Nobel Laureate series

Werner Forssmann Nobel Prize for physiology or medicine 1956

Mark Nicholls looks at the courageous role Werner Forssmann played in the development of cardiac catheterization and the subsequent award of the 1956 Nobel Prize for his endeavours.

Not only was the experiment Werner Forssmann conducted on himself in 1929 of immense significance in paving the way for a monumental leap forward in cardiovascular care, it was also an outstanding act of selfless courage. Now recognized as a key figure in the development of cardiac catheterization, for which he was awarded the 1956 Nobel Prize, Forssmann’s role risked his personal well-being in the process.

While still a young man relatively new to medicine, Forssmann inserted a catheter into a vein in his arm and threaded it through to his heart, all the while not knowing whether the catheter would pierce a vein with a potentially fatal outcome.

Despite putting his life at risk, Forssmann was successful in safely passing the ureteral catheter into his heart, having hypothesized that a catheter could be inserted directly into the heart for applications such as directly delivering drugs, injecting radiopaque dyes, or measuring blood pressure. It proved one of the landmark breakthroughs in cardiovascular medicine and was arguably the start of cardiac catheterization as we recognize it today, becoming an integral part of the routine care and treatment offered to heart patients.

Yet while living to tell the tale, Forssmann paid a high price; for many years facing opposition and criticism—rather than respect and recognition for advancing the field of cardiac care—with his medical career impeded as a result. However, in the early 1940s, André Frédéric Courmand and Dickinson W. Richards—working in close collaboration at Columbia University and Bellevue Hospital in New York—began to advance the technique, whilst constantly acknowledging Forssmann’s contribution and also facing opposition to their own work. This ultimately led to the trio together being awarded the Nobel Prize in Physiology or Medicine in 1956 ‘for their discoveries concerning heart catheterization and pathological changes in the circulatory system’.

Werner Theodor Otto Forssmann was born in Berlin on 29 August 1904, the son of Julius Forssmann and Emmy Hindenberg. Educated at the Askanische Gymnasium in Berlin, he went to the University of Berlin in 1922 to study medicine and after further clinical training and anatomical study, received his clinical instruction in surgery in 1929 at the August Viktoria Home at Eberswalde near Berlin.

It was during this time as a young physician that he conducted his experiment, having been inspired by a sketch in his physiology textbook depicting a long tube being placed into a horse’s jugular vein and guided into the animal’s heart. That convinced him that a similar experiment—albeit one that went against his department chief’s wishes—could be conducted on humans. Persevering, he persuaded Gerda Ditzen, the operating-room nurse in charge of the sterile supplies at Eberswalde, to assist him as she held the keys to the closet where there was a catheter of sufficient length.

She agreed, but only on condition that Forssmann would do it on her rather than himself. However, Forssmann tricked her and while she was restrained on the operating table, performed the experiment on himself during the hospital’s quieter lunchtime period.
Inserting a cannula into his left antecubital vein, through which he passed a 65 cm long catheter, he recalled feeling progressive painless warmth as the tube moved along. Then, with Ditzen, he walked to the X-ray department, where under the guidance of a fluoroscope he further advanced the catheter into his right ventricular cavity. Once the tube had reached its destination, the technician took the X-ray image before it was removed.

The account of Forssmann’s experiment was published in the journal Klinische Wochenschrift in November 1929, by which time he had moved to work at the Charité hospital in Berlin for a short period. However, despite little interest from the medical community, Forssmann continued with his experiments, later developing the use of groin catheterization to reach the inferior vena cava through the femoral veins.

At this time, unable to find a suitable job, he gave up on cardiology and began work as a urologist. His wife, Dr Elsbet Engel, who he married in 1933 and had six children with, was also a urology specialist.

He served in the German Army in World War Two as a Surgeon-Major and was captured and held prisoner until 1945. It was during this period that Courand and Richards read of his work and began developing ways of applying his technique to heart disease diagnosis and research. From 1950 onwards, Forssmann practised as a urological specialist at Bad Kreuznach and in 1956, the year he became a Nobel laureate, was also appointed Honorary Professor of Surgery and Urology at the Johannes Gutenberg University, Mainz. In 1958, he became Chief of the Surgical Division of the Evangelical Hospital at Düsseldorf.

In delivering his Nobel Lecture on 11 December 1956, entitled ‘The Role of Heart Catheterization and Angiocardiography in the Development of Modern Medicine’ Forssmann not only reflected on those who before him had expanded knowledge of circulation of the blood but also touched on the opposition his work had attracted.

‘Further development of the technique’, he noted, ‘was impeded not only by the absence of technical essentials and consequent lack of knowledge. To some outsiders, ethical considerations also weighed heavily in the balance against it’.

He went on to speak about the ongoing resistance faced by his co-laurates but added: ‘The work of Courand and Richards and their pupils had fanned a small flame into a blazing fire which began to rage all over the world’. He felt frustration at people who ‘did not hesitate to obstruct practical research work with threadbare ethical and moral objections’ yet he also foresaw that ‘further development will in many cases enable us to dispense with the massive and dangerous quantities of contrast media’ . . . and ‘to manage instead with smaller, less harmful amounts of radioactive isotopes’.

Discussing the issue later in his life, Forssmann said he found the negative response from the medical community ‘very painful’. He said ‘I felt that I had planted an apple orchard and other men who had gathered the harvest stood at the wall, laughing at me’. But without his courageous self-experiment nine decades ago, routine cardiac procedures such as angioplasty or percutaneous valve repair may not have developed as they did.

Forssmann died in Schopfheim, Germany, on 1 June 1979, aged 74. Courand died on 19 February 1988, aged 92, while Richards had died in February 1973, aged 77.

Today, the Klinikum Barnim Werner-Forssmann-Krankenhaus is named after him because of his connection to the hospital as a registrar when he conducted his self-experiment in 1929. A teaching hospital with 16 main departments, it is associated with the Charité—University Medicine Berlin.

### Werner Forssmann—Legacy

Professor Ulf Landmesser, medical chair of the Cardiovascular Center at Charité University Berlin and chairman of the Department of Cardiology, outlined the contribution Forssmann made to modern cardiac catheterization. ‘Werner Forssmann has laid the ground for cardiac catheterization, a mainstay of modern cardiovascular medicine, in a self-experiment, which also required a lot of courage’, he said ‘Courand and Richards advanced this approach towards clinical application’.

He said Forssmann’s work was a ‘very important step, since it was believed before that cardiac catheterization would be life threatening’ and that the further work on right heart catheterization by Courand and Richards in New York were certainly ‘encouraged’ by the experiences of Forssmann. ‘Courand and Richards moved the technique forward towards clinical application, in particular for right heart catheterization’.

Prof. Landmesser, who has a particular interest in advancing catheter-based treatment of coronary disease and prevention, said the legacy of their work was catheter-based diagnostics, now being an essential approach in modern cardiovascular medicine.

He added: ‘Heart catheter-based diagnostics is a mainstay for assessment and characterization of pulmonary hypertension and assessment of coronary disease. A major recent development has been the development of catheter-based treatment of heart valve disease’.
Conflict of interest: none declared.

The First ‘Paul Vanhoutte Lecture’ by Filippo Crea at the University of Zurich

Professor Paul M. Vanhoutte left us unexpectedly at the age of 78 years on 23 August 2019. The sad event left his family, many of his colleagues and friends as well as scientists around the world stunned and was reported by several prestigious scientific journals worldwide.1–4 This merely reflected the scientific weight of his outstanding career and the generosity of his personality.

Professor Vanhoutte will be remembered for his pioneering work on endothelium-dependent relaxation and its key role in the early phases of cardiovascular disease, a stage better known as endothelial dysfunction. His scientific achievements made him one of the best-cited scientists of all times as underlined by his stratospheric h-index of 128. During his career, he published almost 1000 manuscripts including original research articles, reviews, and editorials.

In addition to the above, Professor Paul M. Vanhoutte will be surely remembered for his outstanding mentoring capabilities which produced excellent and successful scientists holding chairs all over the globe.

Among his mentees, Professor T.F. Lüscher who is Chair of Research and Education at the Royal Brompton and Harefield Hospitals, Imperial College London, UK, Chairman of the Center for Molecular Cardiology at the University of Zurich, Switzerland and Editor-in-chief of the European Heart Journal, was a close friend of Paul M. Vanhoutte and kept working with him up until the end. Indeed, Paul M. Vanhoutte was a research consultant for the Center for Molecular Cardiology and regularly visited the laboratories 2–3 times a year.

In recognition of his longstanding precious contribution to the Center for Molecular Cardiology, Prof. Thomas F. Lüscher and Prof. Giovanni G. Camici, Chairman and Director and the Center for Molecular Cardiology, respectively, recently organized a ‘Paul Vanhoutte Lecture’ series. The first lecture was inaugurated on 10 January 2020 and the invited speaker was Professor Filippo Crea, Director of the Department of Cardiovascular and Thoracic Sciences, the Postgraduate School in Cardiology, and Coordinator of a PhD programme in Molecular Medicine at the Catholic University, Rome. For the occasion, Prof. F. Crea gave a wonderful lecture on the