Second John Vane Memorial Symposium on Prostacyclin Science and Pulmonary Vascular Disease

Supported by an unrestricted educational grant from United Therapeutics



30-31 March 2007
Royal Society, London, UK

Co-Chairs

Professor Lewis RubinUniversity of California,
San Diego, USA

Professor Sir Magdi Yacoub, FRSThe Magdi Yacoub Institute,
Imperial College, London, UK



Foreword by Lady Vane

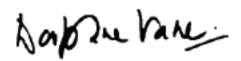
I welcome this Second John Vane Memorial Symposium on Prostacyclin Science and Pulmonary Vascular Disease, which is made possible by an unrestricted educational grant given through the generosity of United Therapeutics (UT).

UT's understanding and appreciation of 'Blue Sky Research' and the vital part it plays for 'life', along with the need to advance it, are well established.

The Symposium offers another significant occasion at which scientists, like artists can 'brush stroke' their ideas, certainties, results and meanderings. These will be the mix for both days.

Lively debates, energetic and colourful, substantial and rewarding in themselves, will bring fresh enthusiasm and from this can spring progress anew. It matters that you, with your contributions, are here now.





The Road to the Discovery of Prostacyclin in the words of John Vane

I was born in Tardebigg, Worcestershire, on the 29th March 1927, one of three children, with an elder sister and brother. My father, Maurice Vane, was a son of immigrants from Russia and my mother, Frances Vane, came from a Worcestershire farming family.

At the age of 12, my parents gave me a chemistry set for Christmas and experimentation soon became a consuming passion in my life. At first, I was able to use a Bunsen burner attached to my mother's gas stove, but the use of the kitchen as a laboratory came to an abrupt end when a minor explosion involving hydrogen sulphide spattered the newly painted decor and changed the colour from blue to dirty green! Shortly afterwards, my father, who ran a small company making portable buildings, erected a wooden shed for me in the garden, fitted with bench, gas and water. This became my first real laboratory, and my chemical experimentation rapidly expanded into new fields.

At High School I progressed through the pure sciences, and in 1944 it seemed natural to move to the University of Birmingham to study Chemistry. However, the enthusiasm with which I had approached experimentation in Chemistry in the garden shed was soon dampened, for at university experimentation was nonexistent. The only unknown in the practical class was the percentage yield in the chemical synthesis involved. It was, I suppose, at this stage that I began to realise that my interest lay not in chemistry but more in experimentation. Thus, when Maurice Stacey, the Professor of Chemistry, asked me what I wanted to do when I graduated, I said "anything but chemistry". Stacey then told me that he had received a letter that morning from Professor Harold Burn in Oxford asking whether he could recommend another young chemist (he had sent one the previous year) to go to Oxford to be trained in pharmacology. Without hesitation I grasped the opportunity and immediately went to the library to find out what pharmacology was all about! That brief exchange with Stacey reshaped my whole career.

I went to Burn's department in 1946. I had no biological training of any sort and very little motivation. I found inspiration in working with him and caught his enthusiasm for pharmacology. If anyone can be said to have moulded the subject of pharmacology around the world, it is he. He did this through his particular style of research, through the lucidity of his writings, but most of all through the school which he founded. Young, impressionable scientists from various disciplines and older, less impressionable pharmacologists all came to work with him. It was Burn who reinforced for me the essence of experimentation and that is, never to ignore the unusual.

After qualifying for a B.Sc. in pharmacology, I went back to Oxford to the Nuffield Institute for Medical Research in order to study for a D. Phil. with Dr. Geoffrey Dawes. In 1951 I was awarded the Stothert Research Fellowship of The Royal Society. Oxford was also an important milestone for it was there that my wife and I made our first home, and it was there that my daughters Nicola and Miranda were born.

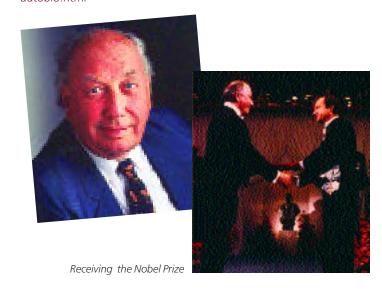
In 1953, we all went to Newhaven, Connecticut where, at the invitation of Dr. Arnold Welch, who was then Chairman, I joined the Department of Pharmacology at Yale University as Assistant Professor in Pharmacology. After two years we returned to the U.K, where I started work with Professor W. D. M. Paton at the Institute of Basic Medical Sciences of the University of London in the Royal College of Surgeons of England. I stayed there for 18 years, progressing from Senior Lecturer to Reader to Professor of Experimental Pharmacology. From 1961 to 1973, Professor G. V. R. Born, a close friend from my Oxford days, was the Chairman of the Department and we enjoyed a strong symbiotic relationship, each maintaining an active group of graduate students and research workers. Interestingly, our fields of research endeavour (platelets and prostaglandins) only coalesced in a significant way after we had both moved on.

It was here that I developed, together with my group, the cascade superfusion bioassay technique for measurement of, dynamically and instantaneously, the release and fate of vasoactive hormones in the circulation or in the perfusion fluid of isolated organs. In the mid-1960's, our attention was focused on prostaglandins, leading in 1971 to the forging of the link between aspirin and the prostaglandins.

In 1973, I was offered the position of Group Research and Development Director for The Wellcome Foundation. I took with me from the Royal College of Surgeons a nucleus of colleagues, and this has expanded into a Prostaglandin Research department. It was in this department that prostacyclin was discovered and its pharmacology developed.

Adapted from Sir John Vane's Nobel Autobiography

 $http://nobelprize.org/nobel_prizes/medicine/laureates/1982/vane-autobio.html\\$



30 March 2007

9am-10am Registration, Tea and Coffee

10am Welcome by Lewis Rubin and Sir Magdi Yacoub

10.10am The Discovery of Prostacyclin

Richard Gryglewski, Jagiellonian University, Crakow, Poland

10.40am Tissue Protection with Prostacyclin and Analogues

Karsten Schrör, University of Düsseldorf, Germany

PAH in Developing Countries

11.10am Overview

Sir Magdi Yacoub, The Magdi Yacoub Institute, Imperial College, London, UK

11.40am Pulmonary Hypertension in Developing Countries

Rogério Souza, University of São Paulo Medical School, Brazil

12.10pm Pulmonary Hypertension in India

Sheila G Haworth CBE, University of London, UK

12.40pm Lunch

Pathophysiology

1.40pm Ion Channels in PAH

Jason Yuan, University of California, San Diego, USA

2.10pm TASK Channels in Pathogenesis in PAH

Andrea Olschewski, Medical University of Graz, Austria

2.40pm RHO-Kinase Pathway and PAH

Paul McLoughlin, University College, Dublin, Ireland

3.10pm Tea and Coffee

3.30pm Role of Endothelin in PAH

Michael Bauer, University of Jena, Germany

4pm BMPR2 Dysfunction in Familial Pulmonary Arterial Hypertension

Nick Morrell, University of Cambridge, UK

4.30pm Effects of BMPs in the Vasculature

Adrian Chester, The Magdi Yacoub Institute, Imperial College, London, UK

5pm Adjournment

7pm Conference Dinner

31 March 2007

Current Treatment Strategies

9-9.30am Tea and Coffee

9.30am Current and Future Management of Chronic Thromboembolic Pulmonary Hypertension:

from Diagnosis to Treatment Responses

Gerald Simonneau, Hospital Antione Beclere, University Paris-Sud, France

10am Manifestations of Pulmonary Hypertension in Childhood

Sheila G Haworth CBE, University of London, UK

10.30am Long-Term Outcomes in Pulmonary Arterial Hypertension Patients Treated with Parenteral Prostacyclin Analogues

Robyn Barst, Columbia University College of Physicians and Surgeons, New York, USA

11am Inhalation Therapy as part of Combination Therapy

Vallerie McLaughlin, University of Michigan, Ann Arbor, USA

11.30am Tea and Coffee

11.50am Combining Prostacyclin and other Remedies

Lewis Rubin, University of California, San Diego, USA

12.20pm Treating Left Heart Disease with Prostacyclin and its Analogues

Robert Bourge, University of Alabama, Birmingham, USA

12.50pm Lunch

1.50pm PDE5 Inhibitors and PAH

Nazzareno Galie, University of Bologna, Italy

2.20pm Clinical Indications for Prostacyclin in Lung Injury/Pulmonary Fibrosis

Jane Mitchell, Imperial College, London, UK

2.50pm Tea and Coffee

New Therapeutic Approaches – Stem Cells

3.10pm Cell Therapy for Acute Lung Injury and ARDS

Duncan Stewart, University of Toronto, Canada

3.40pm Protecting the Heart using Adult Stem Cells - Experimental Evidence

Ken Suzuki, The Magdi Yacoub Institute, Imperial College, London, UK

4.10pm Stem Cells and PAH: An Overview

Nadia Rosenthal, European Molecular Biology Laboratory, Rome, Italy

4.40pm Close

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Delegates and Speakers from the Inaugural John Vane Symposium 2006.

William Harvey Press was established in spring 1996 and since has published Monographs and Highlights of the proceedings of selected conferences organised by William

Harvey Research Conferences.

Monographs and Highlights have been purchased in bulk (5,000 to 20,000) by various pharmaceutical companies.

Abstract books and delegate materials have been printed for all Conferences. In some instances, copies of these materials can be purchased separately from the Conference Office.

We have published five Monographs, which are being sold through

Kluwer Academic Publishers, Netherlands and by Gazelle Book Service, UK.

www.williamharvey.co.uk/whPress/whpress.htm



William Harvey Research Institute



The William Harvey Research Institute

2006 proved to be an exciting year for the William Harvey Research Institute (WHRI). Not only did it herald the Inaugural John Vane Memorial Symposium but it was also the twentieth anniversary of the founding of the Institute by Sir John Vane. During these two

decades WHRI has become world-renowned as a centre of excellence for research, both basic and clinical, in the areas of cardiovascular, inflammation and endocrine disease. WHRI is now ranked as one the leading pharmacological research institutes in the world and has over 200 researchers.

WHRI is delighted that one of the Memorial Symposium's speakers, Ken Suzuki, will be joining its faculty at Charterhouse Square in April 2007. Also in April 2007, an inflammation research group headed by Professor Costantino Pitzalis will be joining WHRI and moving into newly refurbished laboratory space.

Under the current WHRI Director, Professor Mark Caulfield, a state-of-the-art Cardiac Research Centre is presently being constructed at Charterhouse Square on what was the last remaining World War II bombsite in London. It is anticipated that the Cardiac Research Centre will open at the end of 2008 and will provide world-class facilities for research, including clinical trials. The academic clinicians within WHRI provide care for the wide range of ethnic communities represented within the East End of London and this new centre will place special emphasis on research pertaining to their specific healthcare needs. The results of this research will therefore not only benefit the community that WHRI serves but will also have a global impact.

www.whri.qmul.ac.uk



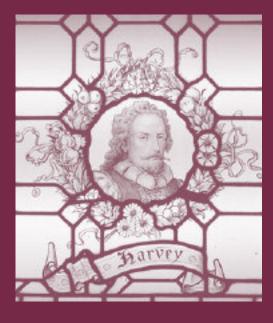
Professor Adrian Smith FRS (Principal of Queen Mary, University of London) and Professor Mark Caulfield (Director of WHRI) at the opening of the new laboratories



Artist's Impression of the Cardiac Research Centre.

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