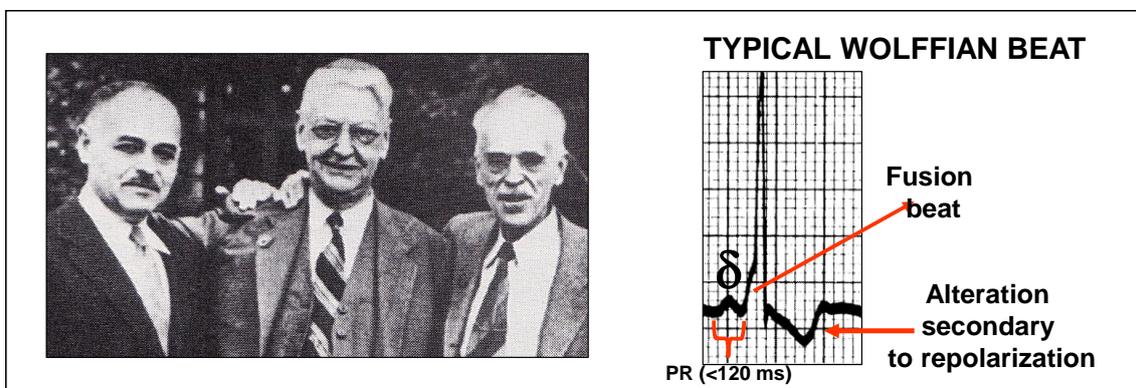


Figure 53.

Brief Sequential Walk through the History of Ventricular Pre-excitation

In **1876, Paladino** described muscle fibers responsible for the communication between the atria and the ventricles (Paladino G, 1876). This the reason why the parallel bundles are sometimes called Paladino-Kent bundles.

In **1893, Stanley Kent** reported lateral muscular AV communications (Rosenbaum, Chiale et al. 1974, Rosenbaum, Klein et al. 1997), that constituted the normal AV conduction system in humans; while these were probably the first reports of VA pathways. The normal conduction system was clearly defined by **His, in 1893 and Tawara, in 1906** (Schmitt C, 2006).

In **1909, Hoffman** described patients with ECGs presenting wide QRS complexes, that were considered by these as atypical forms of branch block (Von Knorre 2005). In fact, these were the first reported ECG data relative to ventricular pre-excitation syndrome.

The first complete description of WPW syndrome was published in the American Heart Journal, in **August 1930** (Wolff L et al, 1930) by **Wolff, Parkinson and White**. These authors described 11 young patients with no structural heart disease, with short PR, paroxysmal tachycardia runs associated to ECG pattern of branch block. Nevertheless, these features were not initially associated to electrical conduction by anomalous VA pathways.

In **1932, Holzmann and Scherf** proposed that the AV communications described by Kent may conduct the impulse from the atria to the ventricles, thus explaining ECG alterations and tachyarrhythmias. Consequently, they described that the mechanism of WPW syndrome consisted of the rapid passage of the impulse from the atria to the ventricles and not of a block (Hanon, Shapiro et al. 2005).

In **1944, Ohnell** introduced the term “pre-excitation” into medical literature, and just as Wood, confirmed the presence of VA pathways in histological studies.

Also in **1944, Segers** called the initial part of slow QRS as “delta wave” (Von Knorre 2005), observed in these cases.

In **1945, Rosenbaum** (not our Mauricio, though) classified WPW syndrome into types A and B, considering leads V1, V2 and VE (esophageal) (Rosenbaum FF, 1945).

In **1952, Holzmann and Scherf** were the first to describe pre-excitation as a result of extranodal VA pathway (Scheinman 2005). These data were not well accepted at the time, and originated many alternative ideas.

In **1956, Guiraud** concluded that types A and B represented the left posterobasal and right lateral pathways, respectively (Giraud, Latour et al. 1956).

In **1999, the North American Society of Pacing and Electrophysiology (NASPE) and the European Society of Cardiology (ESC)** proposed a new classification of VA pathways locations, based on the analogy of the heart in anatomic position, being more useful for the EPS (Cosio, Anderson et al. 1999).

Pick, Langendorf and Katz greatly contributed to our understanding of this syndrome. They concluded that the characteristics present in this syndrome could only be explained by the existence of extranodal VA pathway. By a detailed analysis of literature on thousands of ECGs, they described the differences between the refractory periods of the nodal pathway and the VA pathway for the onset of paroxysmal supraventricular tachycardia. They also clarified the relationship to paroxysmal tachycardia and Wolff-Parkinson-White syndrome (Giraud G et al, 1945) AF, and made a differentiation between nodal and extranodal AV pathways. Their ideas strongly influenced subsequent cardiac EPS (Scheinman 2005).

Durrer and Wellens were the first to use programmed electrical stimulation of the heart to better define the mechanism of arrhythmias. They showed that tachycardia could be induced by early atrial or ventricular stimulation; that tachycardia could be orthodromic or antidromic; and defined the relationship of refractory period of VA pathway with ventricular response during AF. Their work constituted the basis for intracardiac studies, in the sense of defining the location and physiology of these pathways (Scheinman 2005). Until the 1960s, the treatment of patients with WPW syndrome was pharmacological, based on antiarrhythmic drugs with significant side and proarrhythmic effects.

However, **Durrer and Roos in 1967**, were the first to conduct intraoperative mapping to locate the VA pathway.

Burchell et al, in the same year, showed that pre-excitation could be inhibited by procainamide injection.

Sealy and Duke in 1968 made the first successful surgical intervention on a VA pathway. Their results showed conclusively that most WPW patients could be healed by right surgery or by cryoablation of these pathways. In the 1970s, surgery substituted pharmacological therapy for the treatment of these patients. Identifying and locating the VA pathway became essential, and it was made by epicardial and/or endocardial mapping in pre-operative EPS studies (Scheinman 2005).

The catheter ablation technique was introduced by **Scheinman et al, in 1981** (our dear and beloved master Melvin!!!!) who used high energy to destroy cardiac tissue.

Fisher in 1984 attempted the ablation of left VA pathway through the coronary sinus, a technique that was dropped because of its limited efficacy and by the high incidence of cardiac tamponade.

The introduction of radiofrequency energy at the end of the 1980s, completely changed catheter ablation procedures. Simultaneously, other significant advancements recorded included the improvement of the quality of the catheters used, and it was shown that the location of the pathway could be facilitated by identifying the potential of the pathway[8]. Radiofrequency ablation is now the treatment of choice for WPW syndrome patients, because of its high rate of success and low morbi-mortality.

In **2003, guidelines** were published for the approach to patients with supraventricular arrhythmias, that comprehended in a more consensual way, the best follow-up strategies for patients with extranodal VA pathways (Blomstrom-Lundqvist, Scheinman et al. 2003, Blomstrom-Lundqvist, Scheinman et al. 2003).

1931

In this year, Dr. Wilson (Wilson FN, 1931) (Bayley 1955) (Wilson, Johnston et al. 1946) developed the concept of ventricular gradient (VG). This is in a single ECG lead a net time integral of the ECG voltage from the beginning of the P wave to the end of the U wave. Its spatial counterpart is the ventricular gradient vector determined from the orthogonal XYZ leads.

The practical utility of the ventricular gradient in differentiating primary from secondary repolarization abnormalities has not been demonstrated until today. In summary, the ventricular gradient is the sum of the areas within the QRS complex and the T wave on the electrocardiogram.

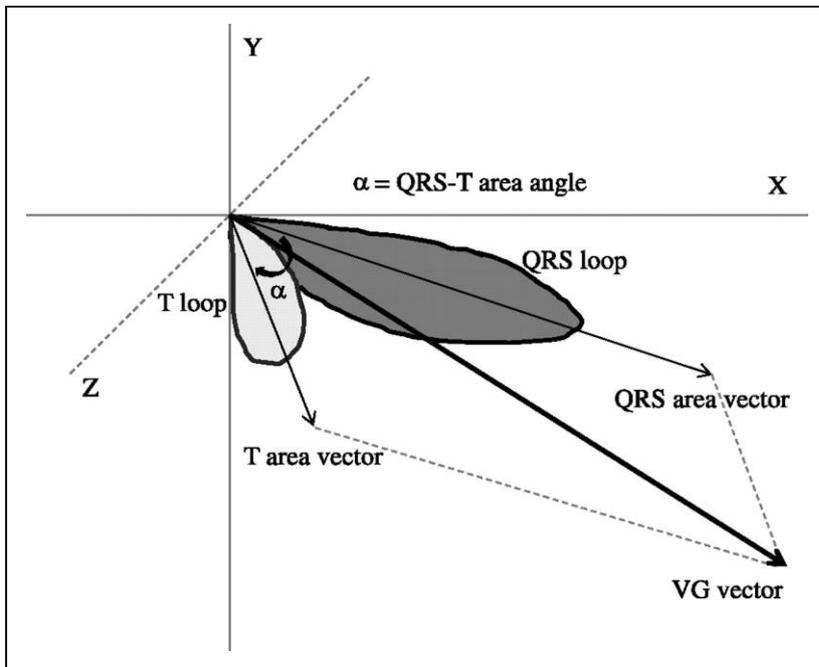
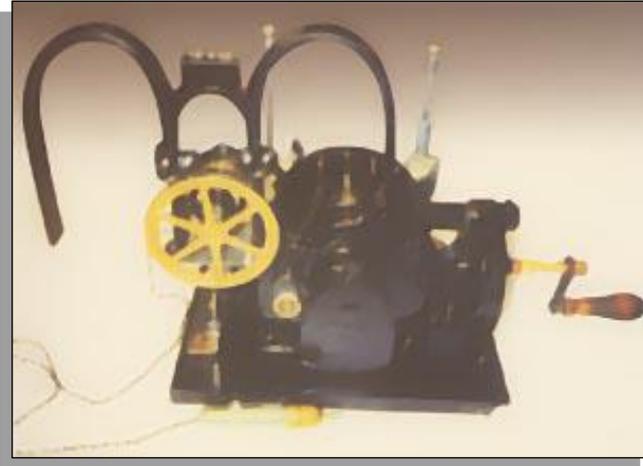


Figure 54. The VG is the vector sum of the QRS area (the spatial area under the curve formed by the moving heart vector during the QJ interval) and the T area (the spatial area formed by the moving heart vector during the JT interval). QRS-T area under the curve angle, the angle between the QRS area vector and the T area vector.

Dr. Albert Hyman patents the first artificial pacemaker stimulating the heart, using transthoracic activation. His goal was to produce a small device that would stimulate the area of the atrium. His experiments were always in animals.

In 1942, the first pacemaker successful over a short period of time, is reported in patients with attacks of the Morgagni-Stokes-Adams type (Hyman AS, 1932).



FIRST ARTIFICIAL PACEMAKER



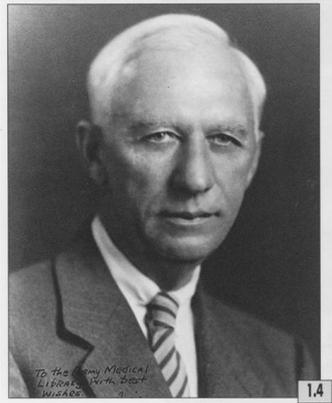
DR. ALBERT S HYMAN

Figure 55.

1931

The current 12-lead ECG results from the conjunction of:

- 1) Bipolar or standard system of the frontal plane: I, II and III (1913 - Einthoven);
- 2) Unipolar precordial system (V_1 - V_6) (1934 – Frank Norman Wilson) of the University of Michigan developed the concept of the ‘central terminal’. By connecting the three limb electrodes, a central negative lead reflecting a ‘ground’ or reference terminal was created. An electrode from the body surface connected through a galvanometer to this ground measured the potential difference between that point on the body and what can be thought of as zero. These ‘unipolar’ leads were in contrast to the ‘bipolar’ leads that measure the potential difference between two sites on the body surface. The unipolar lead could have theoretically been placed at any point on the body and, as a consequence, was termed an exploring lead. In 1938, the American Heart Association and the Cardiac Society of Great Britain published their recommendation for recording the exploring lead from six sites named V_1 through V_6 across the precordium. Thus, the chest leads were born.
- 3) Unipolar system of the limbs: aVR, aVF and aVL (1942 - Emanuel Goldberger).



DR. FRANK NORMAN WILSON
(1890-1952)

Frank N. Wilson M.D.

Figure 56. Frank N. Wilson, MD. (Reprinted from: The Journal of the Michigan State Medical Society, January 1953, with permission). Courtesy of Dr. Thomas N. James.

1931

Arthur Morris Master (1885-1973), got his degree in 1921 at the Cornell University and his post-degree at the Mount Sinai Hospital in New York. He worked in London with the famous English cardiologist and physiologist Sir Thomas Lewis in London. Back to the US, he was the director of the Mount Sinai Hospital and during WWII, he served in the US Navy in the Solomon islands. In 1937, he created the stress test to study cardiac function, performed during 90 seconds, climbing and descending a stair with 2 steps of 23 cm, while he analyzed pulse. The method became known as “two step exercise test”, Master two-step or by the eponym Master’s test (Master AM, 1935 and 1942).



DR. ARTHUR MORRIS MASTER

Figure 57.

1937

The so-called “Katz-Wachtel phenomenon” or pattern observed in VSD with BVE (association of systolic RVE and diastolic RVE), characterized by wide isodiphasism in the intermediate leads from V_2 to V_4 , is described.

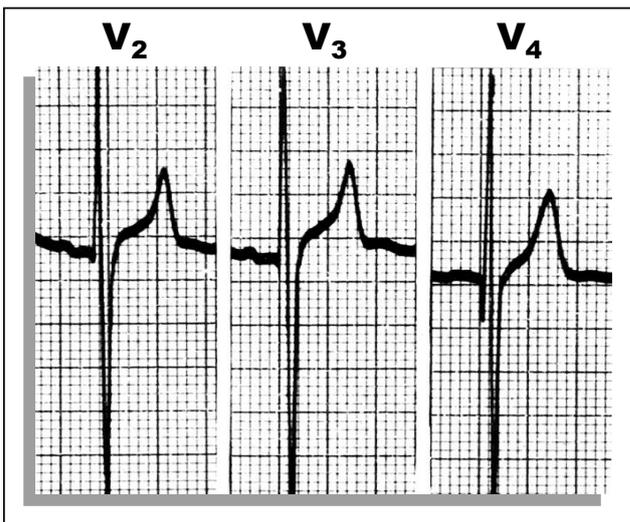


Figure 58. Sign, pattern or phenomenon of Katz-Wachtel. Wide isodiphasism in the intermediate leads, indicates BVE.

1938

In 1938, the American Heart Association and the Cardiac Society of Great Britain published their recommendation for recording the exploring lead from six sites named V1 through V6 across the precordium. Thus, the chest leads were born.

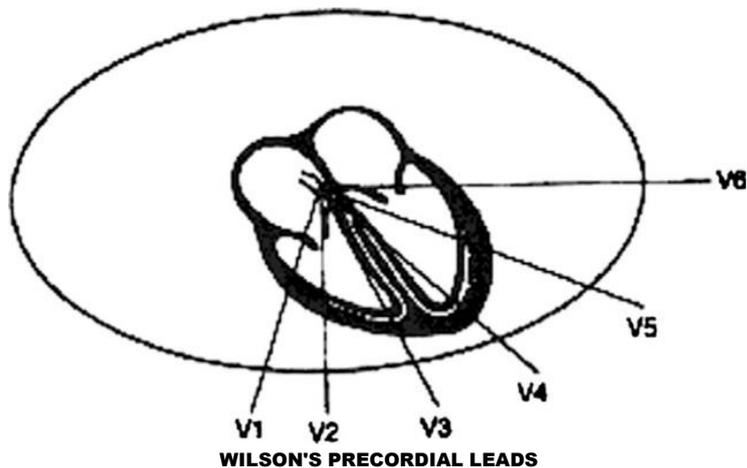


Figure 59.

The J-wave history

Earlier than the Osborn's description, similar deflections on the ECG had already been described in 1920 and 1922 by Kraus (Kraus F, 1920).

In 1938, Tomaszewski et al. provided the description of hypothermic J wave in an accidentally frozen man. (Tomaszewski W, 1938)

In 1953 John J, Osborn (Osborn 1953) were then definitively described and were named with his eponymous in his honor. This author studied the effect of hypothermia on the respiratory and cardiac function in dogs. Experimentally-induced hypothermia caused the development of a distinct deflection at the J point on the ECG, which he called "current of injury". Although there had been several reports regarding an alternation in the ECG at the J point prior to Osborn's article, this deflection came to be called the "Osborn wave" in honor of his systematic and cornerstone manuscript. Osborn considered acidosis induced by hypothermia as a primary cause of the "current

of injury”, because it disappeared if the arterial pH was normalized by hyperventilation during the same degree of cooling. He described the J wave as a very slowly inscribed deflection between the QRS complex and the ST segment of the ECG. Osborn described what he called a “current of injury” in dogs that were acidotic and hypothermic that fibrillated at rectal temperatures less than 25°C. This so called “current of injury” was later named the Osborn wave.

In 1957 Fleming (Fleming and Muir 1957) and Muir described the electrocardiographic changes in induced hypothermia in man (Emslie-Smith, Sladden et al. 1959).

In 1959, Emslie-Smith et al Emslie-Smith, 1959 #3108} found differences in the endocardial and epicardial responses of the ventricular myocardium to cold, and the Osborn wave was more prominent in the epicardial than endocardial leads. These authors questioned the participation of acidosis in the genesis of the Osborn wave on the basis of their observation that the Osborn waves appeared in hypothermic dogs irrespective of the blood pH.

In 1959 West et al (West, Frederickson et al. 1959) confirmed that the spike and dome pattern could be recorded by a microelectrode.

In 1972, Clements and Hurst showed the diagnostic value of ECG abnormalities observed in subjects accidentally exposed to cold (Clements and Hurst 1972).

In 1984 Sridharan and Horan shows the electrocardiographic J wave of hypercalcemia (Sridharan and Horan 1984).

In 1988, Litovsky and Antzelevitch (Litovsky and Antzelevitch 1988) proposed a difference in the electrophysiology of the ventricular epicardium and endocardium as the basis for the J waves. The 4-aminopyridine sensitive transient outward current (I_{to}) was shown to be prominent in canine ventricular epicardium, but not in the endocardium. The more conspicuous notched configuration of the epicardial action potential was supposed to produce a transmural voltage gradient during ventricular activation that manifested as the J wave in the ECG.

In 1994 Di Diego (Di Diego and Antzelevitch 1994) and Antzelevitch demonstrated that high Ca^{2+} (a hypercalcemic conditions) I_o -induced electrical

heterogeneity and premature ventricular contraction activity in isolated canine ventricular epicardium

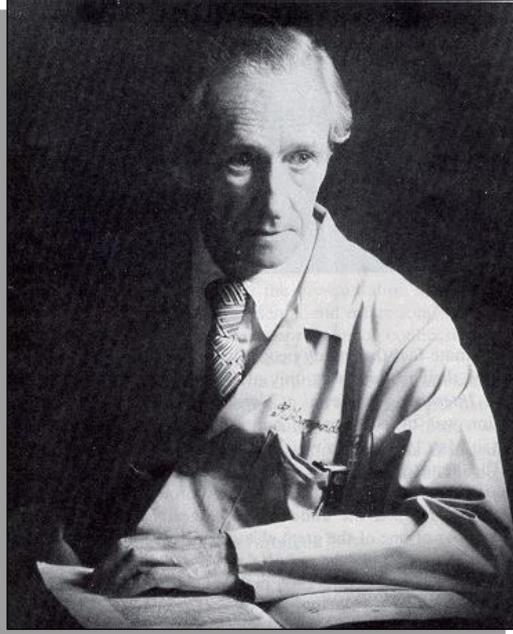
In 1996, Yan and Antzelevitch (Yan and Antzelevitch 1996, Yan and Antzelevitch 1998) clarified their hypothesis using an arterially perfused canine ventricular wedge model, which made it possible to simultaneously record transmembrane action potentials from several sites across the ventricular wall together with a transmural ECG.

In 1996 Lukas and Antzelevitch (Lukas and Antzelevitch 1996) demonstrate Phase 2 reentry as a mechanism of initiation of circus movement reentry in canine epicardium exposed to simulated ischemia that had been reported to trigger the appearance of the J waves.

1939

Richard Langendorf presents a case of atrial infarction, proved in necropsy (Langendorf, 1939), in which he retrospectively deduces that it could have been diagnosed by ECG changes:

1. STa depression
2. P wave with M or W appearance in the acute phase
3. Frequent atrial arrhythmias of all types by occlusion of the SA node artery



DR. RICHARD LANGENDORF

Figure 60.

1942

Emanuel Goldberger unplugs from the central terminal of Wilson (CT), the lead of every limb (b): VR, VL and VF. Thus, he enhances (a) waves voltages. Up to this moment, all unipolar leads of limbs converged in a central terminal, originating waves of less voltage, making the interpretation of tracings difficult. Since the creation of the enhanced leads aVR, aVL, and aVF, the ECG obtains the 12-lead ECG methodology as used currently.

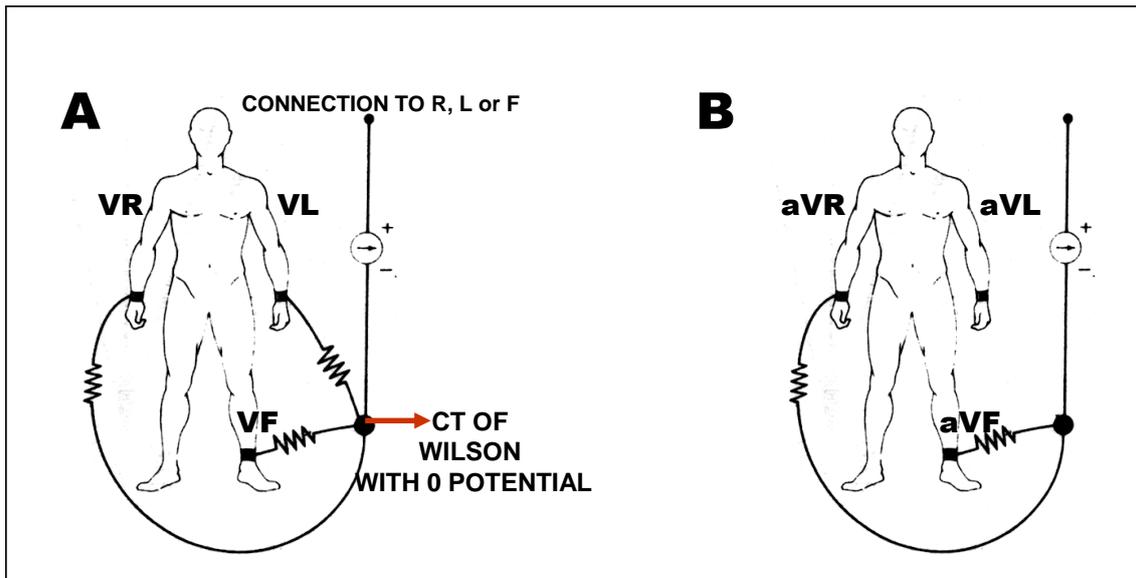


Figure 61.

1942 Augmented unipolar leads

Since the three-lead electrocardiogram covered the frontal plane with 60° increments, it seemed possible that there were uncovered segments potentially increasing the possibility of electrically silent myocardial pathology. In 1942, Dr. Emanuel Goldberger of Lincoln Hospital, New York, using Wilson's central terminal, constructed unipolar leads with the central (zero) terminal and connected to additional positive unipolar leads on each of the left and right arms and the left leg (Goldberger E, 1942). This method provided more detailed coverage of the frontal plane with 30° increments.

Since the signal of these unipolar leads was small, Goldberger designed a method to augment these signals resulting on what we know now as the augmented unipolar limb leads a-VL, a-VR, and a-VF. Of note, this is the first time that a positive electrode was placed over the right arm, against the direction of the electrical activation, leading to the strange looking a-VR. The invention of the unipolar leads concluded the major advancement toward the 12-lead electrocardiogram as we know it now.

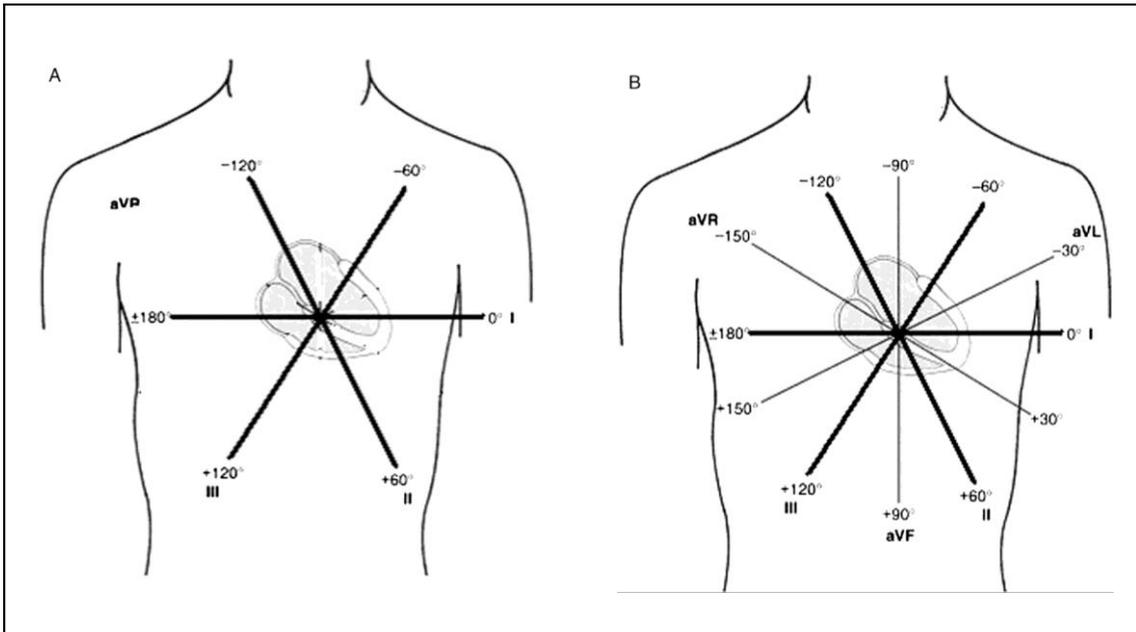


Figure 61. (A) Bipolar limb leads covering the frontal plane in 60° intervals. (B) The addition of the unipolar leads provided a more detailed coverage with 30° intervals.

1947

Gouaux and Ashman described for the first time, the phenomenon that would later be known as Ashman phenomenon.

The aberrant conduction may occur when a short cycle follows a long cycle (long-short sequence) because the refractory period of the branch varies with the extension of the cycle.

In 80% of the cases of aberration, there is CRBBB morphology, because the refractory period of the RB is longer than that of the LB.

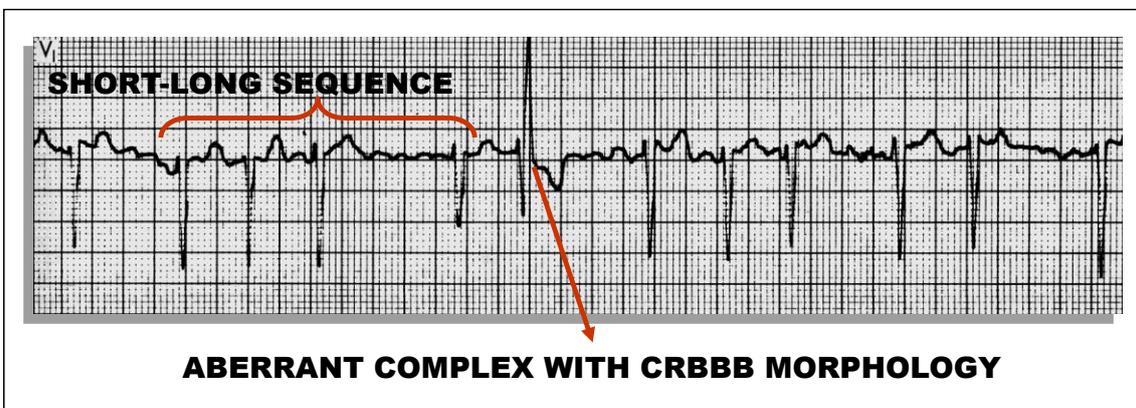


Figure 62.

1949



NORMAN HOLTER



CURRENT HOLTER MONITOR

Figure 63.

The Americans Maurice Sokolow and Thomas P. Lyon proposed an index for the diagnosis of LVE using only precordial leads (Sokolow and Lyon 1949).

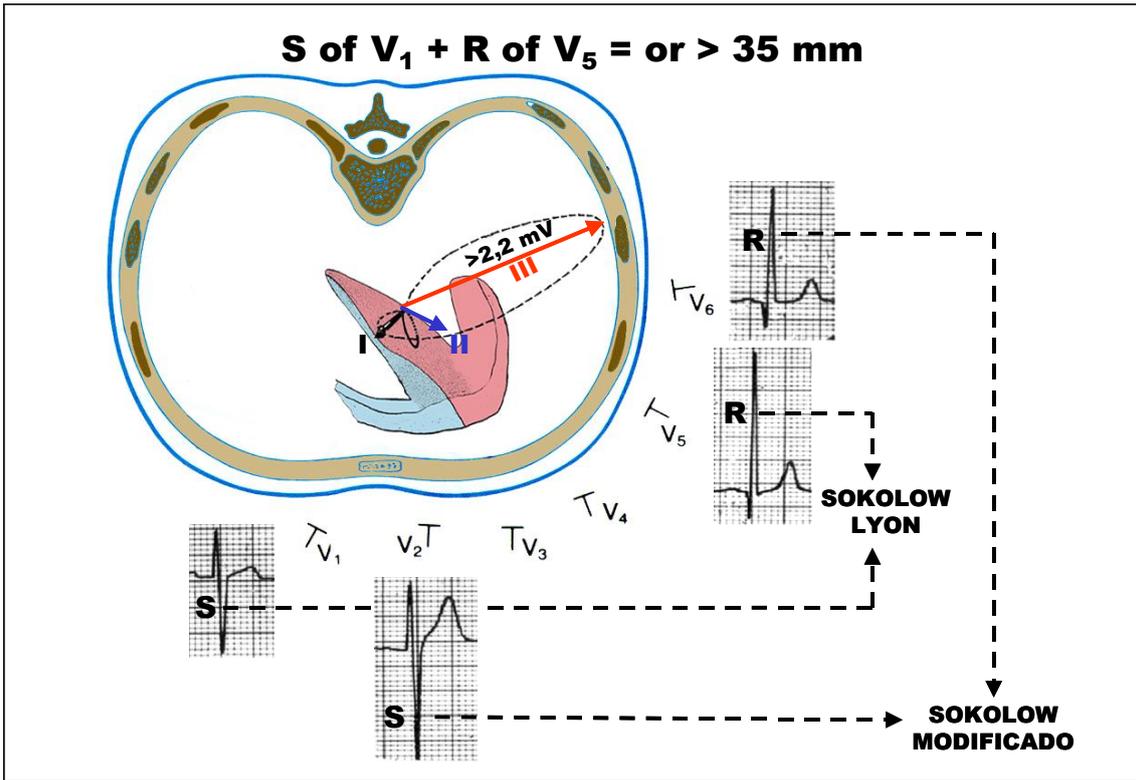


Figure 64.

1952

Cabrera and Monroy (Cabrera and Monroy 1952, Cabrera and Monroy 1952) introduce the concept of two hemodynamic modalities of LVE: systolic or of pressure and diastolic or of volume.

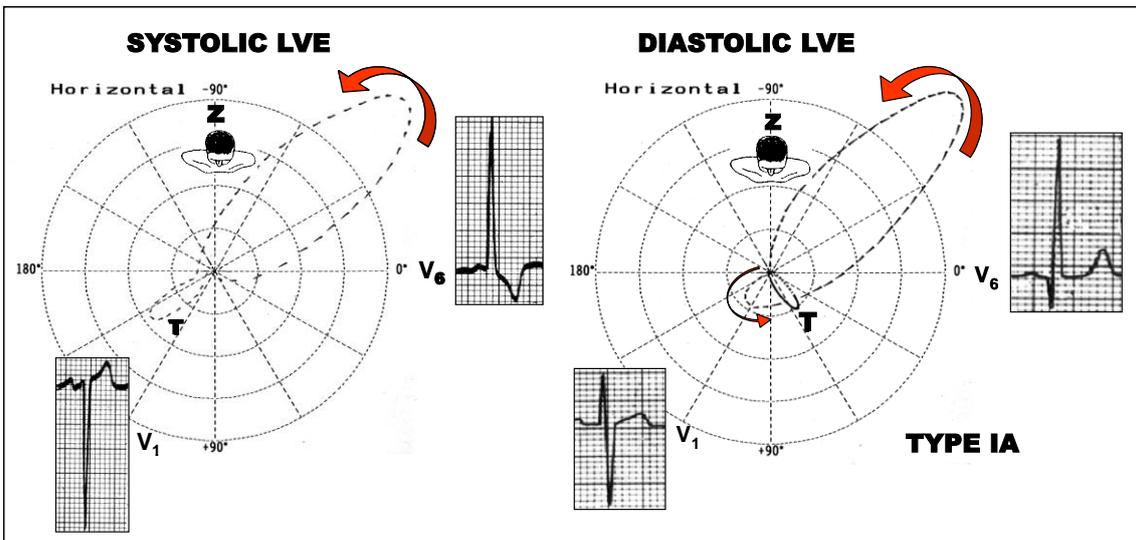


Figure 65. The two classical modalities of LVE.

1953

Osborn, experimentally in dogs, described the prominent J wave known as “Osborn wave”. Osborn interpreted that the J wave was caused by a lesion current caused by acidosis. This interpretation made him infuse bicarbonate (Osborn 1953). Other names: junctional wave, late δ wave, Osborn wave, camel-hump sign, hump-like deflection or lesion potential.



Figure 66. ECG tracing

1954

In this year, Richman & Wolff (Richman and Wolff 1954) identified for the first time the so called “*standard masquerading right bundle-branch block*”. In standard masquerading RBBB the presence of a high degree LAFB in association obscured totally or partially the diagnosis of RBBB only in the frontal plane by abolishing (or becomes very small) the final broad S wave in the leads I and aVL. Consequently, the limb leads may resemble LBBB although the precordial ECG remain typical for CRBBB.

The precordial leads reflect the feature of RBBB. The necessary conditions for the presence of standard masquerading RBBB are: high degree of LAFB + RBBB (bilateral bundle-branch lesions of considerable intensity, which do not completely disrupt the continuity of the branches) + severe left ventricular hypertrophy or marked biventricular hypertrophy + localized block in the left ventricle (frequent severe fibrosis, or truly massive myocardial infarction mainly in anterior wall).

Presumably, the intramural left ventricular block, together with the LVH or the LAFB, or both, produce predominant leftward forces which tend to cancel out the late rightward forces of the RBBB in the left precordial leads. In the next slide we show a typical example.

Example of “Standard Masquerading Right Bundle-branch Block”

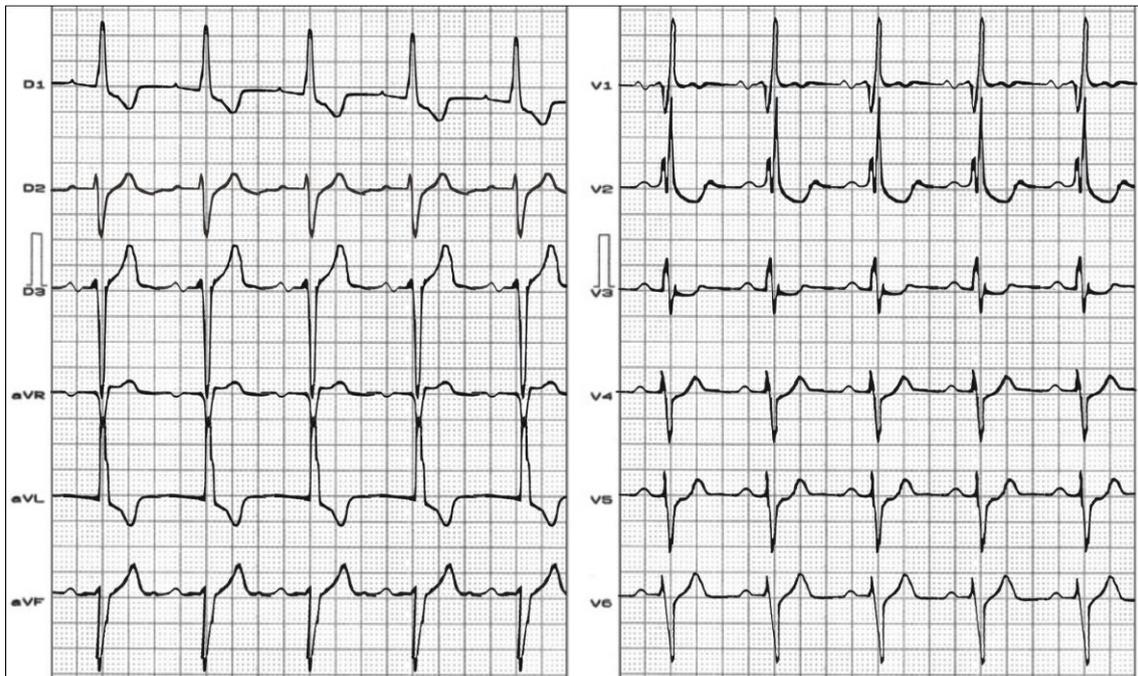


Figure 66. Extreme QRS left axis deviation ($\hat{S}QRS -50^\circ$), $S_{III} > S_{II}$: LAFB. The limb leads show a LBBB-like pattern, but the precordial leads show a RBBB. $S_{III} > 15\text{mm}$: Type IV Rosebaum LAFB: association of LAFB + LVE or LVH.

1956

Initial description of the concealed conduction phenomenon by Richard Langendorf and Pick (Langendorf and Pick 1956).

An interpolated premature ventricular contraction, partially and retrogradely penetrating into the AV node, causes a modification in the dromotropism of the junction, which makes the beat immediately following the PVC, to show PR interval prolongation.



Figure 67.

Ernest Frank, US engineer, proposed using 7 electrodes to minimize errors, 5 of them located in the 5th intercostal space (electrodes A, C, E, I, M), one in the left leg (F) and one in the nape (H). This is the system used currently in all the centers that perform VCG (Frank and Seiden 1956).

He uses the corrected orthogonal leads, which use the three planes of space: F, H and S. They are called orthogonal because they are perpendicular to each other and corrected because they use technical artifacts of resistance and multiple connections that correct the lack of homogeneity of the electrical field of the heart.

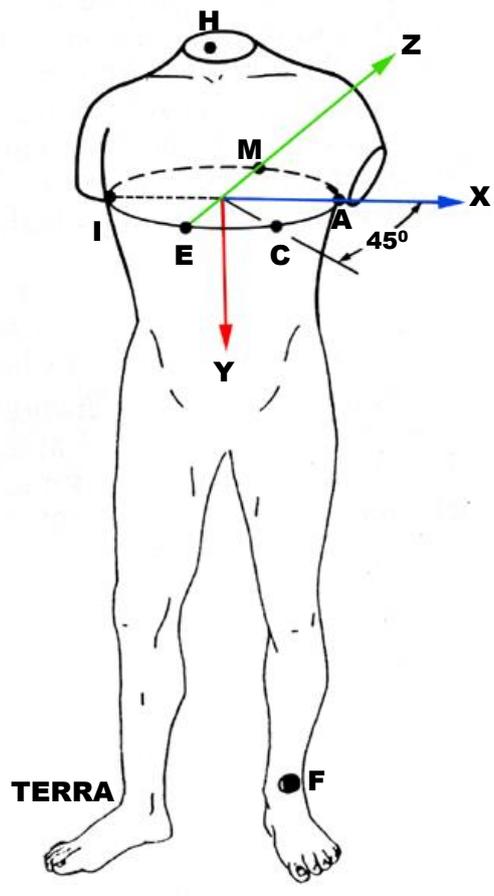
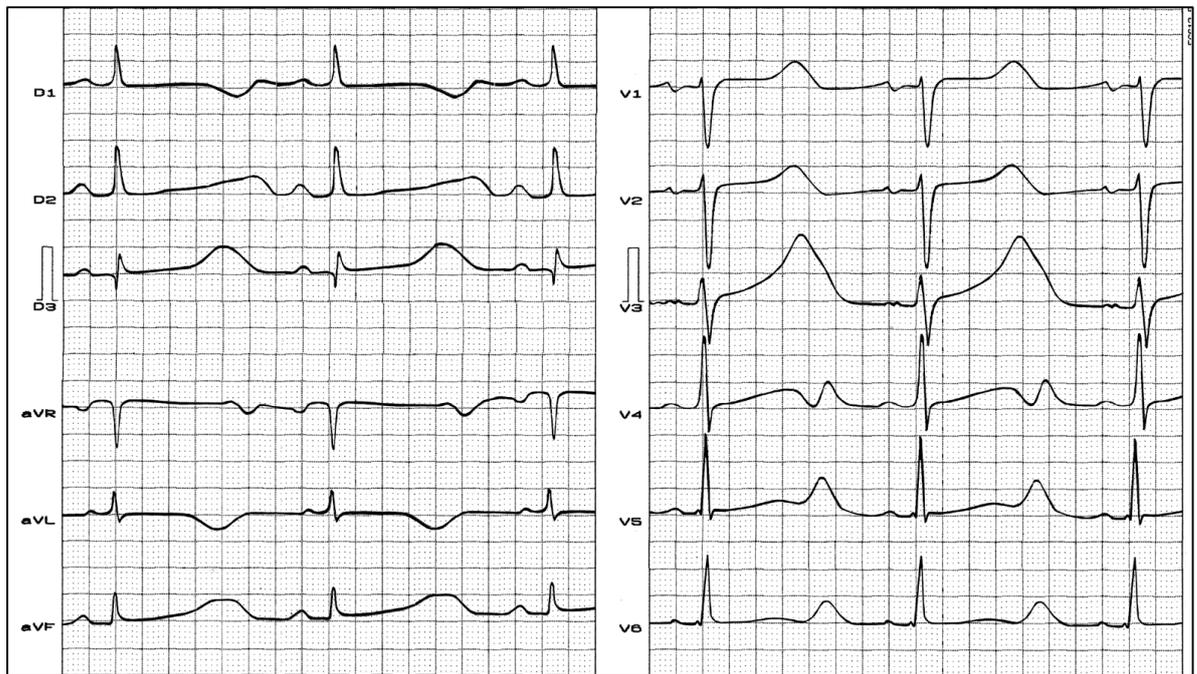


Figure 68. Location of electrodes by Frank's method.

1957

Anton Jervell and Fred Lange-Nielsen from Sweden identified the first family carrier of the LQTS syndrome: inherited, autosomal recessive, with central deafness

associated to long QT interval and sudden cardiac death (Jervell and Lange-Nielsen 1957).



1958

In this year, the Swedish engineer R. Elmqvist developed the first implantable pacemaker in a patient called Arne H.V. Larsson. The surgery was performed by A. Senning in October 8, 1958, at the Hospital of Karolinska, Stockholm, in Sweden. The patient died on December 28, 2001, with 86 years of age. He had a complete AV block.

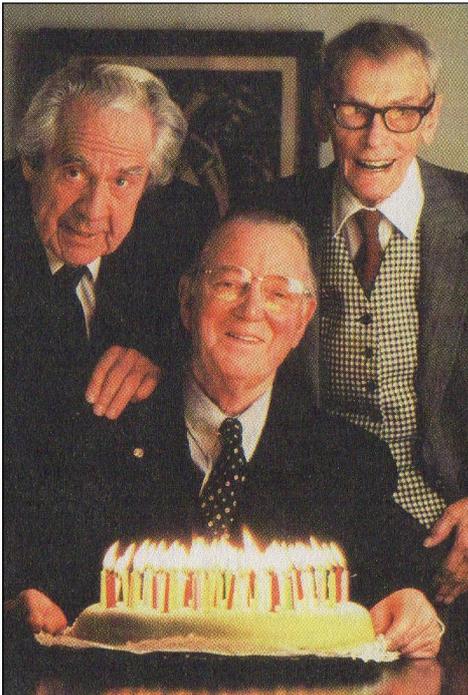


Figure 68. Arne H.W. Larsson (sitting) and the patient that received the first pacemaker. The picture shows the patient celebrating his 80th birthday, on May 26, 1995. At the left, the surgeon Dr. Senning and Rune Eimqvit, the engineer at the right.

1959

MYRON PRINZMETAL et al 1959 (Prinzmetal, Ekmekci et al. 1959, Prinzmetal, Kennamer et al. 1959), draw attention toward an unusual form of angina that they called variant, in which during the event there is ST segment elevation. The variant is attributed to subepicardial lesion, not related to stress, cyclic with a daily and hourly periodicity, and with a tendency to severe ventricular arrhythmias.

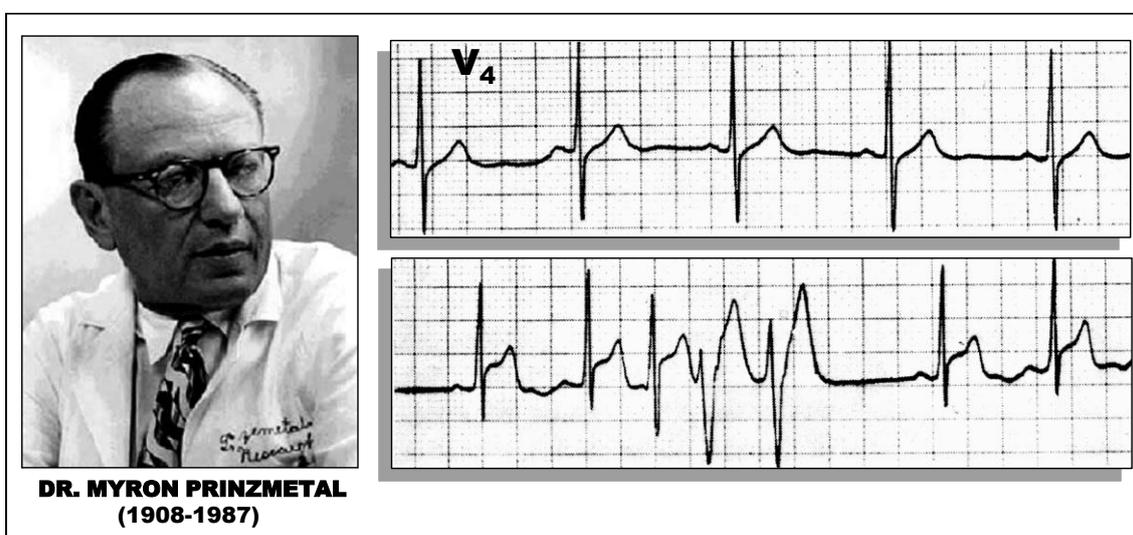


Figure 69.

João Tranchesi (JT), publishes the first modern book on electrocardiography printed in Brazil: *Eletrocardiograma Normal e Patológico – Noções de Vectorcardiografia*.

JT was the most outstanding electrocardiographer of the numerous Brazilian scholars that got their degree at the Instituto de Cardiologia Ignácio Chávez of Mexico, under the influence of the Mexican masters of electrocardiography as Demétrio, Sódipallares and Enrique Cabrera, who trained all of Brazil from north to south, in the Mexican school of electrocardiography.



JOÃO TRANCHESI
1922 - 1978

Figure 70.

JT was the most outstanding electrocardiographist of the numerous JT wrote four books on ECG-VCG:

- “Eletrocardiografia Vetorial”,
- “Eletrofisiologia Experimental”,
- “Exercícios de Interpretação” e
- “Eletrocardiograma Normal e Patológico – Noções de Vectorcardiografia”

This treatise had six editions in Portuguese, five in Spanish and two in Italian (Riera and Uchida 2010).

JOÃO TRANCHESI

Chefe do Serviço de Eletrocardiografia do Hospital das Clínicas
da Faculdade de Medicina da Universidade de São Paulo.

ELETCARDIOGRAMA NORMAL E PATOLÓGICO

NOÇÕES DE VECTORCARDIOGRAFIA

Com a Colaboração de:

Fúlvio Pileggi
Francisco Xavier Pinto Lima
Oswaldo Spiritus
Munir Ebaid
Eduardo Martins de Oliveira Rolim

Prelácio de
LUIZ V. DÉCOURT

FUNDO EDITORIAL PROCIENX
SÃO PAULO - 1962 - BRASIL

Figure 70. Prof. Tranchesi's book.

1960

Smirk and Palmer highlighted the high risk of degeneration into ventricular fibrillation that have short coupled premature ventricular contractions that occur above the T wave of the previous beat; the “R on T” phenomenon (Smirk and Palmer 1960). It is important to emphasize that in long QT syndromes, even though coupling may be telediastolic or long, QT prolongation causes appearance of the phenomenon.

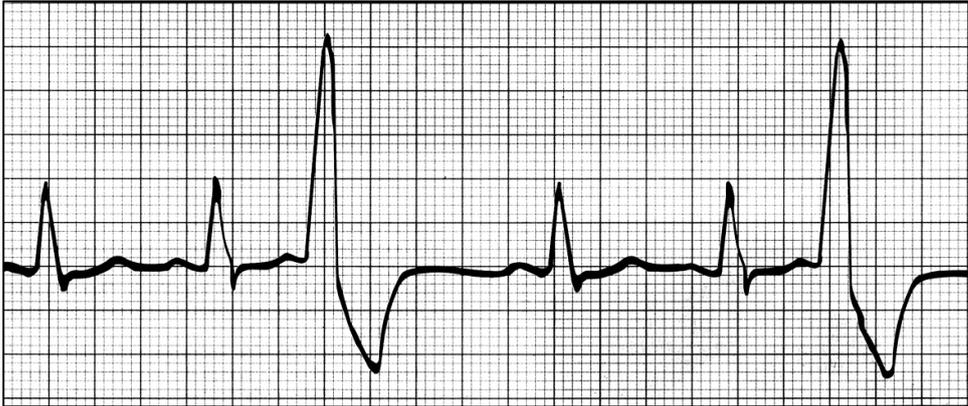


Figure 71.

1963

Robert Bruce et al, published a protocol called “Multistage Treadmill Exercise Test” to be implemented in stress test that came to be known by the eponym of Bruce protocol. The protocol is used nowadays in most ergometry labs. (Bruce and Hornsten 1969)

"You would never buy a used car without taking it out for a drive and seeing how the engine performed while it was running," Bruce says, "and the same is true for evaluating the function of the heart."

Mirowski M. et al 1963, describe the P wave in V₁ with the dome and dart P wave configuration, indicating left atrial rhythm. The initial portion of the P wave, rounded and with lower voltage, corresponds to left atrial activation, and the apiculate end caused by right atrium activation (RA).

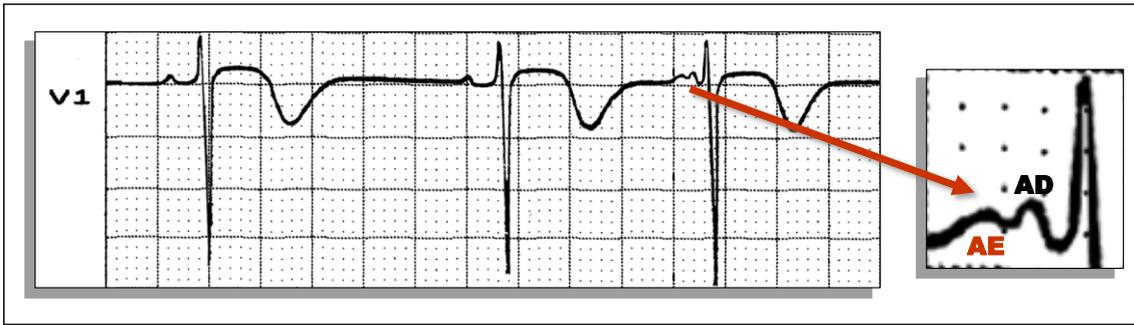


Figure 72.

1963/1964

Description of familial. autosomal dominant Romano-Ward long QT syndrome without deafness.

In Italy, Romano et al., described the autosomal dominant form without deafness, described with rare arrhythmia occurring at a pediatric age and leading to ventricular fibrillation (Romano, Gemme et al. 1963, Romano, Gemme et al. 1963).

Ward in Israel, independently from Romano, described in children, the same form without deafness (Ward 1964). Thus, it remains known as Romano-Ward syndrome, much more frequent than the form with deafness of Hervell and Lange-Nielsen.

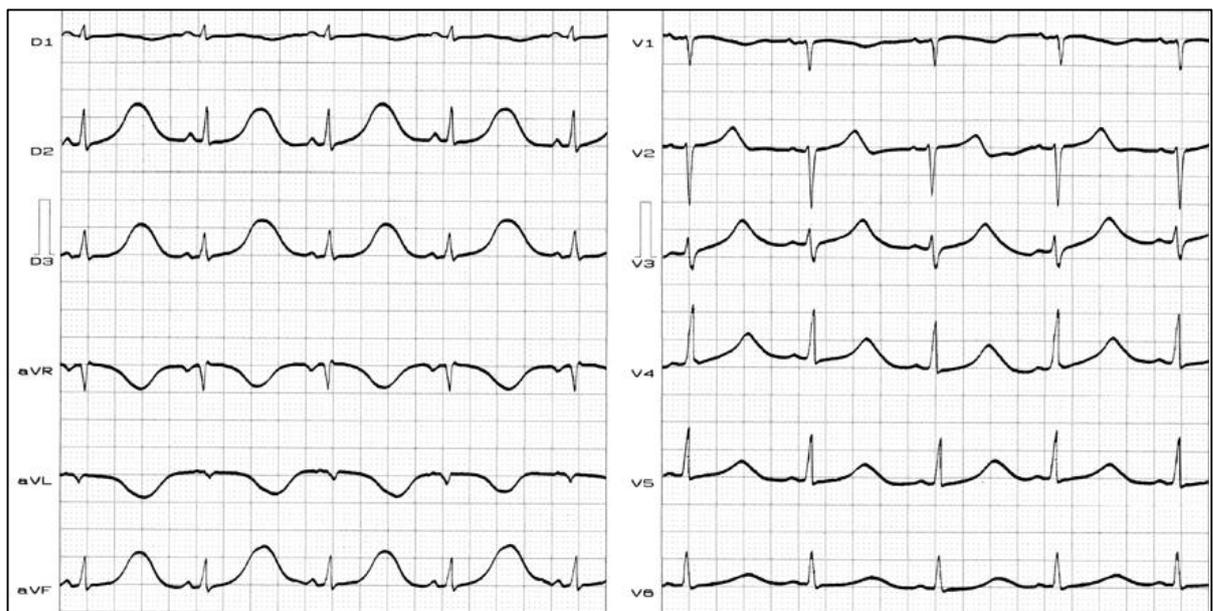


Figure 73.

1966

The Parisian François Dessertenne published the first case of polymorphic ventricular tachycardia with “Torsade de Pointes” (Dessertenne 1966). It is considered as the “cinderella” of arrhythmias.

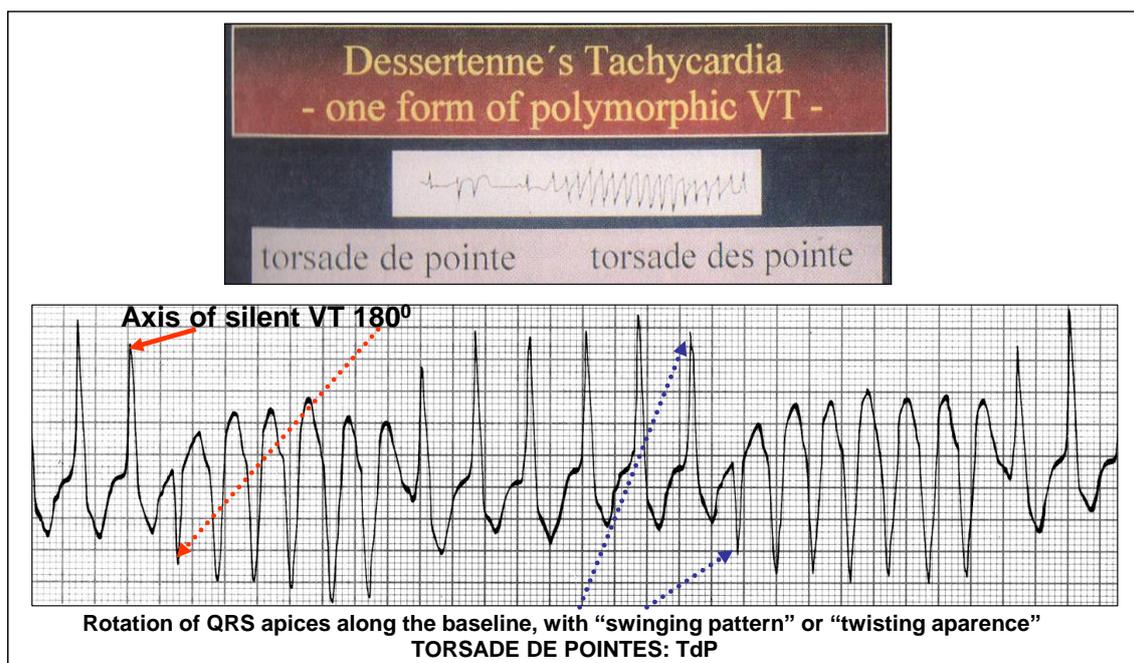


Figure 74.

1969

Mauricio B. Rosenbaum (Figure 75) from the Argentine school classifies premature ventricular contractions and characterizes the benign forms originating in the right ventricle. Thus, they are known as “Rosenbaum Ventricular Extrasystole” or healthy individuals extrasystoles (Rosenbaum 1969).

They are characterized by morphology of LBBB with SAQRS at the right.

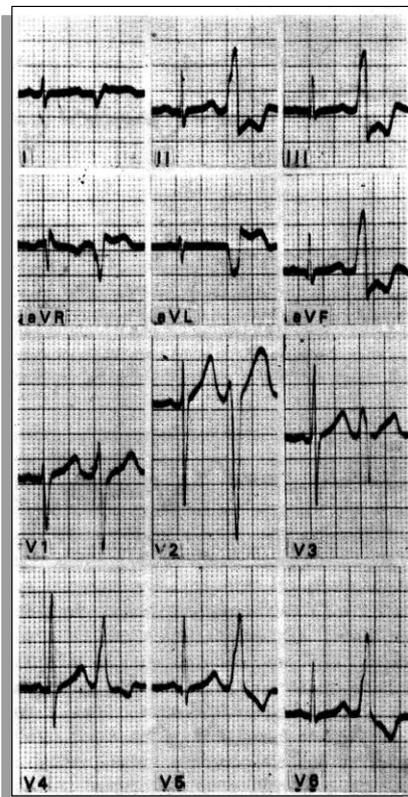
A subset is constituted by the so-called Wolffian premature ventricular contractions originating at the base of the right ventricle.



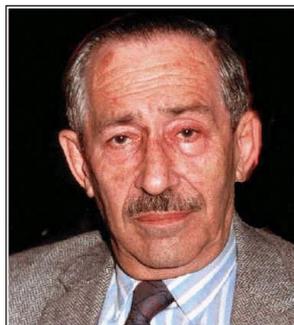
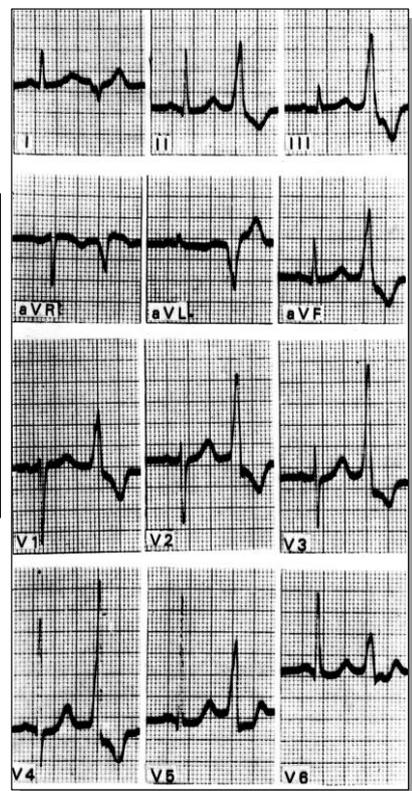
MAURICIO B. ROSENBAUM

Figure 75.

**PVC OF THE RV ANTERIOR
PAPILLARY MUSCLE**



**PVC OF THE RV BASE
OR WOLFFIAN**



**MAURICIO B.
ROSENBAUM**

Figure 76.

In this year, Dr. Kanu Chatterjee et al (Chatterjee, Harris et al. 1969) observed massive T-wave inversion and ST depression occurred in unpaced electrocardiograms of 31 patients after ventricular pacing, whether endocardial or epicardial, and were related to the power of the artificial electric stimulus and not to the presence of the electrode alone. They continued as long as pacing was continued but were always reversible.

They should not be mistaken for evidence of myocardial ischemia or underlying coronary artery disease. This phenomenon later (1982) was called “cardiac memory” by Rosenbaum school (Rosenbaum, Blanco et al. 1982).

Dr. Chatterjee was born in Bangladesh in 1934 and moved to Calcutta, India, as a refugee. He completed medical school at the R.G. Kar Medical College in Calcutta, India, while still living in a refugee camp, and moved to England in 1964 to complete his training in internal medicine and cardiology. At St. George’s Hospital. He was the first to describe post pacing T wave changes on the ECG, an effect that was later termed cardiac memory.

He moved to Los Angeles and worked with Drs. Jeremy Swan and William Ganz in Cedars Sinai Medical Center and described, along with his colleagues, the hemodynamic subsets of acute coronary syndrome and provided insights into hemodynamically guided drug therapy.



**DR. KANU CHATTERJEE
(1934-2015)**

Figure 77.

He was the first to report the beneficial effect of sodium nitroprusside in severe mitral regurgitation.

The major portion of Dr. Chatterjee's career was spent at the University of California in San Francisco, where he taught several generations of innovative, successful cardiologists who became national and international leaders in their field.

From 2001–2009 he directed the UCSF Chatterjee Center for Cardiac Research, named in his honor.

He moved to Iowa in 2009 with his wife, Docey Edwards Chatterjee, an Iowa native. At the University of Iowa, he continued his teaching, clinical work, and writing as the first UI Kanu and Docey Edwards Chatterjee Chair in Cardiovascular Medicine.

Dr. Chatterjee wrote more than 380 peer reviewed publications and 80 reviews and chapters relating to the management of patients with cardiovascular diseases and with the assistance of several Iowa colleagues, he edited the book *Cardiology – An Illustrated Textbook*. He received many teaching and achievement awards including the Gifted Teacher Award from the American College of Cardiology, and the Lifetime Achievement Award of the Heart Failure Society of America. In 2014, he received the Herrick Award, the highest honor in clinical cardiology available from the American Heart Association.

Kanu Chatterjee was a gifted physician, teacher, and researcher, admired and regarded with profound affection by his students, colleagues, and staff. Quiet, modest, and endlessly proud of the many young physicians he had inspired and trained, he changed the practice of cardiology in the world.

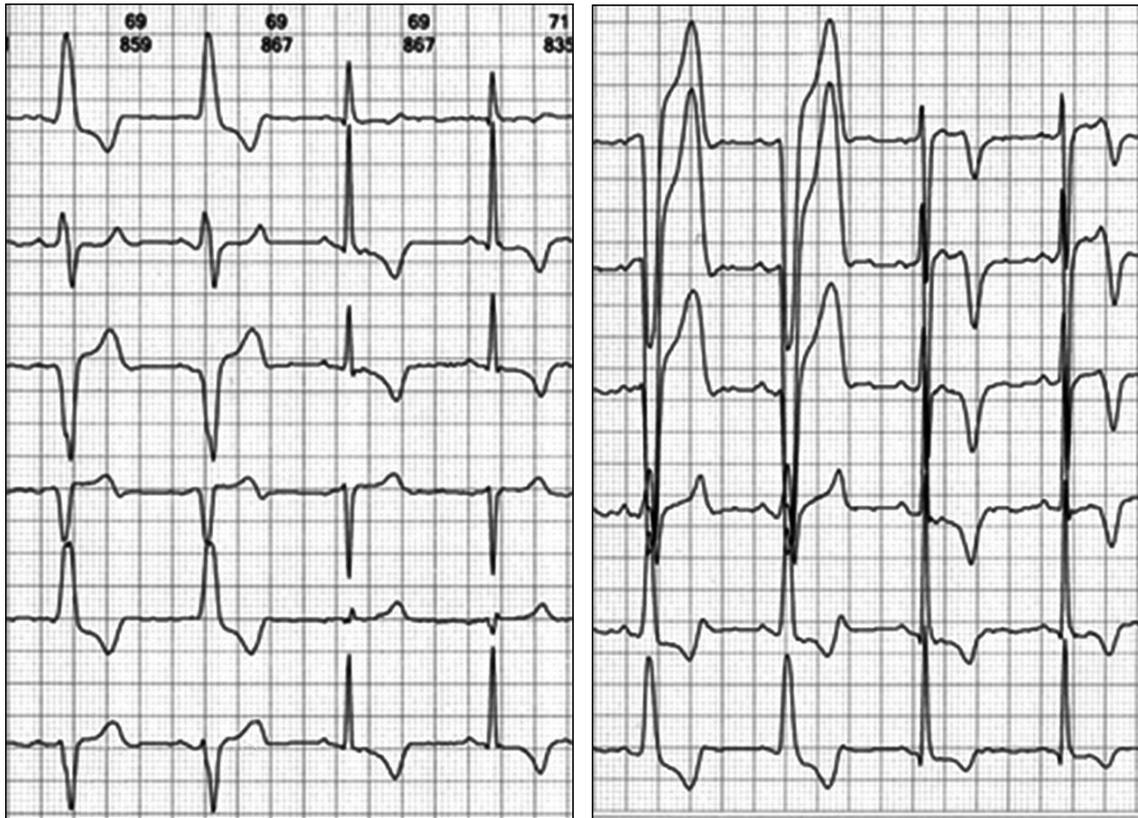


Figure 78. The secondary ST- and T-wave changes associated with transiently altered ventricular conduction such as those that occur with ectopic ventricular complexes or transient bundle-branch blocks (BBB) usually revert promptly to the pattern that existed before the ventricular conduction changes developed. However, some secondary repolarization changes take longer (hours or days) to develop and to dissipate. The repolarization changes associated with prolonged ventricular pacing, transient BBB, transient pre-excitation are examples of this phenomenon.

Dirk Durrer (1918-1984)

This investigator from the Netherlands proved in the human heart, that the initial activation occurs in 3 points and not 2, strengthening the concept of trifascularity of the left His system (Durrer, van Dam et al. 1970).



Figure 79.

1974

Gozensky and Thorne introduced the term “rabbit ear” to distinguish aberration ectopy in electrocardiography (Gozensky and Thorne 1974). The morphology in V1 that suggests ventricular origin or bad rabbit:

- Biphasic RR with R voltage in V1 lower than in R’;
- Monophasic

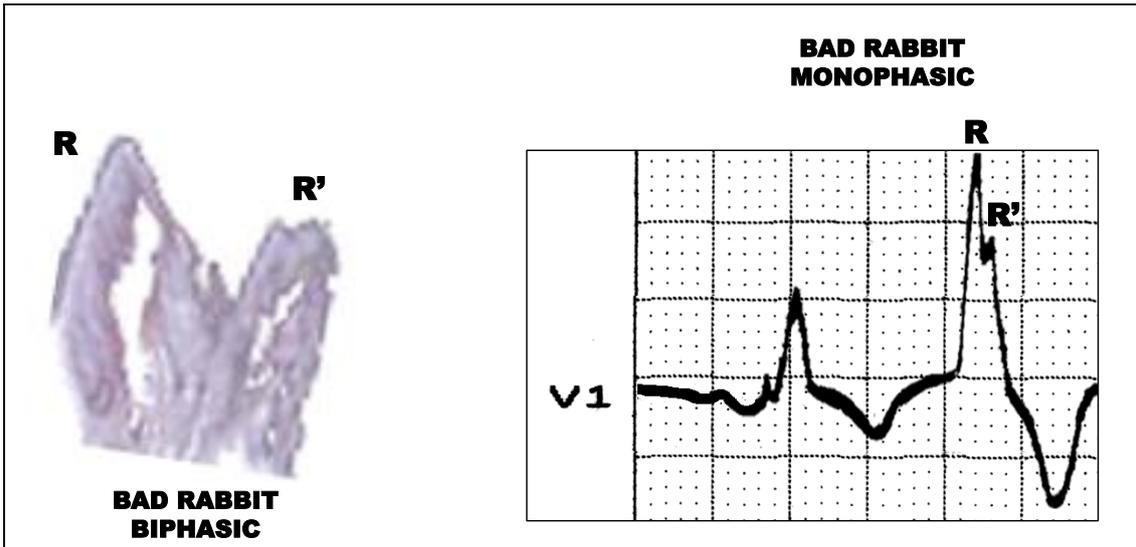


Figure 80. Morphology in V1 that suggests supraventricular origin; i.e. aberration or good rabbit: triphasic of the rSR' type.

1975

South African Prof. Leo Schamroth from the University of Witwatersrand describes the sign of “Dome and Dart QRS Complex configuration” (Schamroth L, 1975). Observed in complicated CLBBB with anterior or antero-lateral infarction in left leads.

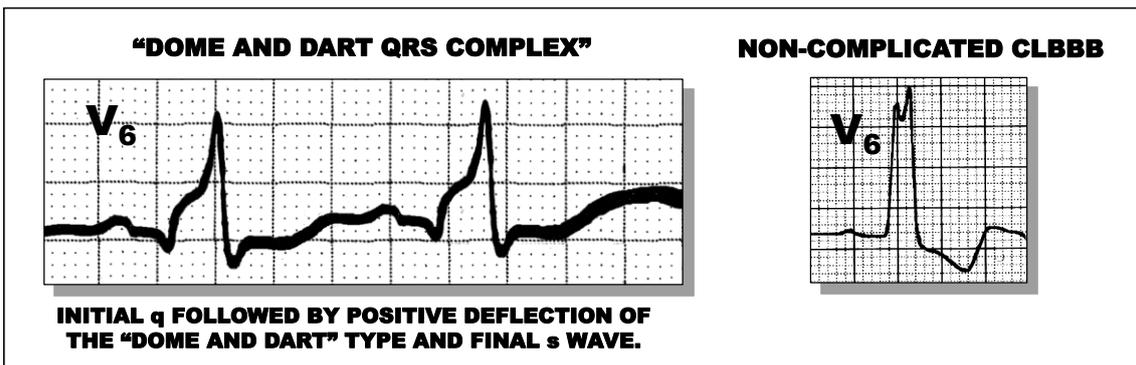


Figure 81.

1977

Professor Guy Fontaine was born in Corbeil Essonnes, a suburb of Paris. He is the son of a bank worker who was responsible for the department of international affairs. His primary school was in the city of Bordeaux, in a Loyola institution, and he moved to the secondary school at the Lycte Montesquieu in Bordeaux and then moved to Paris. During World II, he lived in the city of Orleans at the time his father was a prisoner of war. After the end of World War II he entered second school in Paris.

He works at the Hôpital Jean Rostand in Ivry, France, where he is co-director of the University Department of Clinical Electrophysiology. He has for the past 35 years, been continuously expanding the frontiers of electrophysiology. In 1976, he published **The Essential of Cardiac Pacing**, which was co-authored by his mentors and colleagues, Profs. Y Grosgeat and JJ Welti. Together with his talented and thoughtful surgical colleague, Dr G Guiraudon, Fontaine and his colleagues were the first Europeans to perform successful surgical treatment of an accessory pathway. Fontaine and his associate, Dr. Robert Frank, perfected the technique of epicardial mapping, which permitted them to obtain the first recordings of epicardial delayed potentials in humans. His work led to the discovery of “**arrhythmogenic right ventricular dysplasia**” which resulted in the publication of some of the first clinical descriptions of this conditions (Fontaine G, 1977).



Figure 82. Dr Guy Fontaine discovered and named the ϵ waves Hopital de la Salpêtrière, Université Pierre et Marie Curie, Paris Cardiologie, Electrophysiologie

cardiaque, Cardiomyopathies. Fontaine discovered and named the ϵ wave. He chose the ϵ because it follows δ in the Greek alphabet

1978

In this year the transesophageal procedure of stimulation is published for the first time by the second department of medicine of Landeskrankenhaus Klagenfurt – Austria by Heinz Sterz et al, “Transesophageal rapid stimulation of the left atrium in atrial tachycardias”, via esophageal stimulation with catheter.

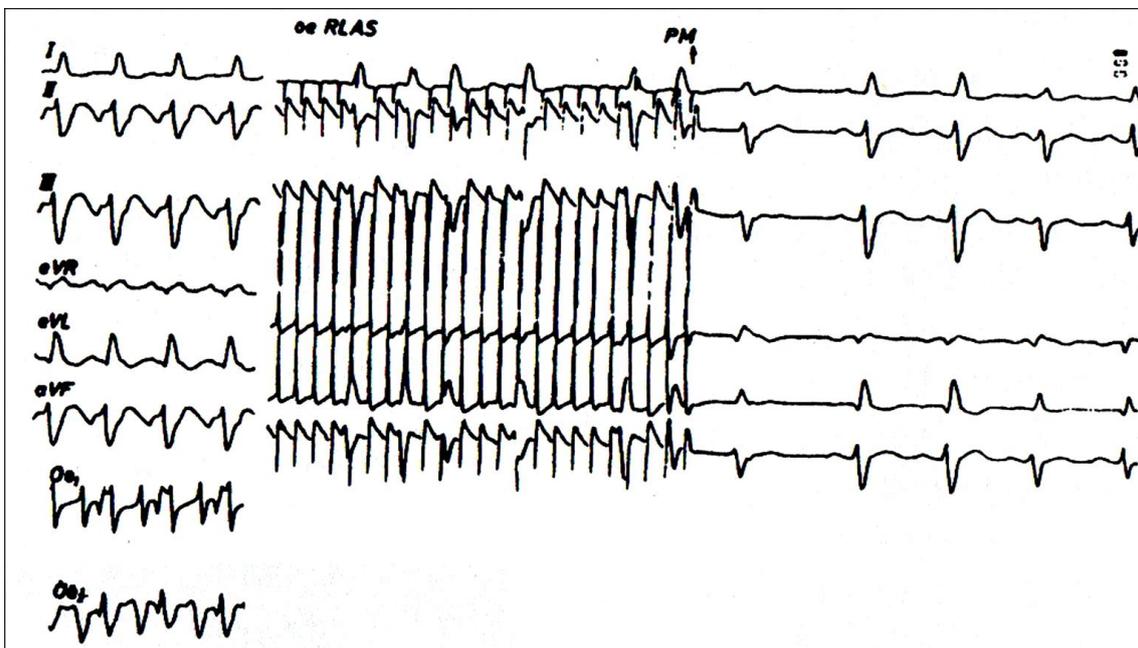


Figure 83.

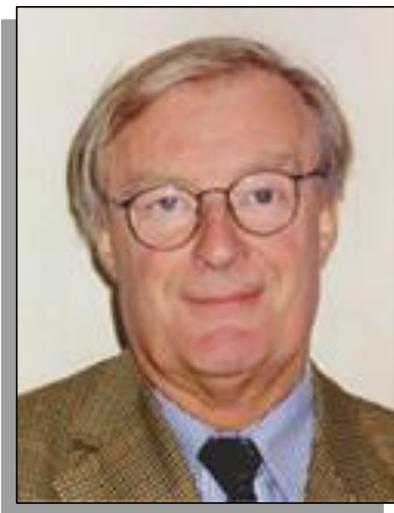
1982 Henrick Joan Joost Wellens

Dr. de Zwaan from the University of Limburg in Maastricht described a syndrome (de Zwaan, Bar et al. 1982) that came to be known with the eponym “Wellens’ Syndrome”, that indicates proximal critical lesion in the anterior descending artery, characterized by:

- Plus-minus T wave with inversion of the final portion (Type 1)

- Deeply inverted T wave in V1 and V2 (type 2);
- ST segment with no elevation or discretely elevated;
- Absence of the loss of voltage in the R wave;
- Normal or discretely elevated enzymes.

When not identified or poorly treated, it quickly leads in 8.5 days to anterior infarction. These patients should never go to previous ergometer test and yes directly to coronary angiography.



HEIN J.J. WELLENS

Figure 84. Dr. Wellens portrait.

Wellens Wellens Syndrome Type 1

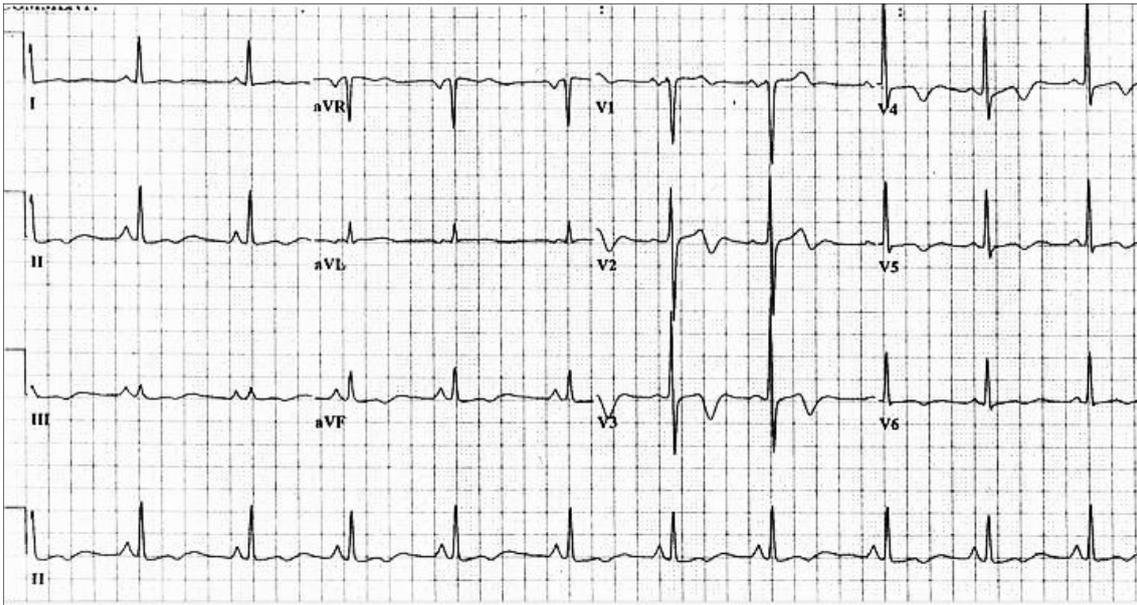


Figure 85.

Wellens Wellens Syndrome Type 2

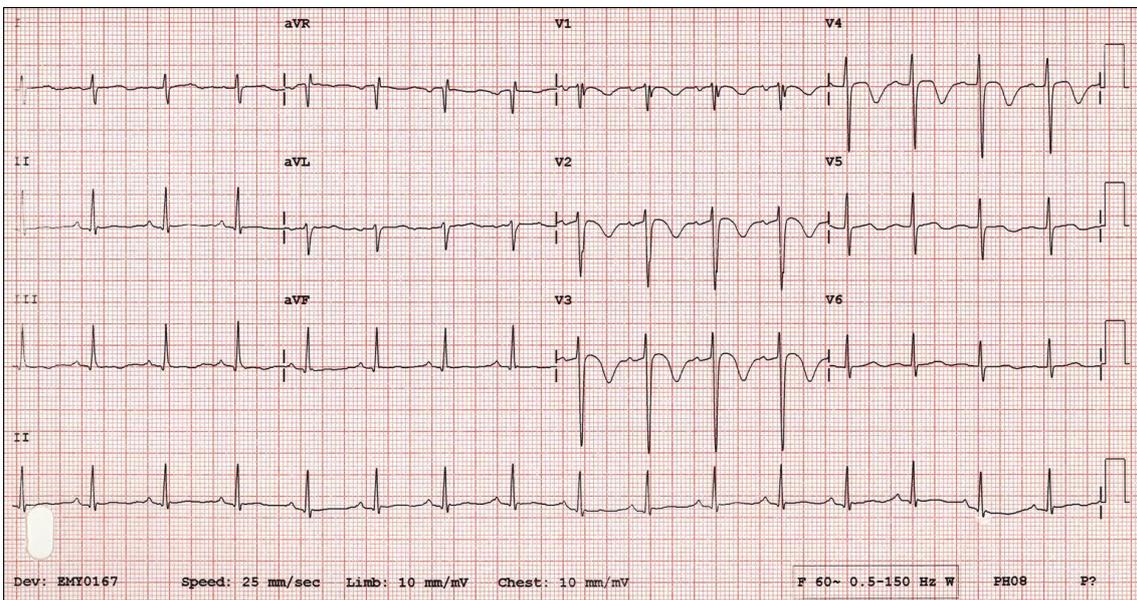


Figure 86.

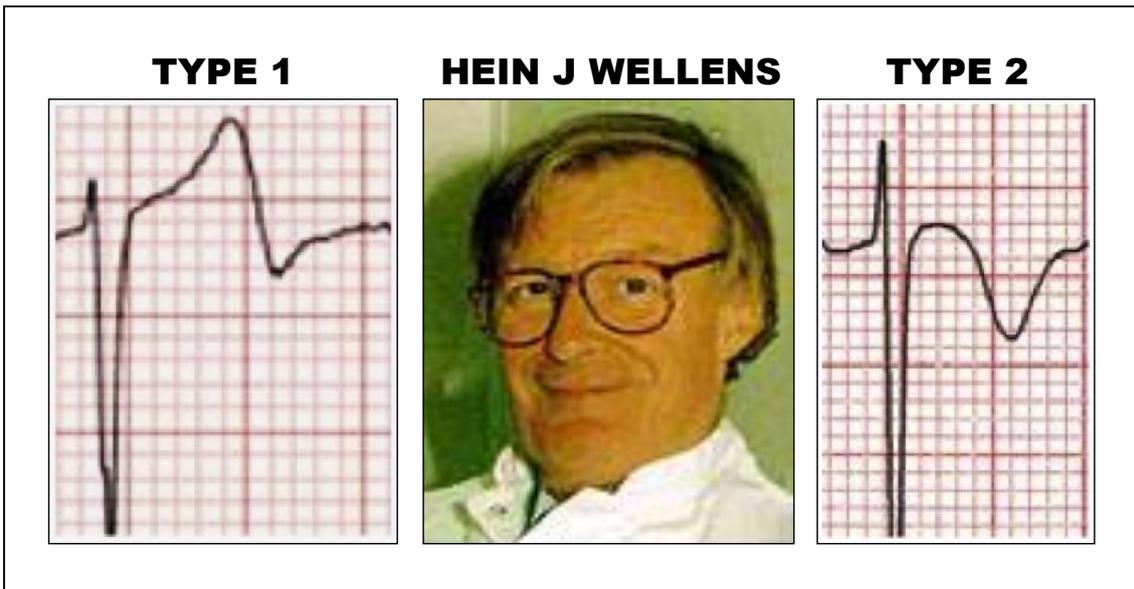


Figure 87.

1988

The following discoveries can be attributed to this investigator and his school of the Masonic Medical Research Laboratory in Utica, NY:

- Mechanism of reentry in phase 2 as trigger of VT/VF;
- Demonstration of electrical heterogeneity in ventricular myocardial thickness;
- Outline of the ion and cellular bases of LQTS and Brugada syndrome;
- Understanding the ion bases of the J and T waves of ECG (Litovsky and Antzelevitch 1988).



CHARLES ANTZELEVITCH

Figure 88.

1992

At the end of the 20th Century, the old technology of ECG, with more than a century of existence, was still capable of enabling the discovery of a new clinical-cardiological entity. The brilliant observation of the Spanish brothers Pedro and Josep Brugada allowed detecting in patients with structural heart disease and with a high tendency to sudden cardiac death, the characteristic ECG. Brugada syndrome was the last clinical-cardiological entity identified at the end of the 20th century (Brugada and Brugada 1992).



Figure 89.

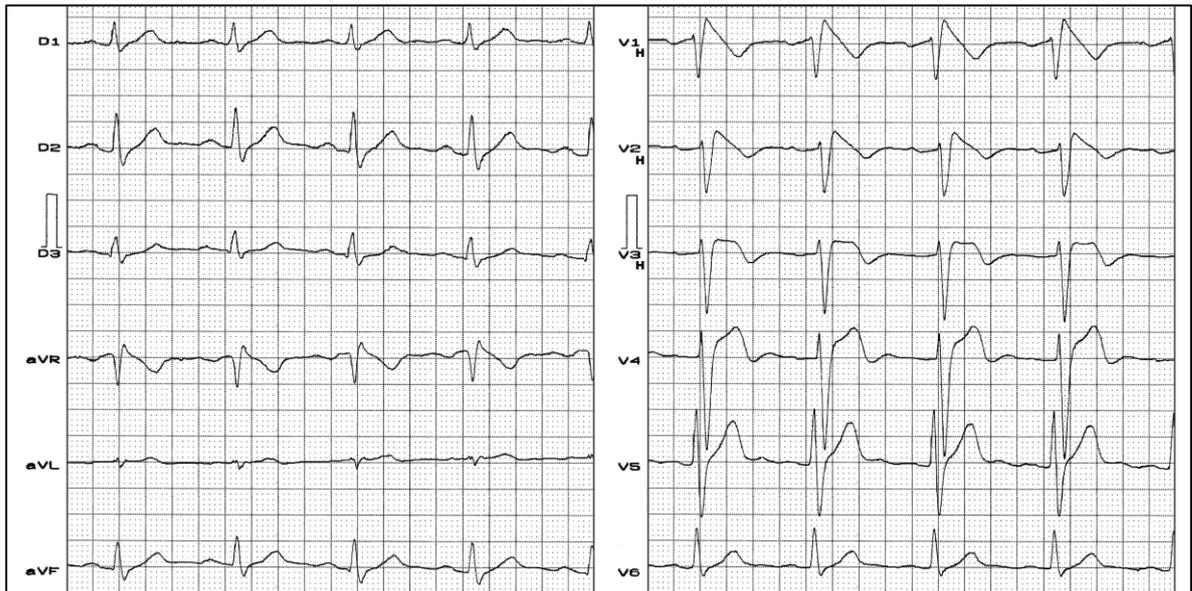


Figure 90. Brugada type 1 ECG pattern

1993

Robert Zalenski et al, professor of the Wayne State University of Detroit, published the influence on the diagnostic sensibility of ACS and MI with the routine use of ECG with 15 leads: the conventional 12 and V_{4R}, V₈ and V₉ (Zalenski, Cooke et al. 1993).



PROF. ROBERT ZALENSKI

Figure 91.

1996

Anton Lukas, performs the initial description of the reentry mechanism in phase 2 as trigger of VT/VF, working as a scientific investigator at the Masonic Medical Research Laboratory and as Associated Prof. at the Department of Physiology of the University of Manitoba, Canada (Lukas and Antzelevitch 1996) (Lukas and Antzelevitch 1989) (Lukas and Antzelevitch 1993).



ANTON LUKAS

Figure 92.

1997

Ramón Brugada et al 1997 (Brugada, Tapscott et al. 1997), identified the first locus of familial AF in chromosome 10q22-24 in three different Spanish families, that later expanded into six, with a total of 132 individuals.



RAMÓN BRUGADA, MD, PhD

Figure 93.

1998

Professor Wellens and his team developed for the first time an implantable atrial defibrillator for the treatment of atrial fibrillation. He was fairly awarded as pioneer of cardiac pacemakers in 1995 and as Distinguished Professor (2000) by the North American Society of Pacing and Electrophysiology (Wellens, Lau et al. 1998).

2000

Issues facing electrocardiography in the year 2000 include a shortage of experienced electrocardiographers, the advent of new noninvasive procedures and, paradoxically, the widespread acceptance by the medical profession.

The shortage of properly trained electrocardiographers in an old issue dating back to the early days of electrocardiography. Carl J. Wiggers, in the preface to his text “Principles and Practice of Electrocardiography” published in 1919, stated “unfortunately, the training of medical manpower in the use of such apparatus and the intelligent interpretation of the electrocardiogram has not kept pace with the increased demand. Few courses in electrocardiography are included in undergraduate and

postgraduate curricula in medical schools, so that opportunity for systematic instruction is decidedly restricted” (Wiggers CJ, 1929).

The issue of manpower addressed by Wiggers 80 years ago is still with us. The widespread use of the ECG is equated by many with ease of interpretation and lack of sophistication, thus, relegating interpretation to individuals with limited experience. The large volume of tracings and the shortage of properly trained personnel stimulate a search for alternate approaches to interpretation, processing, storage and retrieval of the ECG. The computer is suggested as a partial answer. The computer is useful for epidemiologic and large-scale clinical trials. However, its role in analyses of the clinical ECG is limited.

The computer programs, while reasonably reliable for the analysis of the normal ECG and some ECG waveforms, has serious limitation when applied to arrhythmias. The programs lack accuracy and reproducibility. The early hopes for “stand alone” programs are yet to be realized. Clinical ECGs must be overread by trained electrocardiographers. In fact, I would suggest that because of the availability of computer interpretation, the intellectual processes necessary to arrive at an ECG diagnosis are often circumvented and the computer may be, in fact, an obstacle to the acquisition of ECG skills.

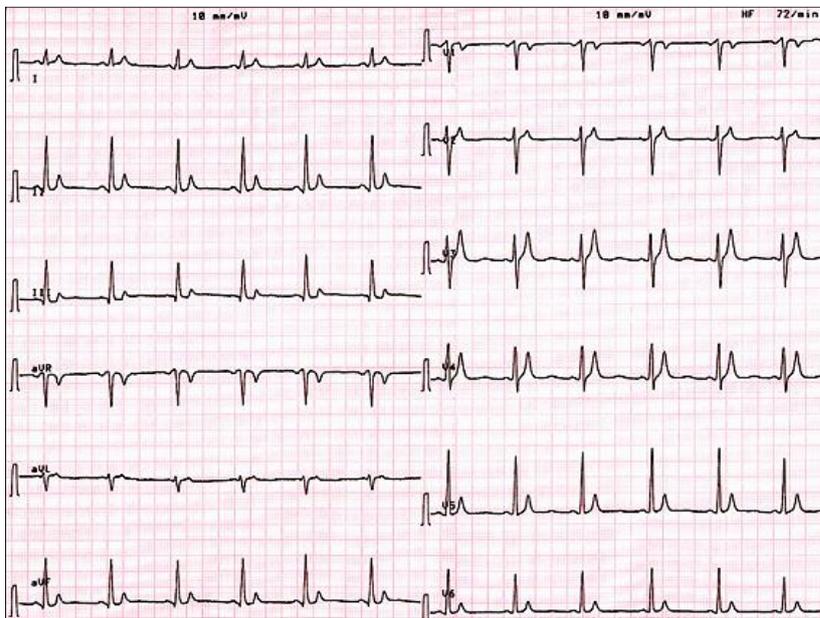
Not all ECGs can be programmed because of their complexity. Despite the problems faced by electrocardiography in the year 2000, until a better method of noninvasive recording of electrical behavior is developed, the future of this discipline is assured.

There is renewed interest in arrhythmias, stimulated by an increased use and increased complexity of cardiac pacemakers, by implantable cardioverters and defibrillators, heart surgery, the ever-present problem of sudden death, the search for new antiarrhythmic drugs, new approaches to the surgical therapy of arrhythmias, ambulatory monitoring, telemetry, heart rate analysis, T-wave alternans and the like. Similarly, new and aggressive approaches to ischemic heart disease rekindled interest in the ECG as an anatomic, qualitative and occasionally quantitative marker of myocardial ischemia, injury and infarction—an important first step in decision-making (Autenrieth, Surawicz et al. 1975).

It is proper to conclude that 117 years after its introduction, the ECG fulfills Webster's definition of a classic. It is of recognized value, serves as a standard of excellence and is traditional, enduring and in fashion year after year (Burchell 1987).

Prof. Ihor Gussak MD, PhD, FACC, et al., described a new form of the congenital short QT syndrome, associated to syncope, paroxysmal atrial fibrillation and sudden cardiac death.

Years later, three genetic forms were identified: SQT1, SQT2 and SQT3 (Gussak, Brugada et al. 2000).



PROF. IHOR GUSSAK MD, PHD, FACC

Figure 94.

2000

The 7th edition of the classical Tranchesi's book is published in Brazil, where important modifications are included in regard to the six first editions.

The book was written by JT's most brilliant disciple, Prof. Paulo Jorge Moffa, with Dr. Paulo César R. Sanches as co-author.



PROF. PAULO JORGE MOFFA

Figure 95. Undoubtedly, Moffa is the greatest living authority –maybe in the world– on the “secrets” of vectorcardiography.

0

2001

The XXVIII Congresso Internacional de Eletrocardiologia is held for the first time in Brazil, in June, in the city of Guarujá SP, at the Hotel Casa Grande. The event had participants from 20 different countries (60 international and 120 national) and it exceeded the average of previous Congresses. We could show the scientific strength and union of Brazilian colleagues devoted to Electrocardiology. The Congress was organized by the International Society of Electrocardiology and the Chair of the event was Carlos Alberto Pastore.



CARLOS ALBERTO PASTORE, MD, PhD

Figure 96.

2002

In this year, the centennial of the first publication by Einthoven on ECG was celebrated (Shalij MJ et al, 1902), thus this year was considered the centennial of Einthoven's ECG (Kligfield 2002). Michael R. Rosen from the Pharmacology Department of the "College of Physicians and Surgeons of Columbia University, New York", wrote two papers on the 100 years of ECG and the contribution of the method to the knowledge of the molecular signaling pathways (Rosen 2002) (Rosen 2002).

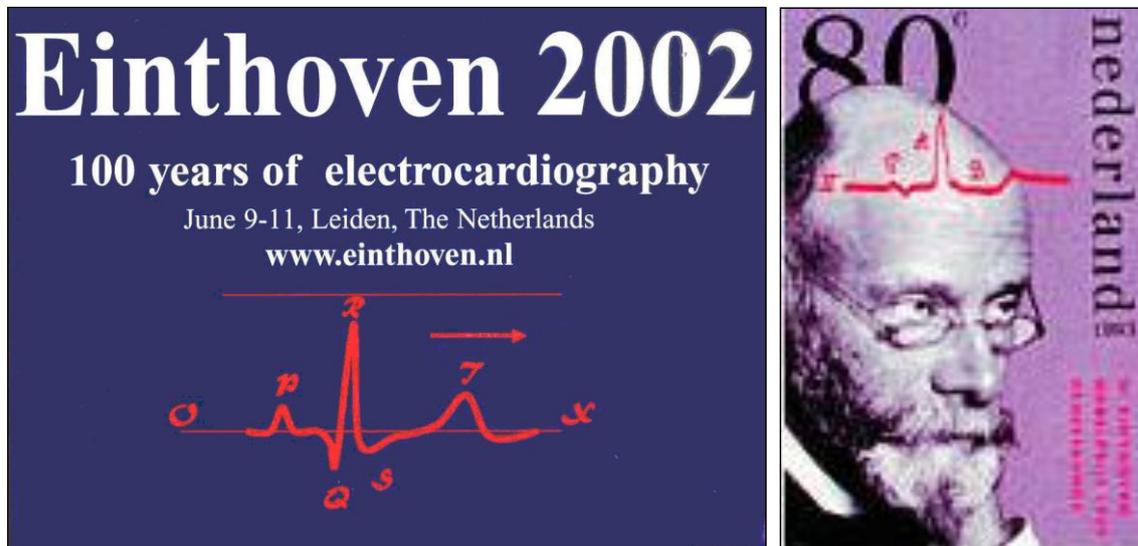


Figure 97.

2004

In this year, Prof. Wellens from Maastricht, the Netherlands, writes a historical paper titled: "**The Electrocardiogram 102 Years after Einthoven**" where he concludes: "that remain essential, therefore, to stress that both old and new ECG knowledge should be in the core curriculum of every cardiologist, not only during his or her training, but especially also during postgraduate education" (Wellens and Gorgels 2004).



Figure 98.

2005

Danish cardiologists, lead by Dr. Peter Clemmensen, showed that using ECG transmitted wireless at a distance, from an ambulance to the portable PC of a cardiologist, may enable an immediate decision making a referral to the hemodynamic lab, saving precious minutes that may make a difference between life and death (Clemmensen, Sejersten et al. 2005).



DR. PETER CLEMMENSEN

Figure 99.

Pérez Riera et al (Perez Riera, Ferreira et al. 2005), published the first case in Latin America, of Congenital Short QT Syndrome.

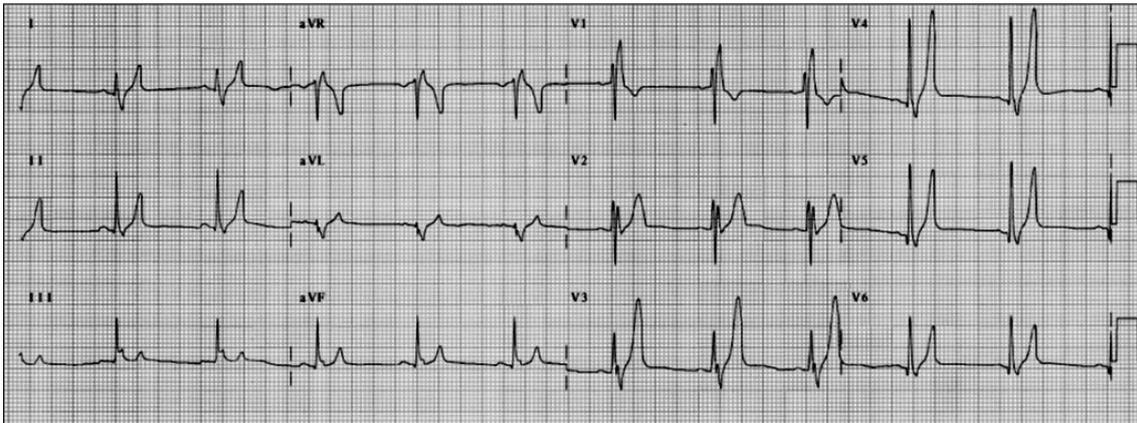


Figure 100.

Pérez Riera et al, show the first VCG of Brugada syndrome.

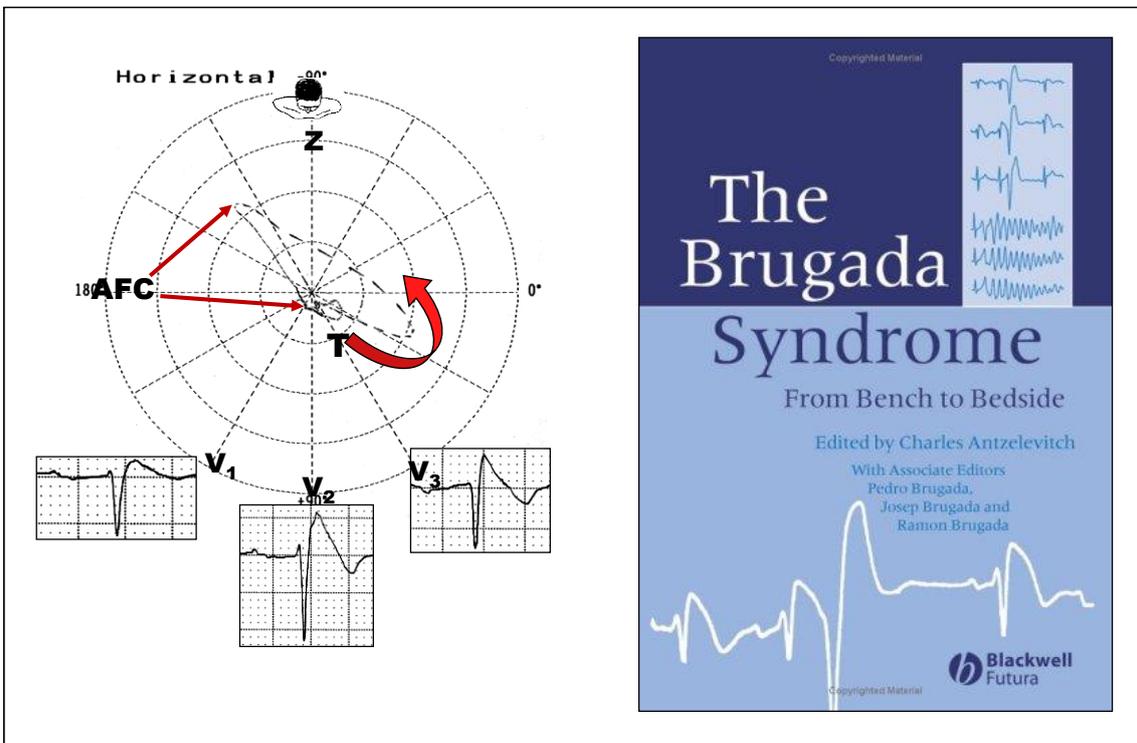


Figure 101.

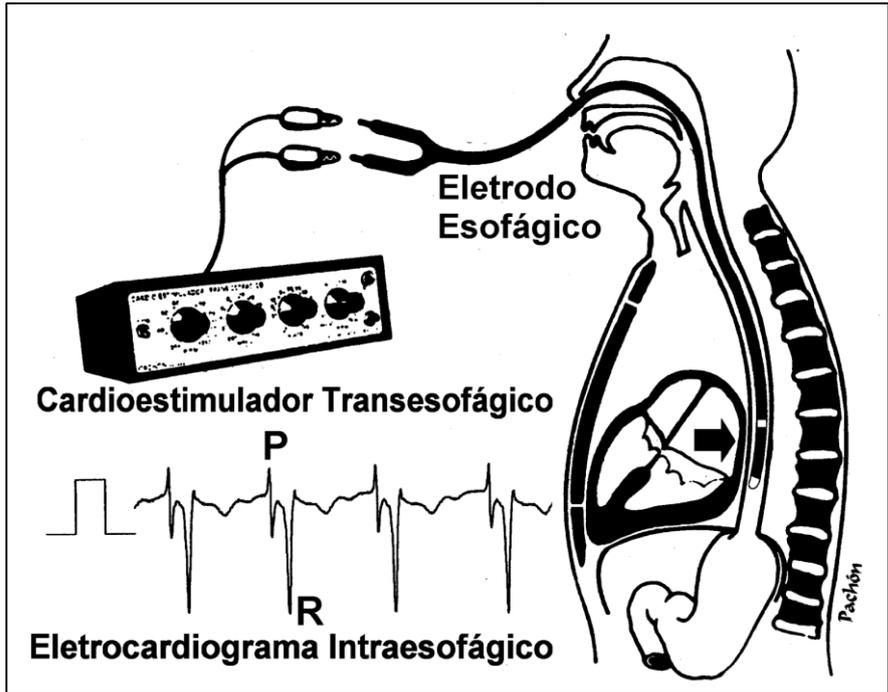


Figure 102. Transesophageal electrophysiology study or transesophageal cardiostimulation (TECS*)

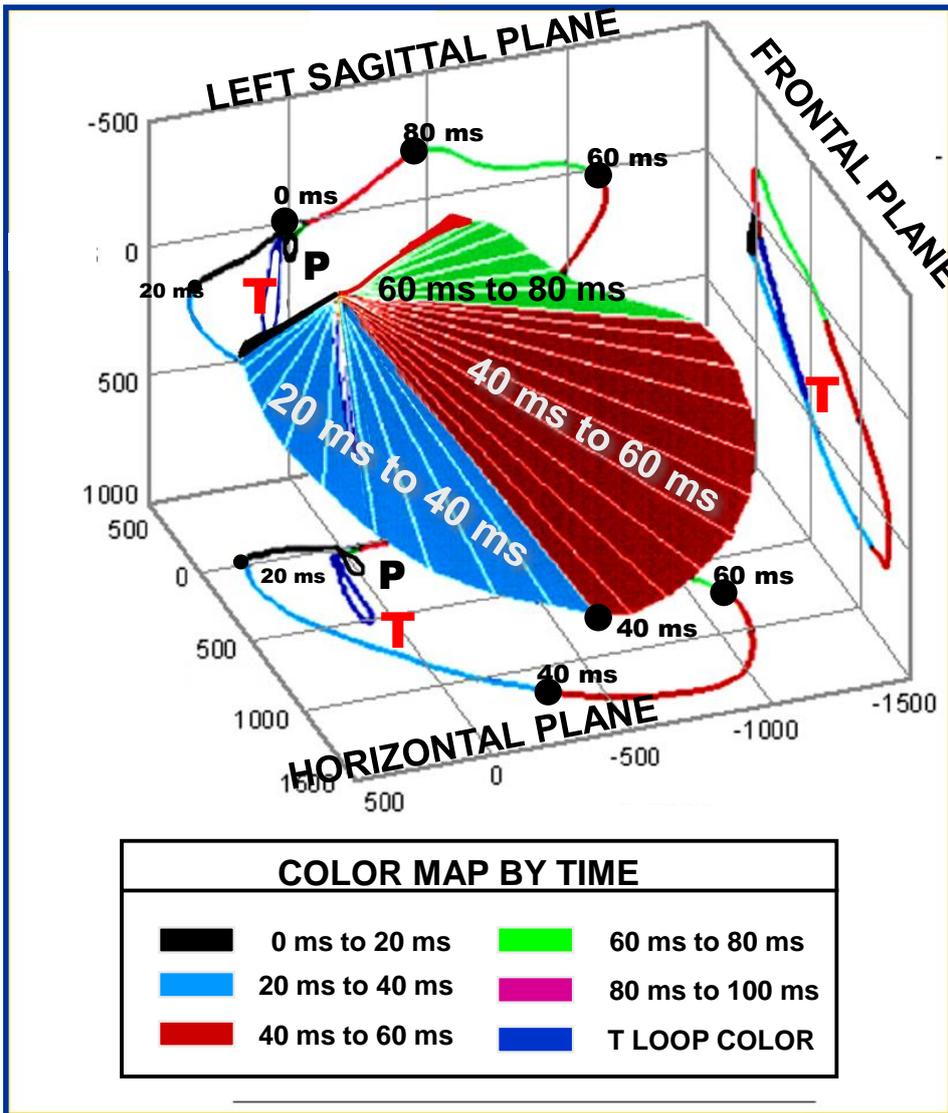


Figure 103. Vectorcardiogram



Figure 104.



Figure 105. The tests of pulmonary function measure the capacity of the lungs to expand, the ease with which air comes in and out of lungs through the airways, and the

ability of the lungs to transfer oxygen into blood and to remove carbon dioxide from the organism. There are different tests of pulmonary function; the most common ones are described below.

Spirometry is a test that measures the amount of air that comes in and out of the lungs.

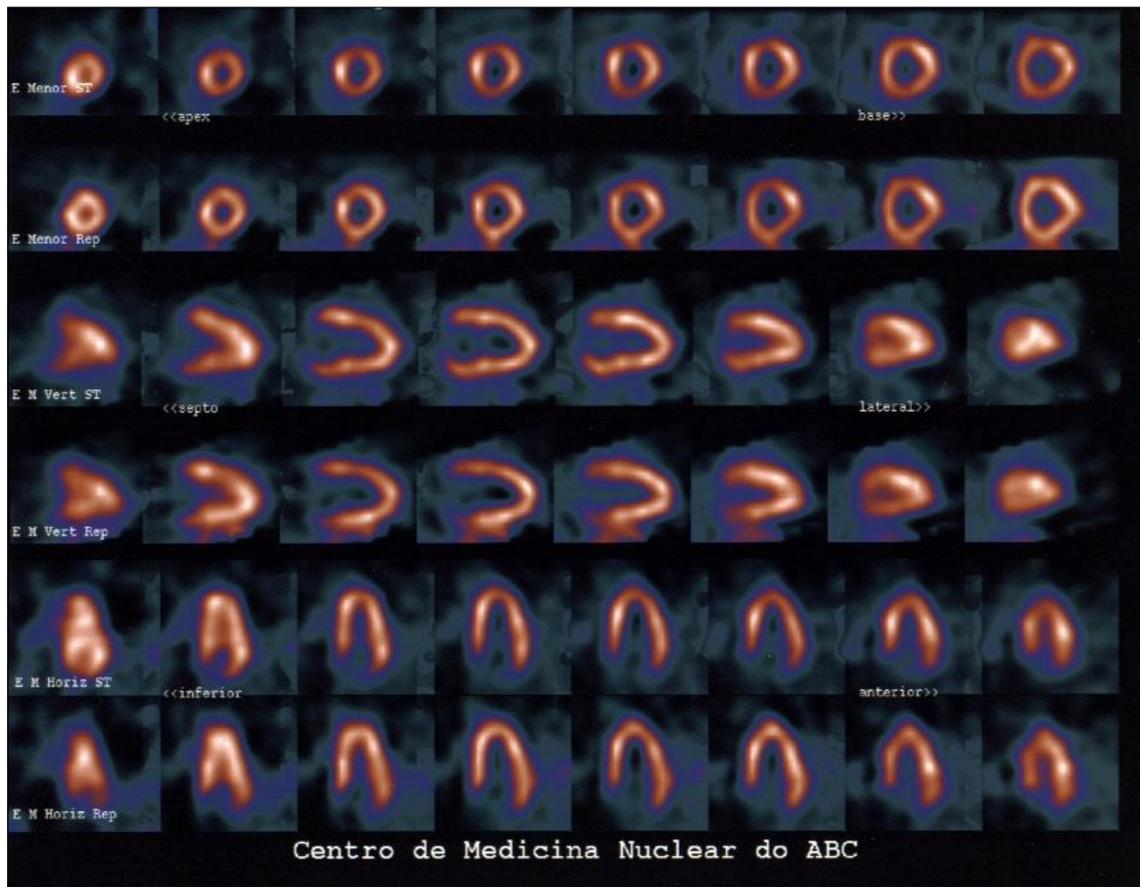


Figure 106. Stress test associated to scintigraphy.

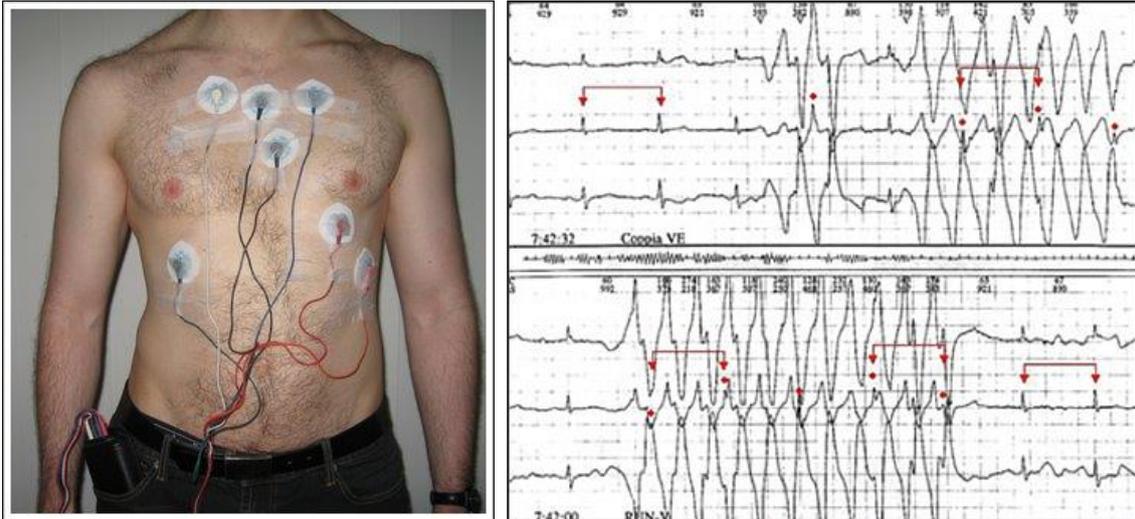


Figure 107. Long-duration ECG or Holter system. Monitor of symptomatic events, graphic recording of events, looping memory system.

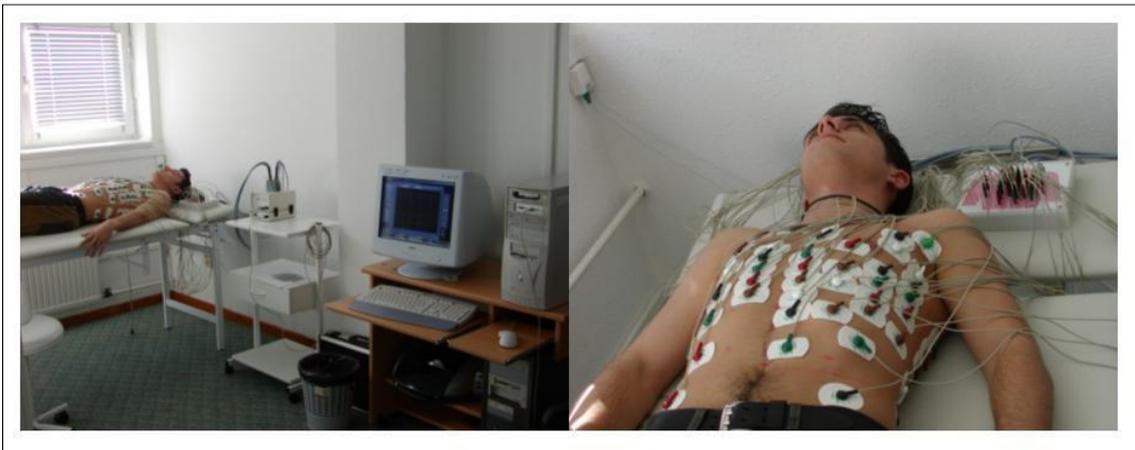


Figure 108. Electrocardiographic body surface mapping, ECG-MAP or Body Surface Potential Mapping.

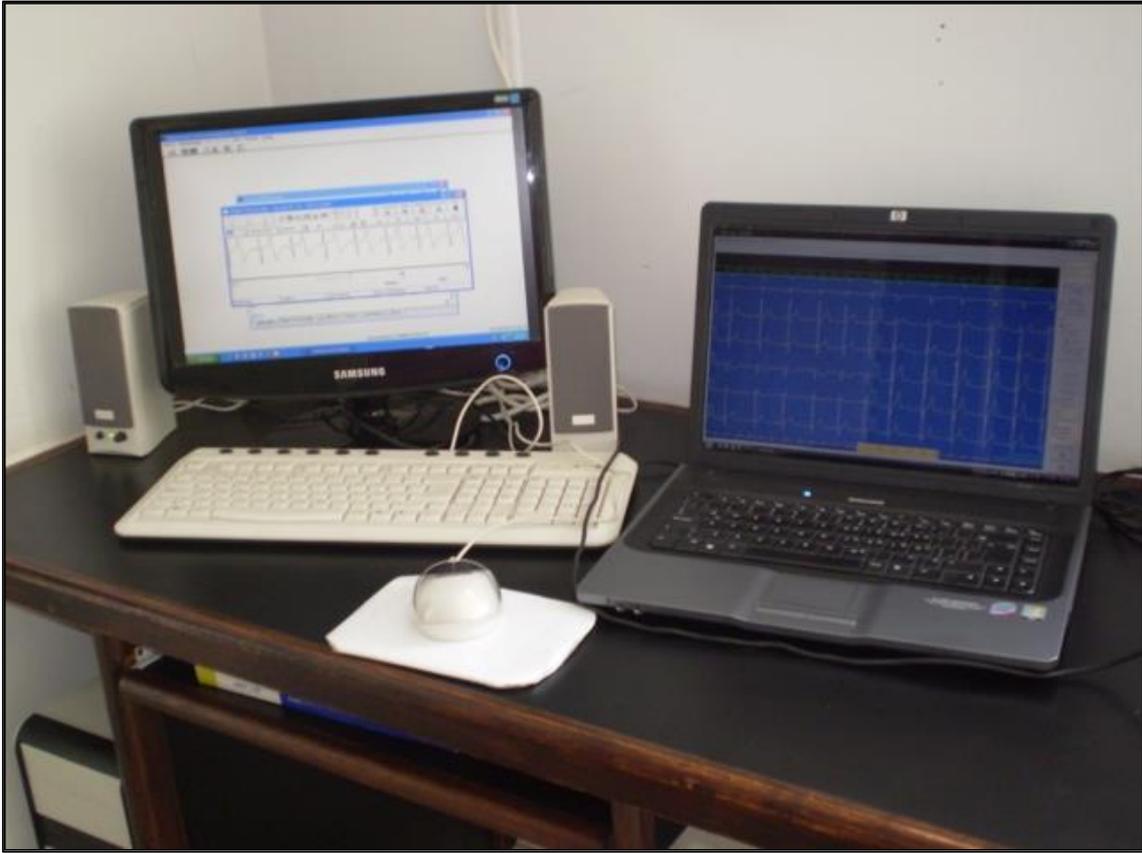


Figure 109. Transtelephonic electrocardiographic monitoring.

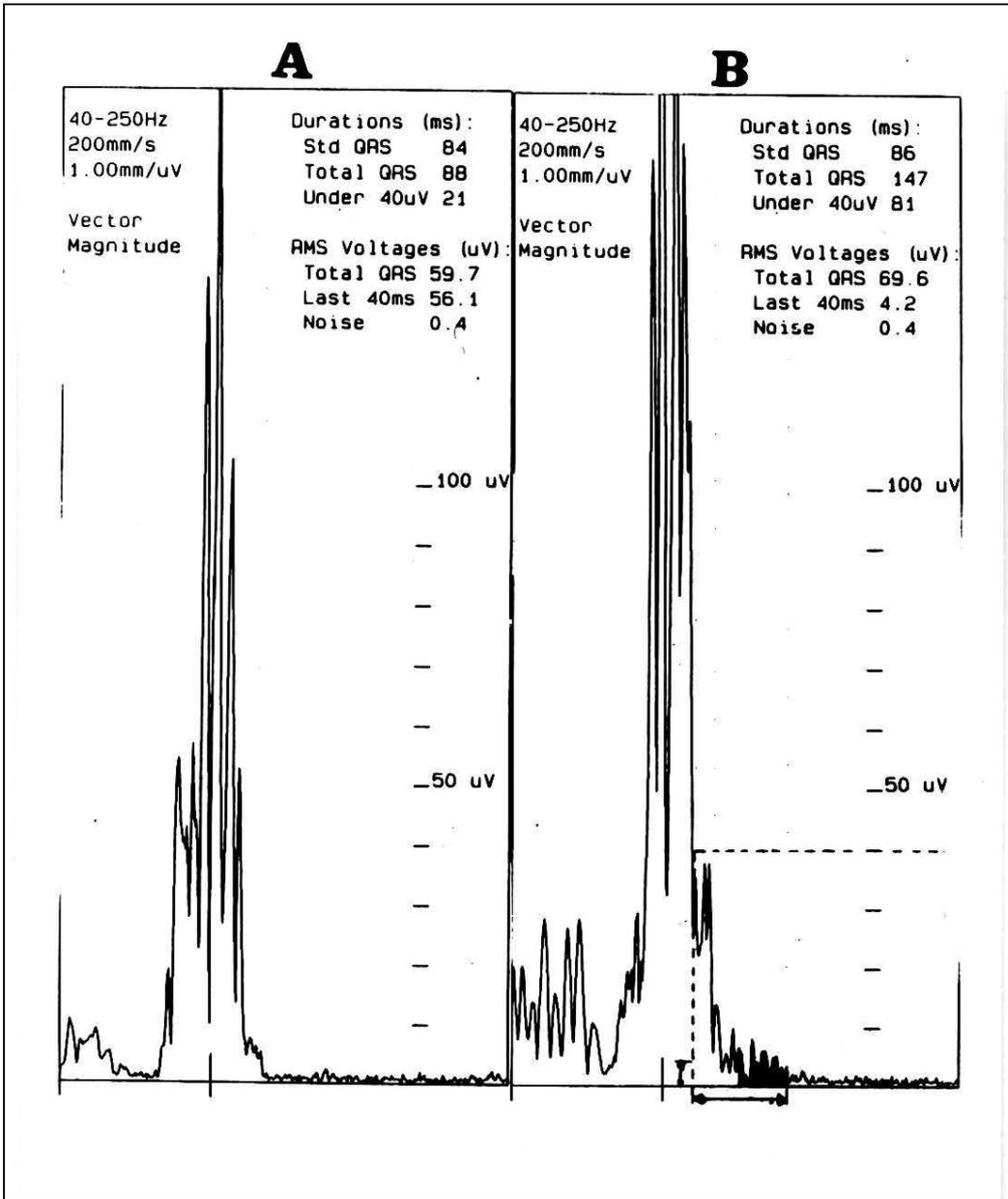


Figure 110. High resolution Electrocardiogram.

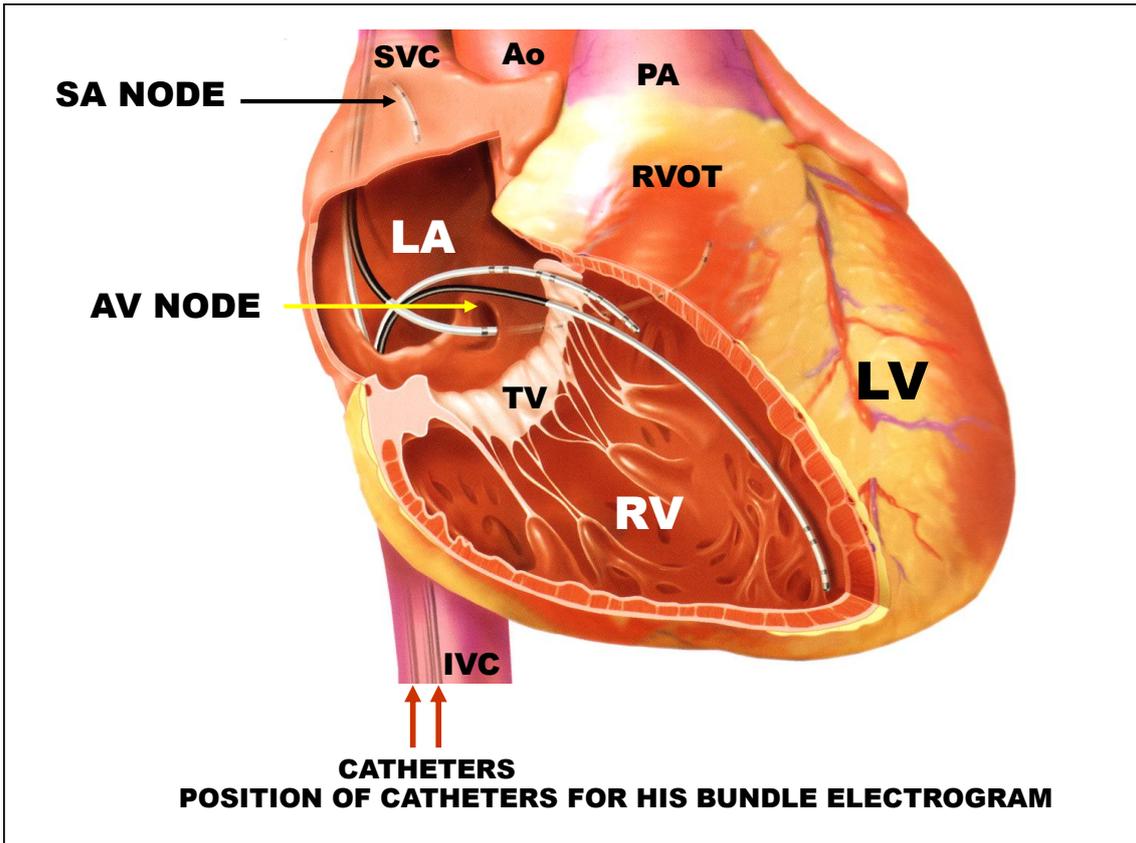


Figure 111. Intracavitary Electrogram.

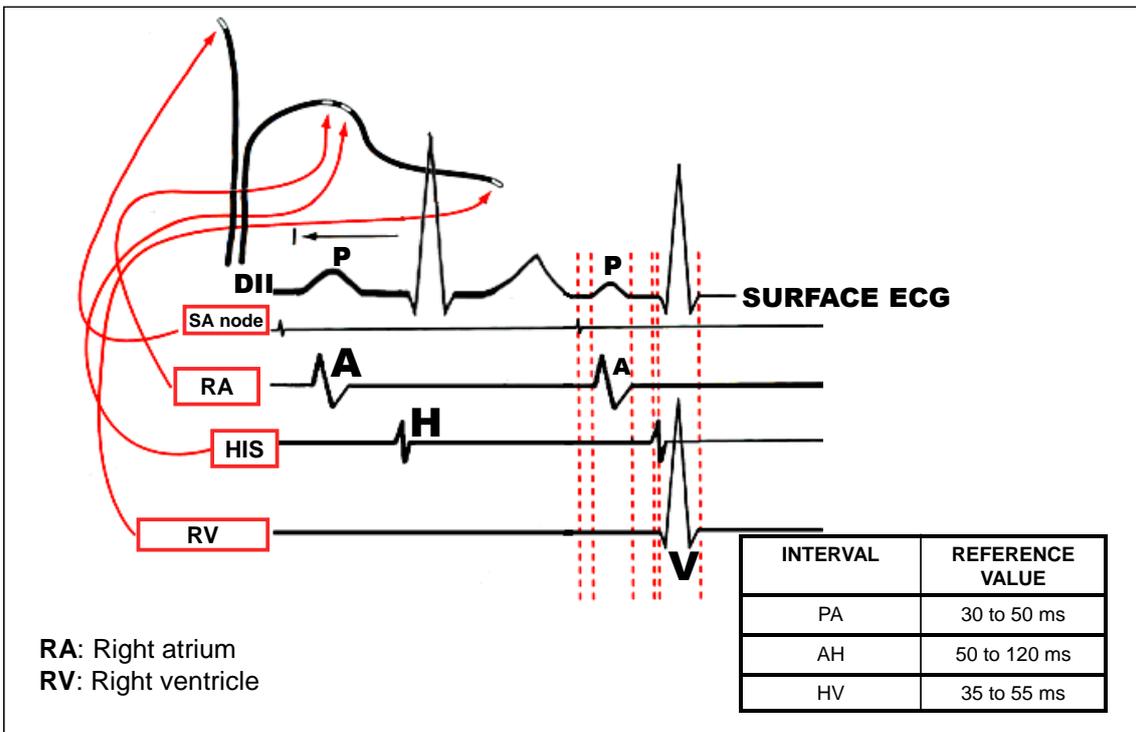


Figure 112. Intracavitary Electrogram and correlation to surface ECG

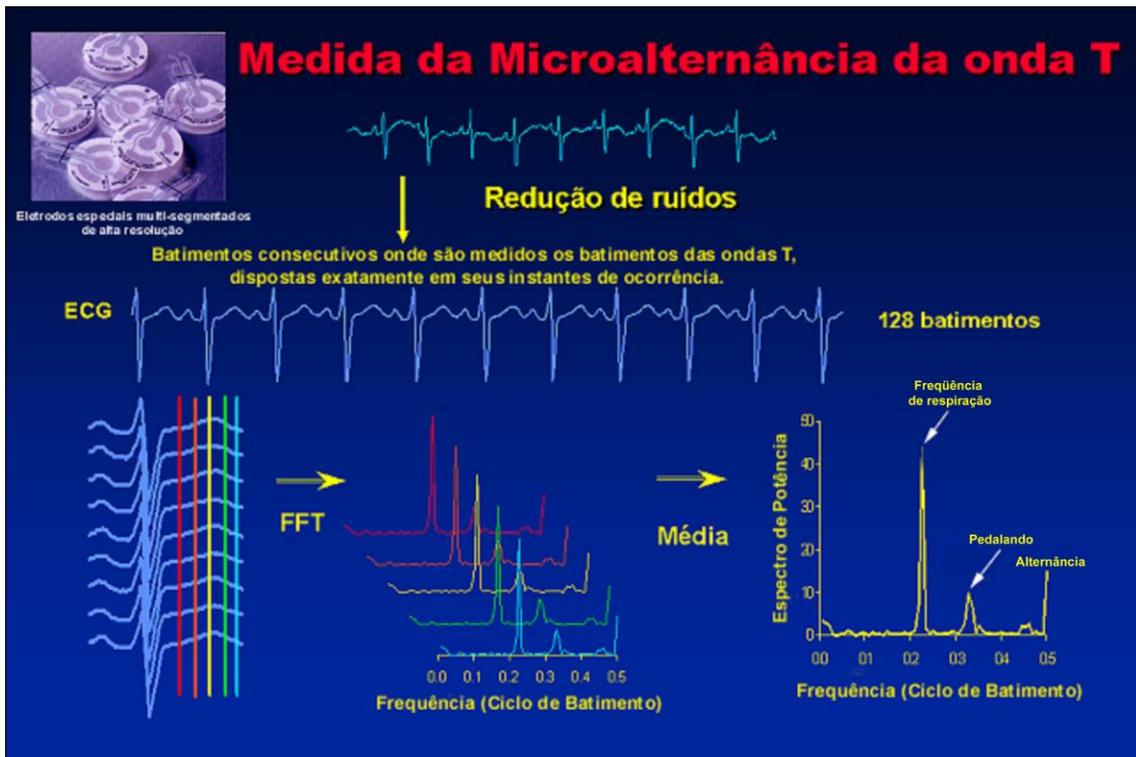


Figure 113. Measure of microvolt T wave alternans (MTWA). Special electrodes jointly with specific signal processing technologies, makes a measurement of MTWA feasible, with minimal interference of artifacts associated to exercise movements. FFT: Fast Fourier Transform Methods.

REFERENCES

- Autenrieth, G., B. Surawicz, C. S. Kuo and M. Arita (1975). "Primary T wave abnormalities caused by uniform and regional shortening of ventricular monophasic action potential in dog." Circulation **51**(4): 668-676.
- Bayley, R. H. (1955). "Vector analysis of the T-deflection of the electrocardiogram." Am Heart J **50**(6): 844-859.
- Blomstrom-Lundqvist, C., M. M. Scheinman, E. M. Aliot, J. S. Alpert, H. Calkins, A. J. Camm, W. B. Campbell, D. E. Haines, K. H. Kuck, B. B. Lerman, D. D. Miller, C. W. Shaeffer, Jr., W. G. Stevenson, G. F. Tomaselli, E. M. Antman, S. C. Smith, Jr., J. S. Alpert, D. P. Faxon, V. Fuster, R. J. Gibbons, G. Gregoratos, L. F. Hiratzka, S. A. Hunt, A. K. Jacobs, R. O. Russell, Jr., S. G. Priori, J. J. Blanc, A. Budaj, E. F. Burgos, M. Cowie, J. W. Deckers, M. A. Garcia, W. W. Klein, J. Lekakis, B. Lindahl, G. Mazzotta, J. C. Morais, A. Oto, O. Smiseth, H. J. Trappe, C. American College of, G. American Heart Association Task Force on Practice and A. European Society of Cardiology Committee for Practice Guidelines. Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular (2003). "ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias--executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias)." Circulation **108**(15): 1871-1909.
- Blomstrom-Lundqvist, C., M. M. Scheinman, E. M. Aliot, J. S. Alpert, H. Calkins, A. J. Camm, W. B. Campbell, D. E. Haines, K. H. Kuck, B. B. Lerman, D. D. Miller, C. W. Shaeffer, W. G. Stevenson, G. F. Tomaselli, E. M. Antman, S. C. Smith, Jr., J. S. Alpert, D. P. Faxon, V. Fuster, R. J. Gibbons, G. Gregoratos, L. F. Hiratzka, S. A. Hunt, A. K. Jacobs, R. O. Russell, Jr., S. G. Priori, J. J. Blanc, A. Budaj, E. F. Burgos, M. Cowie, J. W. Deckers, M. A. Garcia, W. W. Klein, J. Lekakis, B. Lindahl, G. Mazzotta, J. C. Morais, A. Oto, O. Smiseth, H. J. Trappe and N.-H. R. S. European Society of Cardiology Committee (2003). "ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias--executive summary. a report of the American college of cardiology/American heart association task force on practice guidelines and the European society of cardiology committee for practice guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias) developed in collaboration with NASPE-Heart Rhythm Society." J Am Coll Cardiol **42**(8): 1493-1531.
- Brinberg, L. (1958). "A method of analyzing electrocardiac entities in space. III. The electric axis and ventricular gradient as determined from the twelve lead electrocardiogram." J Mt Sinai Hosp N Y **25**(1): 59-73.
- Brinberg, L. (1958). "A method of analyzing electrocardiac entities in space. IV. The QRS-T angle as determined from the twelve-lead electrocardiogram." J Mt Sinai Hosp N Y **25**(6): 539-542.
- Bruce, R. A. and T. R. Hornsten (1969). "Exercise stress testing in evaluation of patients with ischemic heart disease." Prog Cardiovasc Dis **11**(5): 371-390.

Brugada, P. and J. Brugada (1992). "Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report." J Am Coll Cardiol **20**(6): 1391-1396.

Brugada, R., T. Tapscott, G. Z. Czernuszewicz, A. J. Marian, A. Iglesias, L. Mont, J. Brugada, J. Girona, A. Domingo, L. L. Bachinski and R. Roberts (1997). "Identification of a genetic locus for familial atrial fibrillation." N Engl J Med **336**(13): 905-911.

Burchell, H. B. (1987). "A centennial note on Waller and the first human electrocardiogram." Am J Cardiol **59**(9): 979-983.

Burnett, J. (1985). "The origins of the electrocardiograph as a clinical instrument." Med Hist Suppl(5): 53-76.

Cabrera, E. and J. R. Monroy (1952). "Systolic and diastolic loading of the heart. I. Physiologic and clinical data." Am Heart J **43**(5): 661-668.

Cabrera, E. and J. R. Monroy (1952). "Systolic and diastolic loading of the heart. II. Electrocardiographic data." Am Heart J **43**(5): 669-686.

Chatterjee, K., A. M. Harris, J. G. Davies and A. Leatham (1969). "T-wave changes after artificial pacing." Lancet **1**(7598): 759-760.

Clements, S. D., Jr. and J. W. Hurst (1972). "Diagnostic value of electrocardiographic abnormalities observed in subjects accidentally exposed to cold." Am J Cardiol **29**(5): 729-734.

Clemmensen, P., M. Sejersten, M. Sillesen, D. Hampton, G. S. Wagner and S. Loumann-Nielsen (2005). "Diversion of ST-elevation myocardial infarction patients for primary angioplasty based on wireless prehospital 12-lead electrocardiographic transmission directly to the cardiologist's handheld computer: a progress report." J Electrocardiol **38**(4 Suppl): 194-198.

Cohn, A. E. and T. Lewis (1913). "The Predominant Influence of the Left Vagus Nerve Upon Conduction between the Auricles and Ventricles in the Dog." J Exp Med **18**(6): 739-747.

Cosio, F. G., R. H. Anderson, K. H. Kuck, A. Becker, M. Borggrefe, R. W. Campbell, F. Gaita, G. M. Guiraudon, M. Haissaguerre, J. J. Rufilanchas, G. Thiene, H. J. Wellens, J. Langberg, D. G. Benditt, S. Bharati, G. Klein, F. Marchlinski and S. Saksena (1999). "Living anatomy of the atrioventricular junctions. A guide to electrophysiologic mapping. A Consensus Statement from the Cardiac Nomenclature Study Group, Working Group of Arrhythmias, European Society of Cardiology, and the Task Force on Cardiac Nomenclature from NASPE." Circulation **100**(5): e31-37.

de Zwaan, C., F. W. Bar and H. J. Wellens (1982). "Characteristic electrocardiographic pattern indicating a critical stenosis high in left anterior descending coronary artery in patients admitted because of impending myocardial infarction." Am Heart J **103**(4 Pt 2): 730-736.

Dessertenne, F. (1966). "[Ventricular tachycardia with 2 variable opposing foci]." Arch Mal Coeur Vaiss **59**(2): 263-272.

Di Diego, J. M. and C. Antzelevitch (1994). "High [Ca²⁺]_o-induced electrical heterogeneity and extrasystolic activity in isolated canine ventricular epicardium. Phase 2 reentry." Circulation **89**(4): 1839-1850.

Durrer, D., R. T. van Dam, G. E. Freud, M. J. Janse, F. L. Meijler and R. C. Arzbacher (1970). "Total excitation of the isolated human heart." Circulation **41**(6): 899-912.

Einthoven, W., G. Fahr and A. De Waart (1950). "On the direction and manifest size of the variations of potential in the human heart and on the influence of the position of the heart on the form of the electrocardiogram." Am Heart J **40**(2): 163-211.

Emslie-Smith, D., G. E. Sladden and G. R. Stirling (1959). "The significance of changes in the electrocardiogram in hypothermia." Br Heart J **21**: 343-351.

- Fisch, C. (1989). "Evolution of the clinical electrocardiogram." J Am Coll Cardiol **14**(5): 1127-1138.
- Fleming, P. R. and F. H. Muir (1957). "Electrocardiographic changes in induced hypothermia in man." Br Heart J **19**(1): 59-66.
- Frank, E. and G. E. Seiden (1956). "Comparison of limb and precordial vectorcardiographic systems." Circulation **14**(1): 83-89.
- Fye, W. B. (1994). "A history of the origin, evolution, and impact of electrocardiography." Am J Cardiol **73**(13): 937-949.
- Giraud, G., H. Latour, P. Puech and J. Roujon (1956). "[Rhythm disorders of the Wolff-Parkinson-White syndrome; endocavitary electrocardiographic analysis]." Arch Mal Coeur Vaiss **49**(2): 101-133.
- Gozensky, C. and D. Thorne (1974). "Rabbit ears: an aid in distinguishing ventricular ectopy from aberration." Heart Lung **3**(4): 634-636.
- Gussak, I., P. Brugada, J. Brugada, R. S. Wright, S. L. Kopecky, B. R. Chaitman and P. Bjerregaard (2000). "Idiopathic short QT interval: a new clinical syndrome?" Cardiology **94**(2): 99-102.
- Hanon, S., M. Shapiro and P. Schweitzer (2005). "Early history of the pre-excitation syndrome." Europace **7**(1): 28-33.
- Henson, J. R. (1971). "Descartes and the ECG lettering series." J Hist Med Allied Sci **26**(2): 181-186.
- Hering, R. (1909). "Disposal of Municipal Refuse." Am J Public Hygiene **19**(1): 10 11-14 11.
- Howell, J. D. (1991). "Diagnostic technologies: X-rays, electrocardiograms, and CAT scans." South Calif Law Rev **65**(1): 529-564.
- Jervell, A. and F. Lange-Nielsen (1957). "Congenital deaf-mutism, functional heart disease with prolongation of the Q-T interval and sudden death." Am Heart J **54**(1): 59-68.
- Johansson, B. W. (2001). "[A history of the electrocardiogram]." Dan Medicinhist Arbog: 163-176.
- Kirby, D. A., J. M. Pinto and B. Lown (1990). "Changes in ventricular fibrillation threshold during the development of perinephritic hypertension." Am J Hypertens **3**(10): 741-748.
- Kligfield, P. (2002). "The centennial of the Einthoven electrocardiogram." J Electrocardiol **35 Suppl**: 123-129.
- Krikler, D. M. (1987). "Electrocardiography then and now: where next?" Br Heart J **57**(2): 113-117.
- Lama, A. (2004). "[Einthoven: the man and his invention]." Rev Med Chil **132**(2): 260-264.
- Langendorf, R. and A. Pick (1956). "Concealed conduction further evaluation of a fundamental aspect of propagation of the cardiac impulse." Circulation **13**(3): 381-399.
- Lip, G. Y. and D. G. Beavers (1995). "ABC of atrial fibrillation. History, epidemiology, and importance of atrial fibrillation." BMJ **311**(7016): 1361-1363.
- Litovsky, S. H. and C. Antzelevitch (1988). "Transient outward current prominent in canine ventricular epicardium but not endocardium." Circ Res **62**(1): 116-126.
- Lukas, A. and C. Antzelevitch (1989). "Reflected reentry, delayed conduction, and electrotonic inhibition in segmentally depressed atrial tissues." Can J Physiol Pharmacol **67**(7): 757-764.
- Lukas, A. and C. Antzelevitch (1993). "Differences in the electrophysiological response of canine ventricular epicardium and endocardium to ischemia. Role of the transient outward current." Circulation **88**(6): 2903-2915.

Lukas, A. and C. Antzelevitch (1996). "Phase 2 reentry as a mechanism of initiation of circus movement reentry in canine epicardium exposed to simulated ischemia." Cardiovasc Res **32**(3): 593-603.

Osborn, J. J. (1953). "Experimental hypothermia; respiratory and blood pH changes in relation to cardiac function." Am J Physiol **175**(3): 389-398.

Perez Riera, A. R., C. Ferreira, S. J. Dubner, E. Schapachnik, J. D. Soares and J. Francis (2005). "Brief review of the recently described short QT syndrome and other cardiac channelopathies." Ann Noninvasive Electrocardiol **10**(3): 371-377.

Prinzmetal, M., A. Ekmekci, H. Toyoshima and J. K. Kwoczynski (1959). "Angina pectoris. III. Demonstration of a chemical origin of ST deviation in classic angina pectoris, its variant form, early myocardial infarction, and some noncardiac conditions." Am J Cardiol **3**(3): 276-293.

Prinzmetal, M., R. Kennamer, R. Merliss, T. Wada and N. Bor (1959). "Angina pectoris. I. A variant form of angina pectoris; preliminary report." Am J Med **27**: 375-388.

Richman, J. L. and L. Wolff (1954). "Left bundle branch block masquerading as right bundle branch block." Am Heart J **47**(3): 383-393.

Riera, A. R. and A. H. Uchida (2010). "Prof. Dr. Joao Tranchesi: chronology of a fruitful life, 8 February 1922 - 12 October 1978." Cardiol J **17**(2): 211-213.

Romano, C., G. Gemme and R. Pongiglione (1963). "[Rare Cardiac Arrhythmias of the Pediatric Age. I. Repetitive Paroxysmal Tachycardia]." Minerva Pediatr **15**: 1155-1164.

Romano, C., G. Gemme and R. Pongiglione (1963). "[Rare Cardiac Arrhythmias of the Pediatric Age. II. Syncopal Attacks Due to Paroxysmal Ventricular Fibrillation. (Presentation of 1st Case in Italian Pediatric Literature)]." Clin Pediatr (Bologna) **45**: 656-683.

Rosen, M. R. (2002). "[The ECG 100 years later: electrical contribution to molecular signal pathways]." Kardiologija **42**(12): 70-79.

Rosen, M. R. (2002). "The electrocardiogram 100 years later: electrical insights into molecular messages." Circulation **106**(17): 2173-2179.

Rosenbaum, M., G. J. Klein, A. Krahn, M. Basta, C. Le Feuvre and R. Yee (1997). "Utility of full electrophysiological study before accessory pathway ablation in Wolff-Parkinson-White syndrome." Can J Cardiol **13**(4): 359-362.

Rosenbaum, M. B. (1969). "Classification of ventricular extrasystoles according to form." J Electrocardiol **2**(3): 289-297.

Rosenbaum, M. B., H. H. Blanco, M. V. Elizari, J. O. Lazzari and J. M. Davidenko (1982). "Electrotonic modulation of the T wave and cardiac memory." Am J Cardiol **50**(2): 213-222.

Rosenbaum, M. B., P. A. Chiale, D. Ryba and M. V. Elizari (1974). "Control of tachyarrhythmias associated with Wolff-Parkinson-White syndrome by amiodarone hydrochloride." Am J Cardiol **34**(2): 215-223.

Scheinman, M. M. (2005). "History of Wolff-Parkinson-White syndrome." Pacing Clin Electrophysiol **28**(2): 152-156.

Smirk, F. H. and D. G. Palmer (1960). "A myocardial syndrome. With particular reference to the occurrence of sudden death and of premature systoles interrupting antecedent T waves." Am J Cardiol **6**: 620-629.

Sokolow, M. and T. P. Lyon (1949). "The ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads." Am Heart J **37**(2): 161-186.

Sridharan, M. R. and L. G. Horan (1984). "Electrocardiographic J wave of hypercalcemia." Am J Cardiol **54**(6): 672-673.

- Von Knorre, G. H. (2005). "The earliest published electrocardiogram showing ventricular preexcitation." Pacing Clin Electrophysiol **28**(3): 228-230.
- Ward, O. C. (1964). "A New Familial Cardiac Syndrome in Children." J Ir Med Assoc **54**: 103-106.
- Wellens, H. J. and A. P. Gorgels (2004). "The electrocardiogram 102 years after Einthoven." Circulation **109**(5): 562-564.
- Wellens, H. J., C. P. Lau, B. Luderitz, M. Akhtar, A. L. Waldo, A. J. Camm, C. Timmermans, H. F. Tse, W. Jung, L. Jordaens and G. Ayers (1998). "Atrioverter: an implantable device for the treatment of atrial fibrillation." Circulation **98**(16): 1651-1656.
- West, T. C., E. L. Frederickson and D. W. Amory (1959). "Single fiber recording of the ventricular response to induced hypothermia in the anesthetized dog: correlation with multicellular parameters." Circ Res **7**: 880-888.
- Wilson, F. N., F. D. Johnston and et al. (1946). "On Einthoven's triangle, the theory of unipolar electrocardiographic leads, and the interpretation of the precordial electrocardiogram." Am Heart J **32**: 277-310.
- Wolff, L., J. Parkinson and P. D. White (2006). "Bundle-branch block with short P-R interval in healthy young people prone to paroxysmal tachycardia. 1930." Ann Noninvasive Electrocardiol **11**(4): 340-353.
- Yan, G. X. and C. Antzelevitch (1996). "Cellular basis for the electrocardiographic J wave." Circulation **93**(2): 372-379.
- Yan, G. X. and C. Antzelevitch (1998). "Cellular basis for the normal T wave and the electrocardiographic manifestations of the long-QT syndrome." Circulation **98**(18): 1928-1936.
- Zalenski, R. J., D. Cooke, R. Rydman, E. P. Sloan and D. G. Murphy (1993). "Assessing the diagnostic value of an ECG containing leads V4R, V8, and V9: the 15-lead ECG." Ann Emerg Med **22**(5): 786-793.