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CARDIOPULSE

The King and I: royalty, Nobel laureates, and English soccer

In an article exploring the influence of Nobel laureates, Mark Nicholls speaks to the sons and daughter of Hans Krebs, who was awarded the 1953 Nobel Prize, about his influence on their lives and careers.

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Amid the pomp and splendour of the 1953 Nobel Prize Ball, it was a brief conversation between a young boy and the King of Sweden which caught the eye of journalists.

John Krebs, now Lord Krebs and one of the world's leading zoologists, remembers the moment vividly:

> Gustaf VI Adolf was very nice to me. He asked me what I was interested in, and I told him football and that I supported Sheffield United. I have a lovely photograph of me chatting with the king about football.

John and older brother Paul—then 14—also remember staying at the luxurious Grand Hotel in Stockholm, but the central reason for the occasion—his father Hans Krebs award of the Nobel Prize for his discovery of the Citric Acid Cycle—was only of passing interest.

'I was eight and like most young children, focused on my own life', he said. 'I do remember there being a lot of fuss about my father in the newspapers'.

Their sister Helen—11 at the time—recalls the Queen of Sweden and princesses in stunning gowns and tiaras.

Krebs was awarded the Nobel Prize in Physiology or Medicine for discovering the citric acid cycle—a series of chemical reactions used by all aerobic organisms to release stored energy—after fleeing Nazi Germany before World War II because of his Jewish ancestry.

Pressure to succeed

Yet how did having a Nobel laureate for a father impact on their lives, and was there pressure to similarly succeed in science?

Of the three siblings, only John went on to pursue a scientific career, despite their father's intent otherwise. Born in April 1945 in Sheffield, England, where his father headed the University's Department of Biochemistry, the family moved in 1953 when Hans Krebs became head of the Department of Biochemistry in Oxford.

Educated at Oxford University, John became a leading zoologist researching in the field of behavioural ecology of birds. Elected a Fellow of the Royal Society in 1984, he was knighted in 1999 and has published more than 300 papers and 5 books on the science of ecology and behaviour. He entered the British House of Lords in 2007 as an independent peer, was the Principal of Jesus College, Oxford (2005–15) and President of the British Science Association (2012–13). He also served as Chief Executive of the UK's Natural Environment research Council and Chairman of the UK Food Standards Agency.

Wild flowers

But rather than the pure science, it was Hans Krebs' love of botany and gardening that stayed with his offspring.

'All three of us were imbued with the notion that science and asking questions about nature was important', said John. 'That was illustrated when we went on holiday; we would collect and identify plants and take them back to wherever we were staying and press wild flowers'.

Hans Krebs enjoyed English humour but despite being forced to flee the Nazi regime, he did not want to cut off his relationship with post-war Germany.

'We often went on summer holidays to the Bavarian alps but what struck me was that when we were in Germany, he felt very much at home and that fed through to all three of us', said John, who with Paul and Helen were also dispatched to Germany as teenagers to work in research institutes or laboratories to absorb the culture.

Languages rather than sciences were John's favoured subjects, yet his father was keen that he did science A-levels, so he took physics, chemistry, and biology. When hopes of his youngest son studying medicine at university foundered, he relented and enabled John to pursue his interest in natural history.

He went to work at the Max Planck Institute where he came under the influence of Austrian zoologist Konrad Lorenz, who shared the 1973 Nobel Prize in Physiology or Medicine with Nikolaas Tinbergen and Karl von Frisch and is regarded as one of the founders of modern ethology.

'That inspired me to apply to university to study zoology rather than medicine', added John.

Helen, who studied botany as an undergraduate but did not pursue a career in science, embraced her father's love of wild flowers and with her husband regularly recorded wild plants for the Botanical Society of the British Isles. Her daughters subsequently read biochemistry/microbiology at university, the older went into social work, while the

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Clockwise from top left: Hans Krebs in his laboratory at the University of Sheffield; Lord Krebs; Hans Krebs and John (left), Helen and Paul Krebs on holiday collecting orchids in Bavaria; the King of Sweden discussing soccer with the 8-year-old John Krebs at the 1953 Nobel Ball.

younger is a Professor in the University of Edinburgh's Centre for Regenerative Medicine.

Meanwhile Paul had felt similarly pressured to lean towards science, even though his favoured subjects were history, geography, and foreign languages. Under guidance from his father, he obtained a place at Oxford to do chemistry, but later switched courses and studied economics and went into retail, worked on computer systems and later for a lobby group, carrying out media work.

Academic inspiration

While his father subtly exerted influence, John has been happy for his daughters Emma and Georgina find their own way, though both did science A-levels and Emma became a science teacher and Georgina a clinical psychologist.

'When my younger daughter Georgina, who has a clinical and research qualification, finished her PhD, I noticed in her acknowledgement, she very kindly wrote "Dad, you were my inspiration for a career in academia"'.

While becoming an eminent scientist in his own right, John was frequently linked with his father and often asked if he was Hans Krebs' son.

'Although I did not say it, I was often thinking, I am not here as my father's son, I am here as me. Over time I grew out of that but it was slightly irritating'.

But was there pressure to succeed, being the son of Nobel laureate?

'I do not think explicitly', reflected John, 'although when I was doing my PhD, I was working in the Department of Zoology at Oxford with Nikolaas Tinbergen, he called me into his office one day and did a bit of 'cod psychology' on me and said 'you know, John, one of the problems you are going to struggle with in your research career is that you will always be trying to emulate your father but you are never going to succeed because he as such an extraordinary scientist'.

'I was shocked by this because I was completely unaware that I had any thoughts like that. I do not know whether he was right or not but I do think the fact that I was very ambitious in my scientific career and wanted to succeed could somehow, on a subliminal level, have been related to wanting to follow in my father's footsteps, although he is much more distinguished scientist than I have been. I have always regretted that he died three years before I was elected to the Royal Society. He would have been so excited about that'.

Cherished paper

John was inspired by close contact with other Nobel laureates—Tinbergen and Lorenz—but he treasures a memory of working with his father to produce a paper focusing on the question of a universal principle that applies to all living organisms vs. diversity and how you reconcile those two approaches in biological science.

'That was a nice little vignette very late on in my father's career and something that I cherish as a memory of my interaction with him', he said.

Asked how he views Hans Krebs' legacy, he remarked that 'everybody who learns biology at school learned about the Krebs cycle' and also recalls his father's style as a scientist as being 'absolutely persistent' with a 'relentless focus'.

'I think that is what enabled him to make such an important discovery', he added.

John Krebs was instrumental in establishing the Sir Hans Krebs Trust with proceeds from the sale of his father's Nobel medal at auction for £225 000.

His father had received donations—primarily from the Rockefeller Foundation—to re-establish himself in England as a researcher after leaving Germany. The trust, which he chairs, works with CARA (Council for At-Risk Academics) to fund places at UK universities for young scientists forced to flee their homeland.

'I hope my father would have approved of it', concluded John. 'It is a way of recognising what happened to him and reflecting that in the use of the money from his Nobel Prize medal'.

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The expert guide to becoming a cardiovascular clinical trialist

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Faiez Zannad MD, PhD, of the Université de Lorraine, France, has led numerous game-changing clinical trials into heart failure (HF). He talks to CardioPulse about why there's never been a better time to become a trialist and how to find support and training

What route did you take to becoming a clinical trialist?

In the 1990s, I came up with the idea of developing a specific medication for HF and it happened that a senior trialist Bertram Pitt, MD, at the University of Michigan, in the USA had had the same idea. After we talked, he was kind enough to invite me to join his steering committee, which gave me experience and exposure and helped me progress. Some people were lucky to have a mentor who was a major trialist and who got them involved in secondary papers until they became visible and made their way up the ladder. There is no real identified way of getting involved in clinical trials, it is often just serendipitous and needs some persistence. Some fellows work at sites that do lots of trials and they become involved in publishing secondary papers and become visible. However, you can also be a great physician and enrol lots of patients in trials, and never end up on a steering committee. For many, clinical trials are a closed world and we really need to open things up and get senior trialists helping young fellows.

What does the Global Cardio Vascular Clinical Trials Forum (CVCT) do to support aspiring trialists?

We started over 20 years ago with the main objective of organizing an annual meeting. I am one of five directors. CVCT has grown into a real community providing information, forums and contributions from regulators, academics, industry, and others involved in clinical trials. It is now based in Washington, DC, USA, and has a good relationship with the Food and Drug Administration (FDA). CVCT has found that most training programmes are orientated to areas such as interventional cardiology, clinical practice, and imaging, and there is much less opportunity to find similar courses in clinical research and clinical trials. We need to get young people interested in evidence generation and clinical trials science, interpretation, and operational aspects. We need to go beyond courses and programmes that are orientated to methodology, design, and statistics, to offer practical guidance and training that is not covered elsewhere, so we came up with our own Young CVCT initiatives, including a new internship and fellowship.

What are the new initiatives?

We have developed the 'career escalator' that takes place during our annual meeting and involves matching young fellows interested in developing a career in clinical trials with major clinical trialists from academia and industry or from a regulatory background such as the FDA. They typically spend half an hour chatting one-to-one about what they should do in order to get into this area of science and this works well even when we had a virtual meeting in 2020. Another thing is to allow every speaker to nominate a fellow to attend the meeting for free. This has benefitted around 50 fellows so far every year and all of them value attending the meeting because it gives them a unique exposure to stakeholders from various fields including industry, regulators, major journal editors, academics, and investigators. We also have specific courses at the meeting and practical master classes covering topics such as interpreting trials, how to get your manuscript accepted by

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