Major achievements in cardiology in the past century: influence on Dutch cardiovascular medicine

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At the occasion of the 75th anniversary of the Netherlands Society of Cardiology, it is interesting to look back on the major scientific achievements in cardiovascular medicine of the last century and to pay attention to the impact of these achievements on Dutch Cardiology. It might be a nice opportunity not only to mention the ten great discoveries in Cardiology in the past century, but also to address the pioneering work in the Netherlands. When honouring and paying tribute to Dutch individuals, this special article only refers to emeriti-professors in cardiology (and some other closely-related retired experts), as this is a historical reflection rather than a cross-sectional view of current attainments. The practising pioneers of today will hopefully be remembered in 75 years from now. (*Neth Heart J* 2009;17:136-9.)

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At the occasion of the 75th anniversary of the Netherlands Society of Cardiology, we review ten major scientific achievements in cardiovascular medicine of the last century and look back on the pioneering work carried out by Dutch cardiologists.

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Electrocardiography

In 1902, Willem Einthoven, born in Java in 1860, first recorded a human electrocardiogram (ECG) in his Laboratory of Physiology in Leiden using a string galvanometer. In 1895, Einthoven had already been able to detect recognisable waves with a capillary electrometer, which he labelled 'P, Q, R, S, and T waves. Within ten years of Einthoven's clinical studies with the string galvanometer, the immense potential of electrocardiography was recognised. In 1924, the 'Father of Electrocardiography' was rewarded with the Nobel Prize in Medicine. In 1927 Einthoven died of gastric cancer at the age of 67 years.

A Dutch contemporary of Einthoven, Karel Frederik Wenckebach, born in Utrecht in 1864, became famous for his sphygmographic analysis of the irregular pulse. His studies led to the discovery of the well-known Wenckebach periods. Interestingly, Wenckebach evaluated the efficacy of the antiarrhythmic drug quinine in patients with atrial fibrillation. With that work, Wenckebach may also be considered to be the founder of pharmacological therapy for arrhythmias. Wenckebach was appointed professor in Groningen early in the 20th century, moved to Vienna before World War I, became honorary president of our Society at its foundation in 1934, and died at the dawn of World War II in 1940. Until now, the ECG remains the diagnostic cornerstone in cardiovascular medicine.

The Einthoven/Wenckebach tradition was continued by the Dirk Durrer (Amsterdam), Chiel Janse (Amsterdam), Jan Roos (Leiden/Amsterdam), Frits Meijler (Utrecht), Ariaen Zimmerman (Utrecht), Etienne Robles de Medina (Utrecht), Hein Wellens (Maastricht), Jan Pool (Rotterdam), and Norbert van Hemel (Nieuwegein). Willem Mosterd (Utrecht/Amersfoort) studied arrhythmias in athletes.

Cardiac catheterisation and coronary angiography

In 1929, a surgical resident named Werner Forsmann (Germany) introduced a catheter into his own antecubital vein and he confirmed the position of the catheter tip in the right atrium by use of radiography. His goal was to find a safe and effective way of injecting drugs for cardiac resuscitation. In 1941, Andre

Cournand (France) and Dickinson Richards (USA) applied catheterisation techniques to measure right-heart pressures and cardiac output. In 1956, Forsmann, Cournand, and Dickinson were honoured with the Nobel Prize in Medicine. In 1958, Mason Sones (USA) performed the first selective coronary angiogram in a series of more than 1000 patients using the brachial approach. In 1967, Melvin Judkins (USA) introduced the transfemoral approach. Coronary angiography laid the basis for later coronary bypass surgery and percutaneous coronary intervention.

Albert Bruschke (Nieuwegein/Leiden) was the first Dutch cardiologists to perform coronary arteriography in the Netherlands in the late 1960s. Other experts in cardiac catheterisation were Evert van der Wall (Groningen), Geert Meester (Rotterdam), Beert Buis (Leiden), and Tjeerd van der Werf (Nijmegen). Jan Baan (Leiden) introduced the conductance catheter to more accurately explore intrinsic cardiovascular dynamics.

Cardiovascular surgery

In 1938, Robert Gross (USA) successfully closed a patent ductus arteriosus using hypothermia. In 1944, Helen Taussig and Alfred Blalock (USA) stood together at the basis of the first corrective operation of patients with Tetralogy of Fallot. In 1949 the Netherlands Society of Thoracic Surgery (NVT) was founded. In 1953, John Gibbon (USA) performed the first open-heart operation using the heart-lung machine in an 18-year old girl with an atrial septal defect. In 1967, Rene Favoloro (Argentina) used a saphenous vein autograft as a bypassing channel for a stenosed right coronary artery. As from 1968, also internal mammary arteries were used as bypass grafts. In 1967, Christiaan Barnard (South-Africa) performed the first heart transplant in a 53-year old patient (Louis Washkansky). Currently, >80% of all heart-transplant patients are still alive after five years of operation.

Gerrit Brom (Leiden) introduced cardiovascular surgery in the Netherlands in the early 1950s, in particular for patients with congenital heart disease. The first coronary artery bypass graft procedure was performed in the late 1960s in Nijmegen by Pierre Kuijpers in cooperation with Jaap Vonk (Nijmegen). The first heart transplant was performed in Rotterdam in 1984 by Egbert Bos (Rotterdam) and Hans Huysmans (Leiden). Minimal invasive bypass surgery (OCTOPUS method) was introduced by Cees Borst (Utrecht) in 1996. Cardiovascular surgery was further developed by Jan Homan van der Heide (Groningen), Jaap Bredee (Eindhoven/Utrecht), Nico Meijne Amsterdam), Leon Eysmans (Amsterdam), and Olaf Penn (Maastricht/Eindhoven).

Preventive cardiology

In 1944, the 'Father of American Cardiology', Paul Dudley White (USA) pioneered the concept of cardiovascular prevention. In 1948, the Framingham study was launched by the National Heart Institute (NHI), which was the first prospective population-based cohort study focussing on risk factors for cardiovascular disease. Based on the Framingham study, William Kannel (USA) showed in 1961 that high blood pressure, smoking, and high cholesterol levels were major factors in cardiovascular disease. In addition, the study provided information crucial to the recognition and management of atherosclerosis, its causes and its complications. Identification and management of risk factors has resulted in a significant decline in morbidity and mortality in patients with coronary artery disease. The Framingham study laid the basis for many other longitudinal cohort studies such as the EUROASPIRE study.

Jaap Nieveen (Groningen) was one of the first cardiologists in the Netherlands to propagate primary prevention, followed by Arend-Jan Dunning (Amsterdam) and Alex Arntzenius (Leiden).

Cardiovascular imaging

In 1952, Inge Edler (Sweden) and Carl Hertz (Sweden) adapted for human use a sonar device for detecting submarines in World War II. In 1954, they reported for the first time continuous recording of the walls of the heart, and in 1956 mitral valve disease was detected by M-mode echocardiography. In 1973, Harvey Feigenbaum (USA) used echocardiography for detection of wall motion abnormalities of the left ventricle. As M-mode echocardiography gained increased acceptance, the technique was expanded with two-dimensional, transoesophageal, and Doppler echocardiography.

Jos Roelandt (Rotterdam), Klaas Bom (Rotterdam), and Cees Visser (Amsterdam) were the first pioneers in echocardiography in the Netherlands. Subsequently, a variety of noninvasive cardiovascular imaging techniques were introduced such as nuclear techniques in the 1970s (Frans Wackers, Amsterdam/New Haven), magnetic resonance in the 1990s, and computed tomography in the 1990s.

Coronary care units

In 1961, Desmond Julian (UK) launched the concept of a coronary care unit. The main initial objective was to reduce the number of deaths due to ventricular arrhythmias. Before 1961, early mortality of patients with an acute myocardial infarction who reached the hospital exceeded 30%. With the institution of coronary care units, Thomas Killip (USA) showed in 1967 that the in-hospital mortality of acute myocardial infarction was reduced by more than 50%. Coronary care units were rapidly spread across the world and became requirements for hospital accreditation. At present, many hospitals create acute-chest pain units in order to serve patients on a rapid basis at the same time being cost-effective for the hospitals.

In the Netherlands, Henk Lie (Groningen/Amsterdam) was involved in initiating coronary care units.

Reperfusion therapy in acute myocardial infarction

In 1979, Klaus Rentrop (Germany) demonstrated rapid recanalisation after local administration of streptokinase directly into an infarct-related coronary artery. The importance of thrombolysis was further emphasised in 1980 when Marcus DeWood (USA) observed a high incidence of total occlusion of infarct-related arteries during the early period of myocardial infarction. Thereafter, the Western Washington trials and ISIS-2 demonstrated both short- and long-term benefits of thrombolytic therapy. Subsequently, many thrombolytic and antithrombotic drugs have been developed. The merits of thrombolytic therapy have been slowed down by the introduction of primary coronary angioplasty predominantly based on the outcome of the Zwolle trial. The Dutch streptokinase trial, coordinated by the Interuniversity Institute of the Netherlands (ICIN), was instrumental in the application of thrombolytic therapy in patients with acute myocardial infarction.

Cardiovascular drugs

Important cardiovascular drugs that came on the horizon in the clinical arena were β-blocking agents in 1962, developed by Sir James Black (UK), for which he was honoured with the Nobel Prize. Also in the 1960s, calcium antagonists were launched on the market by Albrecht Fleckenstein (Germany). In the late 1970s, ACE inhibitors were introduced by Miguel Ondetti and David Cushman (USA). The first HMG-CoA reductase inhibitors, i.e statins, were isolated by Akira Endo (Japan) in 1976. His work was based on the Nobel Prize winning work by Michael Brown (USA) and Joseph Goldstein (USA) who identified the LDL receptor in the early 1970s. Altogether, these drugs have improved the quality of life and prolonged life expectancy in millions of patients worldwide.

In the Netherlands, Pieter van Zwieten (Amsterdam) became expert in the domain of cardiovascular drugs.

Percutaneous coronary intervention

In 1977, Andreas Gruentzig (Switzerland) performed the first balloon angioplasty on an isolated stenosis of the proximal left anterior descending coronary artery in a 37-year-old man. This extraordinary achievement could not have been accomplished without the previous development of coronary angiography, coronary bypass surgery and peripheral vascular dilatation. Gruentzig turned the diagnostic cardiac catheter into a powerful therapeutic device and he created a new subspeciality: interventional cardiology. In 1986, one year after the untimely death of Gruentzig, Jacques Puel (France) inserted the first intracoronary stent, the success of which was proven by Ulrich Sigwart (Switzerland) one year later. Today, bare-metal stents are increasingly being replaced by drug-eluting stents, which are capable of almost completely preventing restenosis. Percutaneous coronary intervention has become one of the most common medical interventions in the world.

In the Netherlands, Sjef Ernst (Nieuwegein) performed the first balloon angioplasty in 1980. Paul Hugenholtz (Rotterdam) recruited a team of interventional cardiologists who attained world-known recognition. Cardiologists from Eindhoven, Zwolle, Amsterdam (OLVG) and Nieuwegein became prominent for fractional flow reserve measurements, primary PCI studies, the radial artery approach, and carotid stenting/alcohol septal ablation, respectively.

Pacemakers/Implantable cardioverter defibrillators

In 1958, Ake Larsson and Arne Senning (Sweden) implanted the first internal pacemaker. Had the first devices been asynchronous, in 1962 the first synchronous pacemaker was implanted mimicking a physiological state. These achievements led to the invention of the automatic implantable cardioverter defibrillator (ICD) in 1970 by Michel Mirowski (Israel/USA). In 1980, the first devices were implanted in patients and reduced the mortality rate to less than 10%. As of 1988, it became possible to combine the ICD with a pacemaker. The ICD became the therapy of choice in patients with life-threatening ventricular arrhythmias. Today, in many patients with drug-refractory heart failure, a biventricular pacemaker/ICD may constitute the optimal therapy.

In the Netherlands, the first pacemakers were implanted by Frans Rodrigo together with Gerrit Brom (Leiden), and Bert Thalen together with Jan Homan van der Heide (Groningen) in 1962. The first transvenous implantation of atrial leads was performed by El-Gamal (Eindhoven) in 1977. The first ICD was implanted in Utrecht in 1984 by Olaf Penn.

From retrospect to the future

What can we learn from the achievements in the past century? First, our field is continuously evolving. In nearly each decade of the past century (apart from the episodes of the two World Wars) tremendous progress was made. Second, apart from major achievements by American and Japanese researchers, we can be proud that many discoveries were made by European investigators. Third, with Einthoven as tycoon, many of these developments were 'Made in Holland'. Dutch cardiologists (together with other experts in cardiovascular medicine) have performed pioneering work in the majority of the ten above-mentioned areas such as in preventive cardiology, myocardial imaging modalities, thrombolysis, percutaneous interventions, and ICD implantations. Many of these research enterprises have been made possible by the ICIN, founded by Durrer (Amsterdam) in 1972, being a fruitful scientific collaboration between the Cardiology Departments of the eight universities in the Netherlands. A non-university counterpart of the ICIN, the Working Group Cardiology Centers Netherlands (WCN), has been successful in coordinating important national and international multicentre trials since 1988.

The ten major challenges for the current era are:

1 Focus on primary prevention/risk assessment
2 Updating and implementation of evidence-based guidelines
3 Genetic screening/pharmacogenomics/development biobanks
4 Gene therapy/stem cell therapy/novel drugs
5 Integration of imaging techniques/receptor imaging/plaque imaging
6 Development of new coronary artery intervention techniques/ biodegradable coronary stenting/ tissue modification
7 Invasive treatment of heart failure
8 Invasive treatment of arrhythmias
9 Percutaneous valve replacement/new surgical techniques
10 Organisation of cardiology practice/EPD/ registries/home monitoring

In 75 years from now, history will tell us how successful Dutch cardiology has been in realising these major challenges. ■

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