Spotlight: Paul Leeson, PhD, FRCP, FESC

Providing the First Evidence in Humans of Global Changes in the Heart Evident in Adult Life Related to Preterm Birth

Paul Leeson, professor of cardiovascular medicine, British Heart Foundation senior fellow, and consultant cardiologist, Oxford Cardiovascular Clinical Research Facility, John Radcliffe Hospital, Oxford, England, talks to Mark Nicholls.

Combining research and clinical work is an important balance for Paul Leeson, PhD, FRCP, FESC, professor of cardiovascular medicine, British Heart Foundation senior fellow, and consultant cardiologist, Oxford Cardiovascular Clinical Research Facility, John Radcliffe Hospital, Oxford, England. His hypertension clinic at the John Radcliffe Hospital highlights this balance and is a key link in connecting his research programme with the clinic.

Professor Leeson’s research interests focus on the identification and trialling of novel approaches to cardiovascular prevention and using cardiovascular imaging to understand predisposition to cardiovascular disease. His current research programme is focused on why pregnancy complications, such as preeclampsia, and its associated complications, such as prematurity, predict cardiovascular disease and risk of hypertension for both mother and offspring.

“Both Structural and Functional Cardiovascular Variations Are Evident and in the Right Heart Are at Levels That Can Be Considered Clinically Relevant”

A study by Professor Leeson and his colleagues published in Circulation in early 2013 showed that young adults born preterm have distinct differences in left ventricular mass, function, and geometry,1 and animal studies suggest that cardiomyocyte changes are evident in both ventricles after preterm birth. His group therefore investigated whether young adults born preterm also have differences in their right ventricular structure and function. This led to their most recent article in Circulation titled “Right Ventricular Systolic Dysfunction in Young Adults Born Preterm,”2 for which preterm-born young adults were followed up prospectively since birth. Their right ventricular structure and function quantified by cardiovascular magnetic resonance were compared to those of term-born control subjects born to uncomplicated pregnancies.

Professor Leeson and his colleagues found that preterm birth is associated with global myocardial structural and functional differences in adult life, including smaller right ventricular size and greater mass. These changes are greater in the right ventricle than previously observed in the left ventricle.

Professor Leeson explains, “One of the major complications of pregnancies complicated by preeclampsia is preterm birth. Therefore, we set out to understand whether prematurity might have an impact on cardiovascular health. In particular, we wanted to know whether the unusual and dramatic early transition from in utero to postnatal circulations could have a long-term modelling impact on relatively immature fetal cardiomyocytes. Both structural and functional variations are evident, and in the right heart are at levels that can be considered clinically relevant. This clearly establishes cardiac and vascular variations related to pregnancy history, which we can explore in more detail as we work towards targeted preventive interventions.”

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Funding: French Federation of Cardiology—Abroad

Recipients of French Federation of Cardiology—Abroad scholarships in 2012 describe their experience and research funded by the scholarship. Page f112
One strand of Professor Leeson’s research programme is focused on why pregnancy complications predict cardiovascular disease and risk of hypertension for both mother and offspring. He says, “If we can understand what is going on here and identify how to reverse the risk then we have an opportunity to have an impact on the health of a large proportion of the population: 10% of pregnancies result in preterm birth, and 2% to 5% of all pregnancies are complicated by preeclampsia. Both appear relevant to the cardiovascular health of the mother and her child. Furthermore, they are associated with the development of clinical signs and symptoms at a relatively young age. Up to 1 in 4 women who have had preeclampsia are diagnosed with hypertension within the next 5 to 10 years, and we have recently identified that young adults who were born after their mother had preeclampsia are up to 4 times more likely to be hypertensive in their 20s. This appears to be quite a specific phenotype of hypertensive disease, which raises the opportunity for targeted advice.”

“I Ran the First Analysis, and Within the Fraction of a Second It Took for the Result to Come up on the Screen, I Was Taken From Uncertainty Into Delight, as I Realised the Hypothesis We Wanted to Test Was Right”

Professor Leeson grew up in Leicestershire, England, where his father was a university engineering lecturer and his mother was a teacher. He and his sisters all studied medicine. Professor Leeson studied at the University of St. Andrews, St. Andrews, Scotland, and was awarded a studentship from the UK Medical Research Council to undertake an additional year of research. This encouraged him to apply to the University of Cambridge, Cambridge, England, to study clinical medicine, and he was accepted onto their competitive (and at that time novel) MB/PhD programme.

For his PhD, undertaken during the 1990s, Professor Leeson worked jointly between 2 research groups: with Professor Alan Lucas, MD, FRCP, FRCPCH, at the MRC Dunn Nutrition Unit, Cambridge; and within the Vascular Physiology Unit at Great Ormond Street Hospital, London, England, headed by Professor John Deanfield, MD, BChir, FRCP (see http://circ.ahajournals.org/content/124/21/f121).

Professor Leeson says, “The PhD explored the development of vascular dysfunction in young people, and for part of the research, I worked in the Cardiology Department at Great Ormond Street Hospital. This provided me with an opportunity to carry our research alongside practising cardiologists and see ‘first hand’ the way cardiology is able to combine cutting-edge diagnostics with procedural and pharmacological interventions to make a real difference to the health of patients. This was an exciting time to be working with the groups that were changing the way we understood cardiovascular disease development and defining new ways to study the early stages of disease in humans.”

After the MB/PhD programme, Professor Leeson completed a postdoctoral year at University College London and then went into full-time clinical work for the next 7 years, moving to Oxford to undertake specialist training in cardiology within the Oxford Heart Centre at John Radcliffe Hospital. He says, “During this time I developed subspecialist clinical expertise in cardiovascular imaging and cardiovascular prevention with a particular interest in hypertension. The intention was always to return to a combined clinical and research career, which was made possible through the award of a clinical science fellowship from the British Heart Foundation. This allowed me to take up a post within the University of Oxford and set up my own clinical research programme alongside my work as a consultant cardiologist at the John Radcliffe Hospital.”

In his current position, Professor Leeson combines leading his research group with a busy clinical practice. He explains, “This provides cardiovascular imaging and acute cardiology expertise for the Oxford Heart Centre, as well as a general cardiology and specialist hypertension clinic.”

The importance of combining research and clinical work for Professor Leeson is rooted in an event that occurred at the end of the first project he undertook for his PhD. Having spent 9 months travelling around towns in the United Kingdom collecting cardiovascular measurements from ≈400 schoolchildren from a range of low- and high-income households, he then analysed the data, which led to an article that he regards as among his most important. “I spent several weeks entering the large amounts of data not really expecting to find anything of value,” he recalls. “Then, sitting over the library computer, I ran the first analysis, and within the fraction of a second it took for the result to come up on the screen, I was taken from uncertainty into delight, as I realised the hypothesis we wanted to test was right. From that point on, there was no going back from wanting to combine a clinical career with research to continue to uncover novel and transformative ways of understanding disease development.”

Professor Leeson also has teaching roles centred on the supervision of PhD students and undergraduate students undertaking research projects, which he particularly enjoys. “The process of working with them over several years, guiding them from their early days in research, talking through and developing ideas with them, and then ending up with their first article, and potentially an independent research career, is a rewarding experience,” he says.

Professor Leeson recently graduated from a 2-year part-time course at the University of Oxford, which he did in his spare time. This provided him with an opportunity to study the writings of a breadth of philosophical and theological writers on scientific thought and discovery. He says, “These noncardiology publications have probably had the greatest impact on my work because they define what makes ‘good’ and ‘bad’ science, while also putting in context and reinforcing why we endeavour to push forward clinical research.”

Professor Leeson is acutely aware that research is a team effort. This includes colleagues and senior investigators as well as research nurses, fellows, PhD students, postdocs, and research administration teams, and that the calibre of people he works with defines the calibre of the work produced. He says, “Within Oxford, the calibre is exceptional. One of my
most important roles is to work at building and supporting a team of people who complement each other and will work together to create those exciting synergies that generate new ideas.”

Professor Leeson’s work is funded by the British Heart Foundation, which is “hugely important as the main supporter” of his research, together with additional funds from local funding sources such as the Oxford National Institute for Health Research Biomedical Research Centre and the National Institute for Health Research Local Research Network, as well as commercial companies that support distinct aspects of his group’s programme.

Professor Leeson lives in Oxfordshire with his wife, Susie, and their 4 children between 2 and 11 years of age. “I enjoy it when I can involve the children in my work,” he says. “For example, one of the figures in my echocardiography textbooks was drawn by my eldest daughter when she was 4 years old, although none of my co-authors or the publishers has realised it yet.” Outside medicine, his interests include his family, the sea, playing the piano, and art.

“The key thing that has shaped my career has been the ability of those supervising me to combine strong support for what I was doing, with a willingness to give me freedom to develop my own research ideas,” says Professor Leeson. “At St. Andrews, I received a solid and traditional training in all the science that underlies medicine, as well as a first taste of research, which established my interest in combining clinical work with research; the time in Cambridge and London provided me with unprecedented opportunities to interact with leading research groups in clinical cardiology, which taught me how to present and be excited about research; and the time in Oxford has provided me with all the specialist skills in clinical cardiology and exposure to rigorous, scientific research methodology, with groups that brought together basic and clinical science. Then, at the right moment, Oxford provided institutional backing through the support of Professor Hugh Watkins, PhD, FMedSci, to develop an independent clinical research programme with the financial support of the British Heart Foundation.”

References

Contact details for Professor Leeson:
Oxford Cardiovascular Clinical Research Facility,
University of Oxford, John Radcliffe Hospital, Oxford, UK.
E-mail: paul.leeson@cardiov.ox.ac.uk

Mark Nicholls is a freelance medical journalist.
Funding: French Federation of Cardiology—Abroad

Scholarships of €35 000 to Study Abroad to Acquire New Skills and Develop Strong Cooperation Between French and Foreign Research Centres

Recipients of 2012 French Federation of Cardiology—Abroad scholarships describe their experience and research funded by the scholarship to Jennifer Taylor, BSc, MSc, MPhil.

The French Federation of Cardiology has an annual call for projects to be funded. In 2012, it awarded 13 scholarships of €35 000 each to study abroad to acquire new skills and develop strong cooperation between French and foreign research centres. The projects are reviewed by a scientific committee of 13 cardiology expert researchers and clinicians who work in different regions of France and are proficient across a wide range of specialties.

“I Learned a Great Deal From Adapting to a Different Medical System and Collaborating With Inspiring Professionals”

Valérie Duchatelle, MD, junior staff (chef de clinique-assistant), Hôpital Bichat-Claude Bernard, Paris, France, used her scholarship to work on the clinical trial “Effects of the P-Selectin Antagonist Inclacumab on Myocardial Damage after Percutaneous Coronary Intervention for Non–ST-Segment Elevation Myocardial Infarction.” P-selectin is an adhesion molecule involved in interactions between endothelial cells, platelets, and leukocytes. Inclacumab is a recombinant monoclonal antibody against P-selectin, with anti-inflammatory, antithrombotic, and antiatherogenic properties.

The study took place at the Montreal Heart Institute, Quebec, Canada. Dr Duchatelle spent 16 months working with Jean-Claude Tardif, MD, head of the research department, Philippe L. L’Allier, MD, head of the interventional cardiology department, and Jean-François Tanguay, MD. Statistical analyses were performed by Daniel Cournoyer, MSc, and Marie Claude Guertin, PhD, from the Montreal Heart Institute Coordinating Center.

The scholarship gave Dr Duchatelle the unique opportunity to collaborate with the Montreal Heart Institute. She says, “As a clinician it was interesting to take part in all aspects of the trial, from patient recruitment to statistical analysis, through to coronary intervention.”

She adds, “The Montreal Heart Institute is a highly experienced institution in teaching and research. Its organisation and resources make it possible for you to develop excellent research skills such as formulation and validation of hypothesis, writing skills, data acquisition, and statistical analyses. I learned a great deal from adapting to a different medical system and collaborating with inspiring professionals. Going abroad to do some research is a fantastic way to develop or strengthen links between universities, hospitals, and research foundations to share knowledge and help science make progress.”

Having Seen a Different Organisation of Medical Care Inspired Me to Improve Our Own in Marseille”

Béatrice Bonello, MD, consultant in paediatric cardiology and congenital heart disease, La Timone University Hospital, Marseille, France, used a scholarship to research 4 projects, including 1 to assess latent ventricular dysfunction in asymptomatic patients with repaired tetralogy of Fallot using cardiac magnetic resonance imaging. They used a new postprocessing tool called velocity vector imaging.

The projects were conducted at the Royal Brompton Hospital, London under the supervision of Sonya Babunarayan, MD, PhD in the Magnetic Resonance Imaging Department led by Professor Dudley Pennell, MD, FRCP (see http://circ.ahajournals.org/content/113/11/f41), and Professor Mickael Gatzoulis MD, PhD, academic head of the Adults with Congenital Heart Disease Department.

Dr Bonello says, “From my experience abroad, I had the great opportunity to meet people, and train with experts in the assessment and management of adults with congenital heart disease, which is an emerging subspecialty. For my research project, I had access to their database and was supervised by expert people in research. Having seen a different organisation of medical care inspired me to improve our own in Marseille. A close network between London and Marseille has been created to conduct multi-institutional studies and to discuss management of complex patients with congenital heart disease. The experience abroad was the first stone of a bridge between Marseille and London.”
“I Had the Opportunity to Learn How Research Is Conducted in a High-Level American University”

Laura Ernande, MD, PhD, postdoctoral research fellow, Cardiovascular Research Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA, is using her scholarship to assess the effect of α- and β-stimulation on brown adipose tissue perfusion by a novel in vivo ultrasound method and to determine the coupling of brown adipose tissue perfusion to brown adipose tissue function. Dr Ernande says, “We will establish whether an increase in perfusion without a direct effect on the function of the adipocytes can lead to an increase in brown adipose tissue substrate uptake and thermogenesis.” The project is being conducted in the lab of Marielle Scherrer-Crosbie, MD, PhD, in collaboration with Kenneth Bloch, MD. When she applied for the project, Dr Ernande was chef de clinique-assistant, Service des Explorations Fonctionnelles Cardiovasculaires, Hôpital Louis Pradel, Lyon, France.

Dr Ernande says, “I have been able to benefit from this rewarding experience abroad. I had the opportunity to learn experimental research (whereas my PhD research was clinical), learn how research is conducted in a high-level American university, and discover the United States. This experience was also an opportunity to reinforce the collaboration with Dr Scherrer-Crosbie and Dr Bloch initiated by my mentor Professor Geneviève Derumeaux, MD, PhD, a collaboration I hope to pursue when I am back in France.”

On her return to France, Dr Ernande will take up the position of associate professor (Maître de Conférence des Universités-Praticien Hospitalier), Service des Explorations Fonctionnelles, Hôpital Henri Mondor, Assistance Publique-Hôpitaux de Paris, Créteil, France.

Together, We Recently Began a Multicentre Clinical Study on Atrial Fibrillation Ablation

Anne Rollin, MD, assistant professor, Arrhythmia Care Unit, Toulouse University Hospital, Toulouse, France, used her scholarship to spend 1 year conducting research at the end of her cardiologist training. From May 2011 to May 2012, she worked in the Arrhythmia Care Unit, University Hospital of Lausanne, Lausanne, Switzerland, under the supervision of Etienne Pruvot, MD, Jurg Schlaepfer, MD, and Professor Martin Fromer, PhD. The aim was to collaborate on a study about the arrhythmogenic role of repolarisation alternans in a pacing-induced sheep model of congestive heart failure. This work was realised in collaboration with the Applied Signal Processing Group, Swiss Federal Institute of Technology, Lausanne. Dr Rollin shared her time between fundamental study in the animal lab and clinical practice in the electrophysiological lab. She says, “During this year, I improved my skills in electrophysiology from fundamental to clinical practice. It was also an opportunity to begin a partnership between the Swiss team and my French team. We recently began a multicentre clinical study on atrial fibrillation ablation. This fulfilling experience was only possible thanks to the scholarship.”

“A Great Opportunity to Meet Passionate People With Whom I Wish to Collaborate in the Future”

Florent Le Ven, MD, MSc, clinician and research fellow, Department of Cardiology, University Hospital of Brest, Brest, France, used the scholarship to join, as a clinical and research fellow, the teams of Philippe Pibarot, DVM, PhD, and Éric Larose, DVM, MD, at Québec Heart and Lung Institute, Québec, Canada. The purpose of his research was to examine the determinants, progression, and clinical impact of myocardial remodelling and fibrosis in prospective series of patients with aortic stenosis. Dr Le Ven says, “I benefitted from the fellowship in multiple ways. The multidisciplinary and fertile environment has provided me with in-depth knowledge in valvular heart disease and multimodality imaging. I have also enjoyed my training in research: I have been involved in the design of the study, recruitment of the patients, collection, analysis, and interpretation of the data, and finally presentation at the American Heart Association Scientific Sessions and preparation of the article. The experience has confirmed my will and wish to pursue an academic career when I return to the University Hospital of Brest next year. It has also been a great opportunity to meet passionate people with whom I wish to continue to collaborate in the future.”

“I Hope to Benefit My Workplace After My Return by Continuing Collaborations With the Montreal Heart Institute, Mainly Through Clinical Trials”

François Roubille, MD, PhD, clinician and research fellow, Intensive Care Unit, University Hospital of Montpellier and University of Montpellier I, Montpellier, France, used his scholarship to investigate the impact of the interleukin-1β modulator gevokizumab on neointimal proliferation and reendothelialisation in a rat carotid denudation model. Interleukin-1β is a potent pleiotropic cytokine involved in atherosclerosis and neointimal proliferation.
Dr Roubille is conducting the research at the Montreal Heart Institute, Université de Montréal, in collaboration with Jean-Claude Tardif, MD, FRCPC, Éric Rhéaume, PhD, and David Busseuil, PhD.

Dr Roubille says, “During this period abroad I am improving my knowledge in both preclinical and clinical research in a world-recognised institution. I hope to benefit my workplace (University Hospital of Montpellier) after my return by extending the research themes investigated at the Montreal Heart Institute, providing new clinical trials as a result of completed preclinical studies at the Montreal Heart Institute, and continuing collaborations with the Montreal Heart Institute, mainly through clinical trials.”

“I Benefited From the Team’s Interdisciplinary Approach to the Clinical Management and Empirical Investigation of Adults With Congenital Heart Disease”

Alexandra Soufi, MD, assistante chef de clinique, Department of Paediatric and Congenital Cardiology, Louis Pradel Hospital, University of Lyon, used her scholarship to investigate nonelective inpatient admissions in adult congenital heart disease. The aims were to describe the pattern of inpatient care in terms of patient demographics, diagnostic and treatment history, reason for hospital admission, clinical resource provision, and length of stay; determine which factors were associated with longer length of stay; and investigate whether there were any changes in resource provision between 2004/2005 and 2009/2010.

The research was conducted at the Toronto Congenital Cardiac Center for Adults, Peter Munk Cardiac Center, University Health Network, University of Toronto, Toronto, Canada. Adrienne Kovacs, PhD (psychologist), was the principal investigator. Two cardiologists, Jack Colman, MD, and Erwin Oechslin, MD, and an adult congenital heart disease nurse practitioner, Qunyu Li, were co-investigators.

Dr Soufi says, “During the study abroad experience, I benefitted from the team’s interdisciplinary approach to the clinical management and empirical investigation of adults with congenital heart disease. I developed critical skills in all steps of the research process, including study design, ethics board submission, data collection, data entry, data analysis, and manuscript preparation.”

“This ‘Once in a Lifetime’ Experience Had a Real Impact on My Daily Practice”

Frédéric A. Sebag MD, associate professor (chef de clinique) in electrophysiology, Hopital Henri Mondor, Creteil, France, used his scholarship to work as an electrophysiology fellow at St. Thomas’ Hospital, London, England. During the fellowship his mentors were Matthew Wright, MRCP, PhD, and Mark O’Neill, DPhil, FRCP, FHRS. Dr Sebag says, “They taught me the state of the art of cardiac electrophysiology they had previously learned in the Bordeaux team.”

Dr Sebag and his mentors were interested in patients who were transitioning from paroxysmal to persistent atrial fibrillation and conducted a study to determine whether additional substrate ablation is beneficial for a subset of patients with persistent atrial fibrillation in whom long periods of sinus rhythm can be maintained. They collected data for such patients with the help of Professor Nicolas Lellouche, MD, PhD, at the Henri Mondor Hospital.

Dr Sebag says, “Our interesting results are in press. This ‘once in a lifetime’ experience had a real impact on my daily practice. Indeed, my confidence in the electrophysiology lab has increased as much as my skills in clinical research.”

Jennifer Taylor is a freelance medical journalist.