In the Cardiology Masters section of *European Cardiology Review* we bring you an insight into the career of a key contributor to the field of cardiology.

In this edition, we feature **Professor Keith AA Fox, University of Edinburgh, Scotland, UK.**

Professor Keith AA Fox is Duke of Edinburgh Professor of Cardiology at the University of Edinburgh.

Previous posts included Assistant Professor of Internal Medicine and Cardiology at Washington University School of Medicine, St Louis, USA; Senior Lecturer in Cardiology and Honorary Consultant Cardiologist at the University of Wales College of Medicine, Cardiff; Head of Division of Medical and Radiological Sciences of the University of Edinburgh; British Heart Foundation Professor of Cardiology and Consultant Cardiologist in the Royal Infirmary of Edinburgh.

His awards include the Silver Medal of the European Society of Cardiology (ESC) in 2010 and again in 2014 and the Mackenzie medal of the British Cardiovascular Society in 2013. He gave the American Heart Association (AHA) "Paul Dudley White Lecture" at the AHA Congress in 2015 and was awarded the Gold Medal of the ESC in 2015.

Professor Fox's major research interest is in the mechanisms and manifestation of acute coronary arterial disease and the work extends from underlying biological mechanisms to *in-vitro* and *in-vivo* studies and clinical trials. He is the author of more than 460 scientific papers. He is chair of the RITA studies, Co-Chairman of the Global Registry of Acute Coronary Events (GRACE) Programme and Co-Chairman of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) and Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) studies of Clopidogrel in unstable angina/NSTEMI and other settings. Professor Fox was a lead investigator for studies on novel anti-thrombins. The GRACE Programme is the largest international programme in acute coronary disease. It runs across 14 countries and aims to define patients with acute coronary disease, to understand the time course and the disease process and to raise questions for testing in randomised trials and in basic science.

Cardiology was never forefront on my mind. I grew up in Central Africa in Zimbabwe where my father was a banker and I went to local schools. I always had an interest in the sciences so during a gap year between school and university I worked in the Queen Elizabeth Hospital in Malawi in the labs and trauma outpatient clinic. This fed my enthusiasm to pursue science and was really quite informative.

It was during my degree in immunology and in pathology that I became very interested in mechanisms although at that stage I still had no idea that I would be veering towards cardiology. That said, increasingly I became preoccupied with the fact that about half of those with ST elevation myocardial infarction (STEMI) died within 30 days of their index event, which I found really shocking. Most of the treatments were aimed at just ameliorating the duration of the complications not dealing with the problem; I wanted to do something about it and that led me to specialise in cardiology.

Towards the end of my training in 1981 I decided it would be beneficial to spend some time in the USA so my family and I spent five wonderful years there. I took up a research fellowship at Washington University in St Louis and later joined the faculty. Most of my research at that time was basic science research looking at key mechanisms of myocardial arterial reperfusion and it was here that we produced the original experimental and first clinical studies with tPA for thrombolysis^{1,2} in collaboration with colleagues at the University of Leuven in Belgium. We also instigated early work on imaging and positron emission tomography looking at the myocardium and its recovery.

After five years in the USA I returned to the UK in a senior lecturer role at the University of Wales where I stayed for four years, but it was my next appointment that took me to Edinburgh where I'm currently British Heart Foundation Chair.

I became Duke of Edinburgh Professor of Cardiology at the University of Edinburgh and it was here that a research group lended itself because there were already groups working in labs across the city in disciplines that included genetics, endocrinology and pharmacology, all with a cardiovascular theme.

When I joined the university there were fewer than ten people in cardiovascular research; now there are more than 200, which is enormously gratifying. In fact I'm proud to say that our research department recently won the Queen's Anniversary Prize, the UK's most prestigious form of national recognition open to UK academic or vocational institutions.

During my career, I've been involved in some key international studies but one of the better-known is the Global Registry of Acute Coronary Events (GRACE) Programme (GRACE) study,³ which is the global registry of acute coronary events. I set this up with my co-chair from the University of Massachusetts and we were very fortunate to get leading individuals from around the world to give up their time for nothing to be part of the steering committee.

The reason it was so important was because we had no robust information at that time about the characteristics of acute coronary syndromes, how they were defined, how they were managed and what the outcomes were; this enabled us to identify the high-risk features. We thought the program would last a couple of years but actually it lasted 10 and included 102,000 patients in 30 countries!

It's very rewarding to think that the GRACE risk scoring system continues to be used widely internationally and in guidelines to help in the management of patients with non-ST elevation (NSTEMI) acute coronary syndromes (ACS). It's also embedded in the National Institute for Health and Care Excellence (NICE) guidelines on acute coronary syndromes.

The risk score identifies people by phenotype in terms of baseline characteristics and those who are most at risk of further events, however I think in the future we're going to be able to base it on both

phenotype and bio- and genetic markers to help only treat people who need it; it's about getting effective treatment to those most at risk rather than blanket treatment for the whole population.

Whilst being involved with the likes of GRACE and Randomised Intervention Trial of Unstable Angina (RITA-3) have always been enormously significant and satisfying to me, and have changed the management of acute coronary artery disease from watchful waiting to expediting admission, reducing clotting and treatment by opening up the artery, I've also always strongly felt that as cardiologists we must be involved in prevention.

In my spare time I became involved in Action on Smoking and Health (ASH) and am now president of the organisation in Scotland. We were delighted to be one of the key lobby groups to get the cessation of smoking in public places through in Scotland and celebrated the 10th anniversary on 26th March this year. It has been a revolution and amazing to see how law-abiding people have been and the impact both on respiratory and cardiovascular disease.

My ambition is to see a smoke free generation; it's not going to be easy but you have to aim high!

Regardless of the progress we've made in cardiology, there's a lot more to do. Some might say that the box is ticked for acute cardiology because the government targets for declining death rates have been exceeded. We have missed out on long-term consequences that occur in people with prior heart attack in those with cardiovascular disease and changing those long-term consequences is of fundamental importance; the possibilities in bespoke treatments for individuals in the future are truly exciting.

One of the really exciting areas that our group in Edinburgh is involved in is identifying plaques that are susceptible to rupture. Cardiology has been predominantly focused on putting out the fire once it has happened, but the exciting potential that we have been working on is identifying inflammation and micro-calcification within the plaque with the aim of preventing rupture in the first place. The critical issue is altering the balance between repair and progression so the work we are doing aims to favourably shift the balance towards repair and potentially switch off vulnerable plaques. This work is one of the reasons we won the Queen's Anniversary Award, so presumably the reviewers think that what we're doing has potential! ■

1. Bergmann SR, Fox KAA, Ter-Pogossian MM, et al. Clot-selective coronary thrombolysis with tissue-type plasminogen activator. *Science* 1983;**220**:1181–3. PMID: 6602378
2. Van de Werf F, Ludbrook PA, Bergmann SR, et al. Coronary thrombolysis with tissue-type plasminogen activator in patients with evolving myocardial infarction. *N Engl J Med* 1984;**310**:609–3. DOI: 10.1056/NEJM198403083101001; PMID: 6537987
3. Fox KAA, Steg PG, Eagle KA, et al. GRACE Investigators. Decline in rates of death and heart failure in acute coronary syndromes 1999–2006. *JAMA* 2007;**297**:1892–900. DOI: 10.1001/jama.297.17.1892; PMID: 17473299

Written by Harriett Seager, based on an interview with Professor Keith AA Fox available online at www.radcliffecardiology.com/gallery/interview-pioneer-and-award-winning-cardiologist-dr-keith-fox