Obituary

John R. Vane (1927–2004)

Sir John Robert Vane, who died on 19 November 2004, was one of the most distinguished British pharmacologists of all time. His greatest scientific achievement was the invention of the blood-bathed superfusion bioassay technique and its application to a number of seminal discoveries.

Vane used to enjoy saying that “bioassay measures biological activity” — an apparently tautological statement that hides the tremendous potential of the technique. For many years, pharmacological bioassay had been mainly carried out by immersing a piece of tissue in a physiological solution and studying its responses to biologically active agents. This method was taken further by B. Finkelman in the 1930s and J. H. Gaddum in the 1950s, who both developed the idea that a tissue could be superfused rather than bathed in a physiological solution, thereby increasing the sensitivity of the bioassay.

In the 1950s, when Vane was a young researcher at The Royal College of Surgeons, he modified the bioassay system so that different tissues could be suspended, one above the other, with the superfusion fluid flowing over each tissue in turn. By doing so, he developed a system whereby the differential sensitivity of three or four tissues gives a unique ‘fingerprint’ for each substance investigated. Most importantly, this system allowed the immediate detection of previously unrecognized biologically active agents. He also realized that, instead of a physiological solution, blood obtained directly from an animal could be used in an external circulation system for the instantaneous monitoring of the fate of bioactive materials.

In the early part of his career, Vane studied the way in which vasoactive substances — those that cause dilation or contraction of blood vessels — are handled by the circulation. This led him to propose that the lungs are metabolically active organs involved in controlling the concentration of certain local hormones or ‘autacoids’. This was a major contribution which spawned a great deal of research around the world.

By the early 1970s, Vane’s bioassay technique was regularly used in his laboratory to investigate the generation and fate of such agents as catecholamines, bradykinin, angiotensin and, most significantly, prostaglandins — hormone-like substances, the functions of which are now known to include modulation of

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vascular tone, inflammation and pain. There was also the intriguing discovery of an ephemeral substance, released from the lungs in anaphylactic shock, which was recognized for its ability to contract rabbit aortic strips and was therefore given the acronym RCS (rabbit aorta-contracting substance). The release of this material was inhibited by aspirin-like drugs.

Soon after my arrival in 1971 at The Royal College of Surgeons, Vane invited me to join the project that led to the discovery that aspirin and aspirin-like drugs inhibit prostaglandin biosynthesis. The importance of this finding, undoubtedly Vane’s major contribution to biomedicine, cannot be overstated. Besides clarifying the mechanism of action of a drug widely used as an analgesic and anti-inflammatory agent for almost a hundred years, it pointed the way to treatments for various diseases, and opened avenues of research and drug discovery that are still being explored.

Notably, in 1974 RCS was identified as thromboxane A_2 , which is derived from the same precursors as prostaglandins: it is released from platelets in the blood and has powerful platelet-aggregating properties. This led to the unravelling of the mechanism of the now well-established anti-thrombotic properties of aspirin and to its successful use in the prevention and treatment of cardiovascular diseases. Vane used to muse that the 1969 experiments on RCS had already indicated aspirin’s mechanism of action,

because the responses of the tissues detecting prostaglandins were also reduced following aspirin treatment.

In 1973, Vane joined the Wellcome Foundation as director of research and development worldwide, and so took on responsibility for more than a thousand scientists. This distanced him from direct involvement in research, and he often complained to me privately about the burden of that job as compared with the delights of being close to the bench. Nevertheless, continuing in his footsteps, his group made further discoveries, significantly that of prostacyclin — a prostaglandin produced in the walls of blood vessels that acts as a vasodilator and inhibits platelet aggregation. This was a milestone in our understanding of vascular biology.

In 1985, Vane left Wellcome and returned to academic life. He then not only rebuilt a successful research team but established what is now a prestigious institute, the William Harvey Research Institute at St Bartholomew’s Hospital Medical School in London.

Although essentially a shy man, John Vane was charismatic and approachable, with a talent for creating an atmosphere in which intense work was combined with the most enjoyable social occasions. People from all over the world joined the group and were made to feel welcome — in many cases this led to lifelong friendships. During the years we worked together, some of our most productive discussions and ideas arose at the home of John and his wife Daphne in conversations after lunch or before dinner, or when travelling abroad to meetings.

John was an ingenious, hands-on pharmacologist, able to generate meaningful hypotheses almost effortlessly. Although his early training was in chemistry, he developed a great understanding of biological processes and a keen eye for the behaviour of the tissues in his beloved bioassay. One of his favourite phrases to students describing results they did not understand was “the tissues never lie” — it is the interpretation that can fail. Together with Bengt Samuelsson and Sune Bergström, he was awarded the Nobel Prize in Physiology or Medicine in 1982, and received many other accolades. Science in general, and the British Pharmacological Society and his friends and colleagues in particular, have lost a guiding light.

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