Profile

Andrew Grace: tackling the rising tide of arrhythmia

As a cardiologist who combines molecular and clinical medicine, Andrew Grace’s rapid progression to become a leading heart rhythm specialist is no surprise to his colleagues. “Few individuals around the globe command cutting-edge insights into genomic medicine while simultaneously caring for the ill and doing practical clinical research”, comments Grace’s collaborator Gust Bardy, Clinical Professor of Medicine at the University of Washington. Based at the UK’s Papworth Hospital, where he is a consultant cardiologist, and Cambridge University, where he leads research on the molecular pathophysiology of cardiac arrhythmias, Grace has had a crucial role in developing technologies for arrhythmia and sudden cardiac death (SCD).

A lead author of The Lancet’s Cardiac Arrhythmia Series, Grace has seen major changes in his chosen field over the years. During medical studies at St Thomas’ Hospital Medical School, London, Grace spent time on the renowned Mead Ward, which gave him insight into physiological approaches to caring for critically ill patients. “The culture of St Thomas’ was very patient-focused and it had a significant impact on all of the students”, he says. In 1983, when Grace was doing his first ward rounds, coronary angioplasty was in its early days and electrophysiology virtually unheard of. “At the time, St Thomas’ didn’t put in pacemakers”, recalls Grace. “The progress in cardiology in general has been remarkable, and today cardiac electrophysiology—which not so long ago was essentially diagnostic—is now often curative. It is very much its own specialty.” As one of six electrophysiologists working in the east of England, Grace is dedicated to correcting arrhythmias and trying to prevent SCD. One of the rewards of this work “is the continuity”, he says. “I have got to know many patients well over the years.”

Although much of his career has been divided between Papworth Hospital and Cambridge University, Grace has also spent time at St George’s Hospital, London, working on arrhythmias with John Camm and Edward Rowland, and as a postdoctoral Fulbright Scholar at the University of California, San Diego. Whilst a registrar at University College Hospital, London, Grace not only met his wife Rachel, a dermatologist with whom he now has four children, but also realised that he wanted to pursue basic research. Yet his interest in basic science was “then viewed as unusual for cardiologists. We were seen by some essentially as technicians passing our time focused on using the newest tools”, he recalls. He persisted, despite some opposition, and has been a member of the Department of Biochemistry in Cambridge since 1989, where he has undertaken pioneering work on the molecular and cellular mechanisms underlying the heartbeat. “Much of this work centred on cardiac ion channels using a range of approaches revolving around stem cell derived mouse models”, he explains. Rowland, now a consultant cardiologist at London’s Heart Hospital, says: “Andrew is one of a rare and valuable breed that has developed programmes that address questions raised by careful clinical observation through cell-based approaches to understanding mechanisms. From his work we know more about why arrhythmias occur, with the potential for new treatments.”

While pacemakers have taken care of symptoms due to slow heartbeats, cases of fast heartbeat remain a serious cause of morbidity that can only be corrected with drugs, devices, or ablation. The past two decades have seen advances in technology to treat these conditions with increasing use of defibrillators and ablation. Grace has played a part in the development of subcutaneous implantable defibrillators—devices that can be implanted under the skin avoiding the problem of indwelling leads in conventional transvenous devices. “Our first task was to work out the exact size of the shock needed to defibrillate the heart in this new location”, says Grace, who predicts this approach, recently approved for use by the US Food and Drug Administration, may eventually become the system of choice for many patients. Bardy, a key member of the project team, values Grace’s contribution: “Andrew embodies the best of academic research, linking molecular insights to manifestations of disease, as well as providing the highest standards of clinical care.”

In the clinic, Grace sees the risk profile of his patients changing: increasing numbers have atrial fibrillation only partly explained by ageing. Accordingly, a current focus of his research is on the metabolic basis of arrhythmia. “Obesity, diabetes, and hypertension need to be controlled if we want to curb this growth”, says Grace. He is also leading work on predicting SCD in young patients using measurements made directly from patients’ hearts and derived from his preclinical models; the idea is to develop this approach and target implantable defibrillators to those whose lives can be saved.

But progress in arrhythmia is not all about technology, and Grace points to the need for new drugs. “Drugs given to people with rapid heartbeats are generally poorly tolerated and potentially toxic”, he explains. “New drugs to tackle increasing patient numbers will be just as essential as more physical approaches using devices and ablation.” Grace sees opportunities and challenges ahead: “Arrhythmia management has been transformed by the application of technology but to provide effective therapy for all our patients we will need to work harder to further understand mechanisms. This can only come by drilling down on the biology and will require community-wide support to allow effective translation to achieve patient benefit.”

Tony Kirby