Cachexia and Cardiology

Stefan Anker, MD, PhD, is a junior professor in Berlin and a clinical research fellow in London whose passion is cachexia research. He discussed his unusual situation with Ingrid Torjesen, BSc.

Dr Stefan Anker is not a typical cardiologist, as his work crosses many fields of medicine and his theories are controversial. He believes that “wasting is about 10 times more important to human society than obesity.” This is not as surprising as it sounds, because his field of expertise is cachexia, a condition found in disease processes from heart failure to cancer.

As a result, Dr Anker’s work takes him into unusual fields for a cardiologist — oncology, gastroenterology, and geriatric medicine, for example. He is also unusual in that his work is based in 2 centres in 2 countries — the Charité Medical School in Berlin, Germany, and the Imperial College School of Medicine at the National Heart and Lung Institute, in London, United Kingdom.

The tremendous potential that Dr Anker’s work has for the development of treatments over a wide spectrum of disease areas was recognised in 2002, when Charité appointed him to the first junior professorship in medicine in Germany.

Dr Anker was born in East Berlin in 1965. He studied medicine at Charité and, as his studies came to an end, the medical school gave him a grant to work in any department he chose for 18 months. It was the early 1990s, and the Berlin Wall had just come down. “At that time, the professor receiving all the new equipment was a cardiology professor, and that promoted the idea of going into cardiology,” Dr Anker said. “But I also chose cardiology because it is something you can do quite a lot with a non-invasive approach, and it is intellectually challenging.”

When he graduated in 1993, he decided to go to the United Kingdom. He contacted Philip Poole-Wilson, MD, FRCP, a professor of cardiology at the National Heart and Lung Institute. As a result, he was given a grant to work for 7 months under the auspices of Andrew Coats, FRCP, professor of clinical cardiology at the same institution, to look at cachexia.

Dr Anker said, “Dr Coats knew there was cachexia in heart failure, and beyond knowing it was something you should have, he did not know much about it. There was not even a definition.”

When the 7 months were up, it was clear that the investigation of cachexia had great potential, and Dr Anker was offered a PhD course, which he began in 1995. It was at around this time that Dr Anker’s wife and child moved back to Berlin so that their son could have a German education; after his family moved, Dr Anker began flying back to Germany every 2 to 3 weeks. Once his PhD was completed in 1997, he had 2 options: Go back to Germany and do clinical training, or stay in London and prioritise clinical research.

“I wanted to put the priority on research and concentrate on noninvasive cardiology,” Dr Anker said. “The credit really goes to my wife for being patient with all this research. I realised having a link with Germany would be a good thing, and I wanted to create a slow transition back, so I persuaded my Berlin home university, Charité, and London to link up and sign an unusual cooperation agreement.” He explained, “What was agreed was like a sliding scale. I would work in the beginning more in England and in the end more in Germany, and since last year I have been working more in Germany.”

The junior professorship that Dr Anker was offered in 2002 was the result of an initiative by the German government, where the recipients receive a 3-year tenure and access to research funding and facilities. Last year this contract was extended for 3 more years until 2008.

Dr Anker explained that cardiology units in England and Germany are very different. “In Germany you have 1 doctor who is the big king with a big kingdom, and he rules absolutely. There can easily be more than 100 beds and 30 doctors under him. In England, a facility would have 6 to 8 consultants, each with 2 or 3 physicians under them. There would be many princes but none of them would be a real king.”

Working with the 2 systems across the 2 countries has its advantages, Dr Anker said. “What I really love about my way of doing things is the freedom. Eighty per cent of the time I can decide where I am, and that allows me to do things at short notice on the academic side.”

His current priority is to recreate a clinical research unit in Berlin with the facilities that he had in London 5 years ago so that he can carry out pathophysiological studies and treatment
research. "We can never have a huge number of patients, so we go into niche areas," he said. The emphasis of the research is on metabolic studies, particularly with insulin sensitivity, muscle, and fat tissue biopsy work. Body composition can be analysed using dual energy absorptiometry.

“One aspect of pathophysiology we are looking at, which is mainly done in London, is treatment research for anaemia, inflammation and cachexia in heart failure,” he said. A key part of the research is looking into the relationship between gut function and inflammation in heart failure; the involvement of endotoxin in the gut and what happens in heart failure; and the relationship between endothelial dysfunction, hypoperfusion in heart failure, and tissue damage in the gut.

Body composition analysis in chronic heart failure (CHF) can be performed using dual energy x-ray absorptiometry

“Our unit is probably the only cardiovascular unit where a heart failure patient can get a bowel biopsy,” Dr Anker said. “We want to study the bowel wall and its function in the context of immune regulation.” He proposes that once the immune response is activated, tissue hypoperfusion in the gut could lead to malabsorption syndrome and consequent weight loss in patients with heart failure.

Dr Anker said most of this part of the research was being conducted in Germany, where he was able to collaborate closely with the gastroenterology department. “I wanted to do this work 6 or 7 years ago in London, but it was almost impossible,” he said. “In London you have specialised hospitals, such as the Brompton for cardiology, the Marsden for cancer, and so on, while in Berlin everything is in one place.”

Dr Anker’s research could have far-reaching benefits and could lead to potential treatments for conditions in many different specialities. He said, “I believe that if you have wasting in human illness, then regardless of the underlying cause, the pathophysiology and the treatment could be very much the same in the future.” As a result, his group is also carrying out intensive pathophysiological studies on patients with cancer and other illnesses associated with cachexia.

“We look for heart failure abnormalities in other cachexias. We have ongoing studies in pancreatic cancer, lung cancer, severe renal failure, chronic obstructive pulmonary disease, and, in the future, liver cirrhosis,” he said. “This is true translational medicine. There is a lot of possible exchange between specialities, and it is under-recognised for finding a source of new initiatives for the benefit of patients.”

The ultimate goal is treatments for all forms of cachexia. “I am extremely keen on using some of our heart failure research in cancer,” Dr Anker said. “There is one common phenomenon in cancer: wasting. If you can prevent or effectively treat cachexia, I believe you can live much longer with cancer.”

Treatments that are successful against cachexia are already being tested across other conditions. In 2003, Dr Anker’s group published a paper in *The Lancet* on the use of an angiotensin-converting enzyme (ACE) inhibitor to successfully prevent cachexia or weight loss in heart failure, and last year saw the first preliminary results of the use of an ACE inhibitor in oncology.

Wasting is a much greater threat to the health of the population than obesity, Dr Anker believes. “Obesity creates problems late in life, and I believe wasting creates problems much sooner in life — much more dramatic problems. I want to collect proper data — huge databases — to show the sceptics. The collection of this data is one of my longer term goals.”

*Ingrid Torjesen is a freelance medical writer.*

**Reference**


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**Assistant Professorships and the Swiss National Science Foundation**

Philipp A. Kaufmann, MD, director of Nuclear Cardiology and professor of Nuclear Medicine and Cardiology at University Hospital Zurich, talked to Jennifer Taylor, BSc, about research professorships.

Young cardiologists in Switzerland wishing to pursue a career in research are being given a boost by the Swiss National Science Foundation (SNSF). Each year the foundation offers a limited number of SNSF assistant professorships to people of any discipline who want to have an academic career. It enables them to form their own group and pursue their own research. It is also important in helping to bridge the gap between the end of training and the availability of a permanent professorship. The grant includes the salary of the applicant, a research grant for team salaries, and a contribution to infrastructure costs.

Paying for their own research enables these young scientists to publish as head of their group as senior author. With
that comes recognition as an independent scientist.

Dr Philipp Kaufmann is board certified in cardiology, nuclear medicine, and internal medicine. He is in the third year of an SNSF assistant professorship, which means he is a member of the faculty of medicine at the University of Zurich and has all the rights and duties of a full professor. He has 1 year left, but his grant is likely to be extended.

Before his professorship, Dr Kaufmann had a Swiss Clinicians Opting for Research (SCORE) grant from the foundation from 1999 to 2000. These grants are for young researchers in clinical medicine. He did this work primarily in Zurich in collaboration with the Hammersmith Hospital in London. Before this he received a grant from the foundation to do a year’s research at the Hammersmith Hospital. The grants are recognised by all the faculties and by the University Hospital in Zurich, and gave Dr Kaufmann a boost to his clinical career, as 20% of his time is spent in clinical work. Ideally, this leaves 80% of his time for research, but the pressures of administrative tasks and lectures mean it is realistically less than this.

Because of the professorship, Dr Kaufmann has been able to build up his own group. He has 2 research fellows paid by the grant, along with a study nurse and a chemist. Helping scientists become independent researchers is one of the primary aims of the grant. All too often, young researchers work on other people’s ideas, whether it be abroad or at home, and it is difficult to break out of this. Having the money to pay your own and your team’s salary, and purchase consumables, enables researchers to pursue their own ideas.

But to obtain a professorship, people need their own ideas and research concept. During the selection process, international experts read an applicant’s curriculum vitae and publications, and then conduct an interview. “They want to find out whether you are presenting your own research or if you are replicating something,” said Dr Kaufmann.

Even the application process is a boost to careers. It includes a letter to the SNSF from the dean of the medical faculty and the director of the university, saying it is important, innovative research. Dr Kaufmann said that this provides “a very comfortable position in the scientific world.” The competition is strong because applicants are competing across all disciplines, including medicine, chemistry, geography, history, mathematics, and philosophy. In the end, only 25 to 30 SNSF assistant professorships are awarded each year within the 5 universities in Switzerland.

The awards are prestigious for the individual and for the university, since competitive funding improves a university’s ranking. In 2005, the University of Zurich received only 2 professorships despite being the largest university in the country. A coaching programme was set up to give advice on how to apply for grants and prepare for the interview. Dr Kaufmann, along with the deputy director of the university, is helping with this process.

The end goal of an SNSF assistant professorship is a fixed academic position at a university in Switzerland, elsewhere in Europe, or in the United States. “The SNSF do not help because they want you to stay in Switzerland, they want you to be successful wherever you are,” Dr Kaufmann pointed out.

During his grant, he is expected to apply for open positions in his field and report back to the foundation on how successful he was. During his SCORE grant he was number 2 for a head of cardiology post, and during his assistant professorship he was placed number 1 for a molecular imaging position. He had to explain why he rejected the latter post, which he says was due to the equipment. Once he has accepted a fixed position — and therefore salary — at a university, he can still apply to the foundation for grants to pay for the salaries of his team and for materials.

The SNSF grant enables Dr Kaufmann to conduct research that will benefit patients directly.

For cardiologists wanting to pursue research, the benefits of this programme are clear: “If you really have the inner fire to want to do research, then you need support,” said Dr Kaufmann. “Getting that grant gives a really big boost to your career. You get the title of professorship, which means your research is respected, and your voice is heard in the faculty of medicine.”

The grant enables him to conduct research that will benefit patients directly. “In Switzerland for many years, clinical research was not supported enough,” he said. “There was either basic science, or clinical work, but nothing in between. We are now filling this gap.”

Because cardiologists are competing equally with other disciplines, winning a grant means “you’ve really made it,” he enthused. Proof of this can be shown by looking at the history of prominent cardiologists in Switzerland. “All of those who are successful cardiologists [in Switzerland] were supported by the SNSF,” commented Dr Kaufmann. “Without that support, it would be very difficult.”

Jennifer Taylor is a freelance medical journalist.

The opinions expressed in Circulation: European Perspectives in Cardiology are not necessarily those of the editors or of the American Heart Association.

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Adults With Congenital Heart Disease

Grown-ups with congenital heart disease in Europe have been described as having a time bomb in their chests. Mark Nicholls discussed the problem with cardiologists who have a special interest.

Grown-ups with congenital heart disease (GUCH) have been described as “the lost tribe” of cardiac surgery. Many of these patients had surgery around 30 years ago that was considered lifelong and fail-safe. Some of these cases have never been followed up, but many are now presenting for revision, sometimes urgently, because many patients are unaware of their deteriorating condition. This situation has arisen because these patients have been lost to the various health systems across Europe, mainly because they regarded themselves as cured or have subconsciously evaded any follow-up processes.

Cardiologists with a special interest in GUCH now want to see greater recognition of the speciality and a better framework for planning health care for this group, with evaluation to ensure care is uniform and to exacting standards. Primary care physicians should be able to identify these patients and bring them back into follow-up in health systems. Some cardiologists with a special interest in GUCH and are a trustee of the GUCH Patients’ Association. She said the ESC Euro Heart Survey discovered more about adults with congenital heart disease. It showed a young population with relatively low mortality but substantial morbidity. It also showed that the care for adults with congenital heart disease has become an established specialty throughout Europe, with guidelines for interventions and with appropriate use of medication adhered to in most cases.

In England, the Department of Health (DoH) is working on a planning guide for services for adults with congenital heart disease to highlight patients’ expectations of the service and to provide advice, guidance, and support for those who commission health care. The DoH will publish its GUCH Guide, which will also recommend indicators of high-quality care, in the spring of 2006. Meanwhile, the UK’s Grown Up Congenital Heart Patients’ Association, based in Ipswich in Suffolk, has undertaken a survey of the levels of service provided by hospitals to help push for better service provision.

In Europe, the European Society of Cardiology (ESC) collected data for the Euro Heart Survey on adult congenital heart disease, which was completed in April 2004. More publications are imminent. Leisa Freeman, FRCP, a consultant cardiologist at the Norfolk and Norwich University Hospital in England, has a special interest in GUCH and is a trustee of the GUCH Patients’ Association. She said the main problems for GUCH patients relate to the repairs carried out in atrial switch and arterial switch operations, with leakage from either the Mustard or Senning procedures.

Dr Freeman said, “Surgical repair for coarctation of the aorta was considered curative and cited merely as past medical history. It is now clear that a repaired coarctation of the aorta is not a benign condition. Not only is it associated with persistent hypertension and premature coronary artery disease, there are important complications relating to the type of repair.”

Dr Freeman explained that many follow-up patients were lost in the transition from paediatric to adult services, and warned that these people have a “ticking time bomb” in their chests. Often, they do not show until they present with other conditions. She described one of her patients, a woman in her 30s, who was 8 months pregnant when an MRI scan happened to reveal an aortic aneurysm; she had to have further corrective surgery. This was detected in time, but others may not be so lucky.

GUCH patients present a Europe-wide challenge. In Holland, for example, it is estimated there are 20 000 adults with congenital heart disease, but only 8000 are seen in hospital clinics.

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But Barbara J.M. Mulder, MD, professor of cardiology at the Academic Medical Center, Amsterdam, who chaired the survey, said that diagnostic procedures in the follow-up of patients were often insufficient. She comments, “Thanks to advances in surgery and other aspects of care, about 85% of infants born with a heart defect now survive into adulthood, versus a mere 15% previously. These patients constitute a rapidly growing population.” But she added that few large-scale data on specific problems and outcomes are available.

Dr Mulder stressed the need to evaluate whether care is provided according to professional standards, not only in a few selected centres, but more widely. The ESC findings could provide a framework for planning health care for this group and for further defining the scope of adult congenital heart disease as a new discipline. Dr Mulder said the survey has allowed her and her colleagues, who see feel works in relative isolation, to see the bigger picture.

Mark Nicholls is a freelance medical journalist.

References