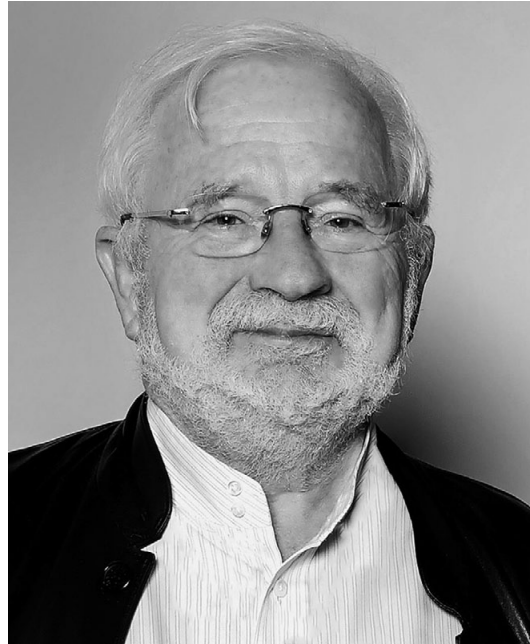




Tribute to Paul M. Vanhoutte, MD, PhD

— 1940–2019 —

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Photograph of Professor Paul M. Vanhoutte
(by his daughter, Valerie, in 2015, with permission)

Professor Paul M. Vanhoutte passed away at the age of 78 on August 23rd 2019. He was an internationally recognized leader in vascular biology and cardiovascular pharmacology and a great charismatic teacher for young researchers. As former Japanese fellows to him, we express our sincere condolences to his wife Jacqueline, children, and grandchildren.

Professor Vanhoutte was born in 1940 in Belgium, where he obtained his degrees at the University of Gent (BS, MS, and MD) and the University of Antwerp (PhD). He received his postdoctoral training at the University of Gent and at the Mayo Clinic (Rochester, MN, USA). His academic career then started at the University of Gent (Assistant, 1969–1971), followed by the Mayo Clinic (Research Associate, 1972–1973), the University of Antwerp (from Associate Professor to full Professor and Head of the Department of Pharmacology, 1973–1981), again the Mayo Clinic (Professor of Physiology and Pharmacology, 1981–1989) and Baylor College of Medicine (Houston,

TX, USA, Professor of Medicine, Pharmacology and Physiology, and Director of the Center for Experimental Therapeutics, 1989–1995). Under his guidance, Shimokawa and Komori studied at the Mayo Clinic, and Nagao at the Baylor College of Medicine. From 1992 to 2002, he was Vice-President R&D, and Director of Discovery Research at the Institut de Recherches Internationales Servier in Paris, France. From 2003 to 2006, he was Distinguished Visiting Professor and Director/Founder of the Biopharmaceutical Development Center at the Faculty of Medicine, University of Hong Kong. From 2006 to 2011, he was Head of the Department of Pharmacology and Pharmacy, and from 2009 to 2015, he was Chair Professor and from 2015 until his death, he was Permanent Visiting Professor in the same department, continuing to co-supervise PhD students and to advise more senior investigators of the department. Since 2013, he held a part-time position of professor at the University of South Denmark in Odense, Denmark. He never retired.

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He had visiting professor positions at many universities worldwide, including the Polish Academy of Sciences (1979), Chonbuk National University, Jeonju (South Korea, 2013–2016), and King Saud University (Saudi Arabia, 2013–2015). He had also been honorary professor at many universities in China, including the Peking Union Medical College, the Institute of Materia Medica of Beijing, the Ocean University of Qingdao, the Second Military Medical University in Shanghai, and the Shanghai Institute of Materia Medica. He was still Visiting Professor at the University of Malaya (Kuala Lumpur), and the University of Zurich (Switzerland).

He also had memberships of many academic societies, including the Academia Europea, the Académie Nationale de Pharmacie (Paris) and the 2 Belgian academies of medicine, and honorary member of the Brazilian Academy of Medicine, the American Association of Physicians, the American Society of Physiology, the American Heart Association (Fellow), the American Society for Clinical Investigation (Emeritus), the American College of Cardiology (Fellow), the American College of Angiology (Fellow), the American Society for Pharmacology and Experimental Therapeutics, the Belgian Society for Physiology and Pharmacology, the French Pharmacological Society. He was member and past-president of the Hong Kong Pharmacology Society. He was honorary member of the Physiological Society (London), the British Pharmacological Society, the Chinese Pharmacological Society, the German Society of Angiology, the Société Française de Cardiologie, and the European Society of Cardiology. Professor Vanhoutte was the founder and the past-president of the Serotonin Club (renamed as the International Society for Serotonin Research) and the Asian Society of Vascular Biology (ASVB). He also was a founding organizer of a series of scientific meetings titled “Mechanisms of Vasodilatation” (MOVD) and “Endothelium-dependent Hyperpolarization” (EDH). It was at the 4th MOVD conference, held in Rochester in the summer of 1986, where Dr. Robert Furchgott and Dr. Louis Ignarro independently reported their findings that endothelium-derived relaxing factor (EDRF) was nitric oxide, which led to the Nobel Prize in 1998. This year, the joint MOVD/EDH 2019 was held in May in Rotterdam, the Netherlands, which was the last meeting for him. As usual, he sat in the front seat and asked valuable and humorous questions of all the speakers.

Regarding editorial works, he served as the editor-in-chief of the *Journal of Cardiovascular Pharmacology* from 1989 to 2007. He was associate editor of the *American Journal of Physiology (Heart and Circulatory Physiology)*, *News in Physiological Sciences*, and the *Journal of Vascular Medicine and Biology*, and a member of the editorial board of many scientific journals, including *Circulation*, *Circulation Research*, *Cardiovascular Research*, *Hypertension*, *Journal of Hypertension*, *American Journal of Physiology*, and *Journal of Pharmacology and Experimental Therapeutics*. He was a member, and chairman, of the Program Project Review Committee of the National Heart Blood and Lung Institute of the NIH (Bethesda, MD, USA). He chaired the International Union of Basic and Clinical Pharmacology (IUPHAR) Committee for Receptor Nomenclature from 1989 to 1998, was secretary general from 1998 to 2002, and then president from 2002 to 2006.

Professor Vanhoutte wrote 3 theses and co-authored or edited 36 books. He published 669 original research papers, and 574 editorials, reviews or chapters in books. He was a

highly cited researcher (ISI) in 3 categories; Biology & Chemistry, Pharmacology, and Clinical Medicine. His last *h*-index was 128.

His scientific contributions have been highly recognized internationally. Early in his career, in collaboration with his mentor, Dr. John T. Shepherd at the Mayo Clinic, he demonstrated the roles of catecholamines and the autonomic nervous system on venous tone.¹ In the 80s, in addition to Dr. Robert Furchgott who demonstrated the obligatory role of the endothelium as a regulator of smooth muscle function, Professor Vanhoutte was among the pioneers who showed the importance of endothelial functions in cardiovascular health and disease.^{2–4} His studies demonstrated for the first time endothelial responses to aggregating platelets,^{5,6} dietary modulation of endothelial function,^{7,8} and endothelial dysfunction in the regenerated state.^{9–11} Furthermore, he will be remembered as a pioneer who discovered the presence of endothelium-derived contracting factors (EDCFs) in 1985,¹² and endothelium-derived hyperpolarization factors (EDHFs) in 1988.^{13,14} The nature of EDCF was thereafter identified as superoxide anions, prostaglandin endoperoxides, and endothelin, playing important roles in pathological conditions such as hypertension, hypoxia, and sepsis.^{15–18} As the 3rd endothelium-derived relaxing factor (EDRFs), the importance of EDHFs should be more emphasized in the microcirculation because the importance of EDHFs increases as the vessel size decreases.^{19–23} When Shimokawa's group identified that the physiological concentration of endothelium-derived hydrogen peroxide (H₂O₂) is an EDHF,²⁴ Professor Vanhoutte strongly supported this notion.²⁵

Professor Vanhoutte was also a great teacher with deep affection for his fellows, a profound passion for science, and outstanding humanity. Throughout his life, he expressed a warm interest in the scientific career and well-being of his fellows. He always referred to his former fellows when he presented the findings of his team during his lectures. He encouraged us by citing Alexander the Great; “There is nothing impossible to him/her who will try”. One of our happiest memories is the “journal club” held at his home every time manuscripts were ready to be submitted from his laboratory. Beer was plentiful and we usually drank 1 or 2 cans to relax before presenting our manuscripts. We then freely exchanged our opinions, just like at a laboratory party. He really enjoyed the atmosphere, and we were also intoxicated by his sense of humor.

Outside of medicine, Professor Vanhoutte was a devoted husband, father, and grandfather. He married Jacqueline Vandenberghe in 1966 at the age of 26; their union was blessed by the birth of 4 children, followed by 7 grandchildren. In 2009, when interviewed by the *European Heart Journal* with the question “What was the best decision you have ever made?”, he quoted ‘In the shadow of every great man is a great woman’ [and a very surprised mother-in-law!], which had been his experience.²⁶ He also mentioned that without Jacqueline's constant and loving support, nothing would have been possible for him. He lived well, enjoying good food, good wine, good laughs, and sometimes a cigar. We are honored and fortunate to have accompanied him on his scientific journey.

Professor Vanhoutte continues to be with us.

Conflicts of Interest

None.

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