Research on the psychosocial aspects of cardiovascular disease is at an exciting stage, according to Andrew Steptoe, MA, DPhil, DSc, FMedSci, director, Institute of Epidemiology and Health Care, University College London, London, England, and British Heart Foundation Professor of Psychology, Department of Epidemiology and Public Health, University College London. He explains, “Aetiological research is becoming well established through the integration of high-quality epidemiological work with mechanistic studies that are helping to define more precisely the pathways to cardiovascular pathology. A major need at present is the integration of psychosocial research into the mainstream of pathophysiological understanding.

“Emotional stress is now recognised as a trigger of acute cardiac events in vulnerable individuals, but the implications for primary and secondary prevention have yet to be fully articulated. Interest in the significance of mental distress and depression in patients with coronary heart disease is increasing because current approaches to treatment have had a limited impact on cardiac morbidity. Promising opportunities for multidisciplinary research involving cardiologists, epidemiologists, and behavioural scientists exist to make real progress in understanding disease development and advancing patient care.”

“His Persistence in the Face of Disappointing Results and His Concern to Embed Scientific Research in the Context of Real Human Problems Has Been an Inspiration”

Having a parent who has achieved greatness in a related field can sometimes be a burden. However, this has never been an issue for Professor Steptoe, who completed his doctorate just 3 years before his father, Patrick Steptoe, FRS, CBE, a gynaecologist who combined a busy clinical practice with research, was responsible for the first in vitro fertilisation or test tube baby, with colleague Professor Robert Edwards, PhD. Their work was recognised with the award of the Nobel Prize for physiology or medicine to Robert Edwards in 2010, an event to which Professor Andrew Steptoe and his wife were invited in acknowledgement of his father’s contribution (Patrick Steptoe died in 1988). Professor Steptoe says, “My father was a major influence.
“Individually Vulnerable to Emotional Triggering Show Heightened Blood Pressure and Platelet Responses to Mental Stress”

“I am particularly interested in the mechanisms through which factors such as low socioeconomic status, work stress, depression, or social isolation ‘get under the skin’ to influence coronary heart disease,” Professor Steptoe says. “Two issues are particularly important to my work. The first is the blending of mechanistic experimental research in humans with the larger population perspective. The second is to carry out research on the longer term psychosocial influences on the aetiology of coronary heart disease and the shorter term effects of emotional factors in the acute cardiac events in patients with advanced coronary heart disease.”

“Our mechanistic experimental studies have demonstrated that stress and other factors stimulate acute cardiovascular, inflammatory, and haemostatic responses relevant to the development of atherosclerosis, and they have also shown wide individual differences in the magnitude and duration of these responses. The likelihood that these responses contribute to coronary heart disease depends on people’s exposure to relevant experiences in their everyday lives, factors such as low socioeconomic status, work stress, loneliness, or social isolation.”

“In our work on acute cardiac events, we have extended previous findings that acute emotional stress triggers myocardial infarction in a proportion of patients, demonstrating that individuals vulnerable to emotional triggering show heightened blood pressure and platelet responses to mental stress.”

“Another key issue, which I believe has been neglected, is the acute distress and fear of dying that some patients experience during a myocardial infarction. These emotional responses have inflammatory and neuroendocrine ramifications that are relevant to future adaptation.”

Having spent many years studying miserable aspects of the human experience, such as stress, depression, social deprivation, and hostility, Professor Steptoe says that it has been a particular pleasure over recent years to turn his attention to more positive aspects of life such as happiness and fulfilment. He comments, “Scientific work in this field is challenging because a great deal of nonscientific ‘stuff’ is written about the positive self. In collaboration with Professor Jane Wardle, PhD [his wife and director, Cancer Research UK Health Behaviour Research Centre, University College London], and Professor Sir Michael Marmot, MD, PhD [director of the International Institute for Society and Health, University College London], I have carried out a series of studies documenting the favourable biological correlates of happiness, demonstrating that positive well-being is associated with survival in older people, independently of their initial state of physical and mental health. These studies suggest that there is really something worth exploring in the positive health domain.”
The First Psychologist Appointed to a British Heart Foundation Research Chair

Professor Steptoe describes his move to University College London as the most significant moment of his career. He explains, “First, I was appointed to a research professorship funded by the British Heart Foundation. This was a brave decision because it was the first time that they have appointed a psychologist to a research chair, reflecting the wider recognition of the importance of psychosocial factors in heart disease. It enabled me to reduce my responsibilities as a regular university professor in teaching and administration and focus more actively on research. It has also led me to understand research on psychosocial factors and cardiovascular disease within the broader perspective of diseases of older age, and one of the major challenges facing the modern world, namely, healthy ageing.”

The move also took Professor Steptoe into the field of epidemiology, providing a vital framework for thinking about the significance of research questions for the health of the population and bringing with it a greater sensitivity to sampling issues in recruitment to studies, questions of statistical power, and sophisticated multivariate statistical methods. His motivation for the move was to work with Professor Sir Marmot, who started the Whitehall II epidemiological study and is a leading figure internationally in understanding the social determinants of health and the devastating health consequences of lower socioeconomic position. “Working with him allowed my group to embed many of our mechanistic studies within the Whitehall II study, so we have been able to take advantage of the wealth of data collected on these participants over >20 years,” says Professor Steptoe. “At University College London, I have also benefitted from working with cardiologist Professor John E. Deanfield, FRCP (see http://circ.ahajournals.org/content/124/21/f121), who alerted me to the importance of endothelial dysfunction in cardiovascular disease,14 and with Professor Brian Henderson, PhD, with whom I have studied the links between stress at the cellular and psychological levels.”7,15

Sustained funding from the British Heart Foundation, has supported Professor Steptoe’s central programme of research and vital graduate student training. He also receives funding from the Medical Research Council and Economic and Social Research Council in the United Kingdom, while the National Institute on Aging has supported much of his ageing research.

“A major theme of my work has been the desire to put research on the links between psychological processes and physical health on a sounder scientific foundation,” Professor Steptoe explains. “I am from a generation in
Outside work, Professor Steptoe has been involved with classical music from an early age. He went to the University of Cambridge, Cambridge, England, as an undergraduate with a singing scholarship, and continued to sing for several years. He is keen on the music of Mozart, and he has written 2 books about the composer and his world (shown on the piano).\textsuperscript{17,18} He is also interested in cultural history and creativity from a historical perspective.\textsuperscript{19} He says, “My most recent ambition is to run a half-marathon; never having run more than a couple of miles before, it is proving to be quite demanding.” Photograph courtesy of Professor Steptoe.

which psychoanalytic thinking was replaced with systematic assessments of behaviour, and this change led to the emergence of the disciplines of behavioural medicine and health psychology.”

Professor Steptoe has been involved in the development of behavioural medicine internationally and served as president of the International Society of Behavioral Medicine in the 1990s. He recently edited a handbook that endeavoured to survey current knowledge.\textsuperscript{16}

Professor Steptoe concludes, “Involvement with population cohorts of older people over the past few years has brought me closer to the policy domain because much of our work is used by government analysts and nongovernmental organisations to inform questions of public policy. It has also led me to become an enthusiast for open access to data. The data we collect in the English Longitudinal Study of Ageing are made available to other researchers and analysts within months of collection, and it seems wrong that some scientists restrict access to publicly funded research data and resources until long after their value and timeliness have diminished.”

References


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The Finnish Foundation for Cardiovascular Research awards scholarships each year to Finns to conduct cardiovascular research. In 2012, >50 scientists received scholarships, including Heikki Ruskoaho, MD, PhD, professor of molecular pharmacology, and head, Department of Pharmacology and Toxicology, Institute of Biomedicine, University of Oulu, Oulu, Finland, who was awarded €180000 to investigate epigenetic regulation of cardiac overload-induced hypertrophy and heart failure.

Professor Ruskoaho’s research group includes 3 other senior and postdoc investigators, 12 PhD students, 4 medical and BSc students, and 4 technicians. The funding will provide salaries for a PhD student and a technician for 3 years (from 2012 to 2014). Professor Ruskoaho’s group collaborates with various research groups in Europe and North America. “The specific objectives are to characterise the regulatory mechanisms of transcription factor GATA-4 and its interactions with cofactors in hypertrophied cardiomyocytes,” says Professor Ruskoaho.

Previously, Professor Ruskoaho and his group have reported that reversal of reduced GATA-4 activity prevents adverse postinfarction remodelling through myocardial angiogenesis, antiapoptosis, and stem cell recruitment. The results suggested that GATA-4-based gene transfer may represent a novel, efficient therapeutic approach for heart failure.
“I believe that our future approaches will allow a better understanding of the molecular mechanisms of the development of left ventricular hypertrophy, myocardial injury, and the failing heart,” says Professor Ruskoaho. “Characterisation of key regulators and signalling mechanisms in the pathogenesis of these diseases is also likely to lead to identification of new diagnostic and treatment opportunities.”

Professor Ruskoaho received his doctorate in 1983. He then worked as an Alexander von Humboldt Foundation Research Fellow from 1984 to 1985 with Professor Detlev Ganten, MD, PhD, at the Department of Pharmacology and German Institute for High Blood Pressure, Heidelberg, Germany. After postdoctoral training, he joined the Department of Pharmacology and Toxicology at the University of Oulu, becoming an associate professor in 1989 and full professor in 1996. His research group is a member of the Finnish Centre of Excellence for Cardiovascular and Type 2 Diabetes Research funded by the Academy of Finland from 2008 to 2013.

Professor Ruskoaho’s research interests include cardiovascular drugs, natriuretic peptides, and identification of signalling pathways and targets for the treatment of cardiac hypertrophy and heart failure. His early research involved studies on the mechanisms of action of antihypertensive drugs on cardiac hypertrophy.

Since 1984, Professor Ruskoaho has been working with natriuretic peptides, particularly on the signalling mechanisms of mechanical stretch-induced natriuretic peptide secretion and gene expression. Professor Ruskoaho and his group recently reported that B-type natriuretic peptide gene delivery may be a potential new therapy after infarction and that B-type natriuretic peptide acts locally as a key mechanical load-activated regulator of angiogenesis and fibrosis. Moreover, B-type natriuretic peptide gene delivery had unique pleiotropic, context-dependent, favourable actions on cardiac function.

“It would thus be attractive to develop novel pharmacological therapies for the enhancement of B-type natriuretic peptide function selectively in the heart,” says Professor Ruskoaho. “This article was published in Circulation: Heart Failure and was one of the Editor’s Picks for the year 2011.”

Professor Ruskoaho concludes, “Funding from the Finnish Foundation for Cardiovascular Research has been important throughout my career, for both scientific productivity and training of PhD students.”

References

Jennifer Taylor is a freelance medical journalist.