Jindřich Špinar, professor of cardiology and head of the Internal Cardiology Department, University Hospital Brno-Bohunice, Brno-Bohunice, Czech Republic, talks to Mark Nicholls.

Jindřich Špinar, MD, CSc, FESC, professor of cardiology and head of the Internal Cardiology Department, University Hospital Brno-Bohunice, Brno-Bohunice, Czech Republic, has played a key role in screening for cardiovascular diseases in the Czech Republic and establishing cardiac registries across the country in recent years. He has also played a part in seeing through the transition of a health system in a country that has moved from a communist regime to one operating in a thriving free market economy. He combines his role as a clinical cardiologist and head of the Internal Cardiology Department at the University Hospital Brno-Bohunice with his research interests, which have focused on heart failure and drug testing, with a particular interest in comparing angiotensin converting enzyme inhibitors and angiotensin receptor blockers. With his wife, Professor Lenka Špinarová, MD, PhD, FESC, and other colleagues, he has also established a heart transplantation programme in Brno, which now has a 1-year survival rate of 82% and a 10-year survival rate of 65%.

Among Professor Špinar’s most important achievements has been his involvement in establishing the Acute Heart Failure Database registry (www.ahead.registry.cz) in 2006 to monitor the diagnostic methods and treatment of acute heart failure at major clinical centres throughout the Czech Republic. Professor Špinar explains, “The aim is to monitor accurately and responsibly the characteristics, treatment, and prognosis of patients with acute heart failure.” Some 6000 patients with acute heart failure have been included from 7 university hospitals in the Czech Republic, and the mortality results were presented at the European Society of Cardiology Congress in Stockholm, Sweden, in 2010. They are also presented each year at congresses of the Heart Failure Association of the European Society of Cardiology. Before 2005, Professor Špinar’s department took part in international registries, such as the Euro Heart Survey programmes I and II. In 2005, however, Professor Špinar’s department began its own research programme for screening cardiovascular diseases, supported by a grant from the Ministry of Education of the Czech Republic. This includes 6 registries in cardiology.

The Brno registry is a registry documenting all 17,000 inpatients of the Internal Cardiology Department of Brno University Hospital from 2006 to 2009, including 1600 with acute myocardial infarction without heart failure, 500 with acute myocardial infarction and heart failure, and 1000 with heart failure without acute myocardial infarction. The in-hospital mortality rate of these 3 groups was 0.7%, 10.7%, and 8.6%, and the 1-year mortality rate after hospital discharge was 6.4%, 22.1%, and 20.2%. Professor Špinar comments, “In conclusion, acute myocardial infarction without heart failure has a 1-year mortality rate (both in the hospital and after discharge) of <8%, but if heart failure occurs, it is >30%.”

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Other registries include the Pharmacotherapy of Myocardial Infarction (FARIM) registry of outpatients with a history of myocardial infarction, which monitors pharmacotherapy and attainment of target values of blood pressure and cholesterol, and the HOBART registry of heart transplantation candidates. In 2011, the Brno centre started a registry of cardiogenic shock in collaboration with Professors Markku Nieminen, MD, and Veli-Pekka Harjola, MD, PhD, of Helsinki, Finland, and Professor Alexandre Mebazza, MD, PhD, of Paris, France. This registry is part of the EURObservational Research Programme—European Heart Failure Registry, which also started in 2011.

Since 2003, Professor Špinar has collaborated with the Thrombolysis In Myocardial Infarction (TIMI) study group, and was national lead investigator for several international trials—MERLIN, AVANT GUARDE, Platelet Inhibition and Patient Outcomes (PLATO), Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischaemic Events (TRA 2P), SAVOR, Effective Anticoagulation with Factor Xa Next Generation (ENGAGE), SOLID, and PEGASUS. His department was the world’s best enrolling centre in the TRA 2P and ENGAGE trials.

“New Drugs Appeared Within a Few Months, Many of Our Colleagues Gained Experience in Europe and the United States, and Many Foreign Professors Came to Teach Us New Techniques”

Professor Špinar was born in the wine-growing region of Kyjov in the Czech Republic in June 1960. He says, “My parents, my wife, and her parents are all doctors, and my daughter, Monika, is a medical student.” His father, Jindřich Špinar, MD, was an otorhinolaryngologist, and his mother, Zdenka Špinarová, MD, worked in general internal medicine and specialised in diabetology. He says, however, “The main reason I looked for a career in cardiology was due to the influence of 2 teachers [Professor Milos Štejfa and Professor Ivos Dvorak] during medical studies.”

At Masaryk University, Brno, where his wife was a fellow medical student, Professor Špinar won an award as the best student of the medical faculty. He then trained at the University Hospital St. Anne’s in Brno, where he held various positions over 18 years, and particularly enjoyed his work in the intensive care unit and coronary care unit at the 2nd Internal Department. In 2003, he became vice head of the 2nd Internal Clinic and vice dean of the Medical Facility at Masaryk University, and he now teaches at the Medical Faculty and the Pharmaceutical Faculty, Masaryk University. In 2004, he became head of the Internal Cardiology Department at University Hospital Brno-Bohunice, where he specialises in acute and chronic heart failure and hypertension. His department was awarded the title Hypertension Excellence Centre in 2007 and the ISO 9001 certification in 2008.

The revolution in 1989 and the end of communism in the Czech Republic paved the way for new opportunities in health care for Professor Špinar and his colleagues. He says, “The revolution in my country changed the lives of millions of individuals. First of all, we became free, we could travel and we could communicate with our friends and colleagues abroad. We were allowed freedom of speech, not only medical, but also social and political. New drugs appeared on our market within a few months, many of our colleagues gained experience in Europe and the United States, and many foreign professors came to teach us new techniques. We started percutaneous transluminal coronary angioplasty, radiofrequential ablation, and many other interventions at that time. It was a lovely time for us, and we believed in a better future.”

“My Favourite Job Is to Compare ACE Inhibitors and Sartans”

Professor Špinar’s research interests focus on the management of acute and chronic heart failure, ischaemic heart disease, and hypertension. He has published >700 articles in Czech-language and 40 articles in English-language journals, and he has been principle investigator of 20 international studies and is the national coordinator of several clinical studies. He says, “My research interest is mainly drug testing, and my favourite job is to compare ACE [angiotensin converting enzyme] inhibitors and sartans.”
In the mid-1990s, Professor Špinar was involved in a trial comparing losartan and captopril, which became a basis for the Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan (OPTIMAAL) trial. A decade later, his group organised a similar comparison with the multicentre, open-label Comparison of Recommended Doses of ACE Inhibitors and Angiotensin II Receptor Blockers (CORD) study, comparing losartan and ramipril in patients with hypertension. He says, “We randomised 7829 patients with essential hypertension. Both drugs had a similar effect on blood pressure and on metabolic parameters, but adverse events were 8 times less frequent after losartan than after ramipril.”

Professor Špinar says that the research testing losartan in acute myocardial infarction and the Moxpiplril and Regression of Left Ventricle Hypertrophy in Combination Therapy (MORE) and CORD studies were the most important and the most enjoyable. His team is currently running a trial comparing losartan and ramipril in patients who have metabolic syndrome and hypertension.” He says, “Because these patients have metabolic syndrome and hypertension, a combination treatment of hypertension is necessary, so there is a second randomisation for either amlodipine or hydrochlorothiazide.”

Professor Špinar is particularly proud of the heart transplantation programme in Brno, which he has been involved with since its inception. With Professor Jirí Toman, MD, he visited Professor Richard Pacher, MD, and Brigitte Stanek, MD, in Vienna, Austria, in 1992, and from that started the heart transplantation programme in Brno with surgeon, Professor Jan Černý, MD. He adds, “The head of the heart transplantation programme today is my wife, Professor Lenka Špinarová, and we perform ≈25 heart transplantations per year. Our 1-year survival rate is 82% and the 10-year survival rate is 65%. As part of the programme, the team has conducted several trials with prostaglandins in patients with severe heart failure, together with Professor Pacher.”

Professor Špinar is scientific secretary of the Czech Society of Hypertension, vice head of the Czech Accreditation Committee Cardiology, and between 2002 and 2005 was head of the Czech grant committee of the Ministry of Health. He cites his best friend and collaborator in cardiology, Professor Jiří Vitovec, MD, PhD, FESC, as a key influence, as well as his wife. Influential collaborators include Professor Mebazza, with whom he organises registries of acute heart failure; Professor Pacher, with whom he collaborates in areas of research in the field of severe heart failure; and Professor Eugene Braunwald, MD, Brigham and Women's Hospital, Boston, MA, of the TIMI group. Professor Špinar adds that his 7 editions of "Braunwald's Heart Disease" are among the works that have had the most impact on his career and the way he thinks.

Selected References

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Mark Nicholls is a freelance medical journalist.
Funding: International Society for Heart Research, European Section/Servier Research Fellowship

€20,000 “for Travelling to Meetings, to Buy Antibodies, and to Pay Microscopy Fees”

Atsuko Kasahara, PhD, postdoctoral fellow, Department of Cell Physiology and Metabolism, University of Geneva Medical School, Geneva, Switzerland, talks to Jennifer Taylor, BSc, MSc, MPhil.

Atsuko Kasahara, PhD, postdoctoral fellow, Department of Cell Physiology and Metabolism, University of Geneva Medical School, Geneva, Switzerland, received the International Society for Heart Research, European Section/Servier Research Fellowship in 2010 at a European Society of Cardiology Frontiers in Cardiovascular Biology meeting in Berlin, Germany. It provided €20,000 for a 1-year postdoc. “I’m using this money for travelling to meetings, to buy antibodies, and to pay microscopy fees,” she says.

As a result, Dr Kasahara was able to present her recent data at the UK National Stem Cell Network congress at the University of York, York, England, in March 2011, and at the European Molecular Biology Organisation conference on stem cells in April 2011 at the Institut Pasteur, Paris, France. She also recently attended a joint meeting of the British Society for Cardiovascular Research, the British Atherosclerosis Society, and the British Cardiovascular Society in Manchester, England, on stem cells, where she had useful discussions.

“I Have Been Working to Generate a Mouse Model That Has a Mitochondrial DNA Point Mutation and Characterised the Phenotype of This Mouse Model, Which Corresponds to Human Mitochondrial Disease”

Dr Kasahara’s postdoctoral fellowship research focuses on how mitochondrial morphology affects cardiomyocyte differentiation in mouse embryonic stem cells. She explains, “The mitochondrial shape is controlled by several proteins, and we downregulate these proteins in embryonic stem cells. We are trying to find out the molecular mechanism that regulates mitochondrial shape during differentiation into cardiomyocytes.”

Dr Kasahara’s PhD at the Graduate School of Life and Environmental Sciences, Institute of Biological Sciences, University of Tsukuba, Tsukuba, Japan, investigated mitochondrial DNA mutation. She says, “I have tried to generate a mouse model carrying a missense mitochondrial DNA mutation in cytochrome c oxidase, and found out that this model shows slight lactic acidosis and respiratory impairment.”

In 2008, Dr Kasahara published a behavioural analysis of the mouse model carrying deleted mitochondrial DNA, which revealed that normal mitochondrial respiratory function is necessary for retention and consolidation of memory trace, and that mutations result in impairment of spatial remote memory.

In Geneva, Dr Kasahara is supervised by Professor Luca Scorrano, MD, PhD. After her current project, which she plans to complete within the next year, Dr Kasahara hopes to find a lab post in London, England, because “there are so many good labs in London, especially in the cardiac field.”

Dr Kasahara explains that, although mitochondria are important in all tissues, cardiac cells need more adenosine triphosphate, so cardiovascular researchers are perhaps the most interested in finding out the mechanisms for clinical problems such as ischaemia and reperfusion. Dr Kasahara says, “I am interested in applying my mitochondrial knowledge to this field.”

In addition to the funding, the fellowship provides fostering and advice from experts of the International Society for Heart Research, European Section and at Servier, as well as the opportunity to present the project at the International Society for Heart Research, European Section meeting. Dr Kasahara comments, “It is a really nice opportunity to talk with specialists from the cardiac field.”

Selected References

Jennifer Taylor is a freelance medical journalist.
Funding: International Atherosclerosis Society Visiting Fellowship Award

“I Felt Part of a Broader European Scientific Network About Lipidology and Cardiovascular Research. I Think This Is Important for a Young Researcher”

Tommaso Fasano, MD, specialist in laboratory medicine, Santa Maria Nuova Istituto di Ricovero e Cura a Carattere Scientifico Hospital, Reggio Emilia, Italy, and Department of Biomedical Sciences, University of Modena and Reggio Emilia, talks to Jennifer Taylor, BSc, MSc, MPhil.

Tommaso Fasano, MD, specialist in laboratory medicine, Santa Maria Nuova Istituto di Ricovero e Cura a Carattere Scientifico Hospital, Reggio Emilia, Italy, and collaborating with the Department of Biomedical Sciences, University of Modena and Reggio Emilia, received an International Atherosclerosis Society Visiting Fellowship Award in 2007. He used it to work with Professor Anne K. Soutar, PhD, professor in molecular genetics, Institute of Clinical Science, Imperial College London, London, England.

In late 2007, Dr Fasano was working in the Lipoprotein Group at the Medical Research Council Clinical Sciences Centre, Imperial College London, and he was looking for some financial support that would give him time to finish his work there. He says, “I received the fellowship at the beginning of 2008, and it allowed me to extend my period in London to the summer of the same year.”

Dr Fasano’s field of research at the time was lipidology and metabolism of the low density lipoprotein receptor (LDLR). In particular, he was studying the effect of some genetic variants of the PCSK9 protein on the LDLR. PCSK9 is a protein involved in the degradation of LDLR, and some gain-of-function mutations of PCSK9 were associated with increased degradation of the LDLR and hypercholesterolaemia. On the contrary, some loss-of-function mutations of PCSK9 were associated with a reduced degradation of the LDLR and hypocholesterolaemia. Dr Fasano identified some mutations of the PCSK9 gene leading to hyper- or hypocholesterolaemia in carriers, and his aim during the fellowship was to study their effect on the LDLR protein and to investigate the mechanism of interaction between PCSK9 and the LDLR.

Dr Fasano explains, “I took advantage of the profound knowledge of the LDLR biology that derived from the work that Anne Soutar and her group did in many years at the Lipoprotein Group. I had the opportunity to experience a productive environment and to work with people who have long experience in the field. In particular, Anne Soutar, Xi-Ming Sun, and Dilip Patel helped me in my research, but I also worked with Isabella Tosi, Bronwen Herbert, and Ann Latham. I was able to attend many seminars at the Medical Research Council Clinical Sciences Centre and to exchange ideas with many leading scientists.”

The work led to an article in which Dr Fasano and his colleagues described a new procedure for assessing the activity of 4 putative PCSK9 gain-of-function mutations identified in hypercholesterolaemic patients. All 4 mutant PCSK9 proteins were demonstrated to be more potent than the wild type in reducing cell-surface LDLR, and their ability correlated with total serum cholesterol in patients. Dr Fasano presented his work at the European Lipoprotein Club in Tutzing, Germany, in September 2008.

The application process for the fellowship was quite simple, but a bit time consuming, says Dr Fasano. He had to write an outline of the project that would be conducted during the fellowship and ensure that his department head at the University of Modena, Modena, Italy, Professor Sebastiano Calandra, MD, and Professor Soutar in London were in agreement about the fellowship’s purpose. Documents from both the Italian and English sides were required.

Dr Fasano concludes, “The International Atherosclerosis Society fellowship gave me a great opportunity to improve my knowledge and experience as a young scientist. At the same time, I felt part of a broader European scientific network about lipidology and cardiovascular research, and I think this is important for a young researcher.”

Selected References


Jennifer Taylor is a freelance medical journalist.
Funding: Pfizer Foundation Award for Research

“The Dietary Sodium/Potassium Ratio May Be More Important Than Only Reducing Sodium Intake for Preventing Hypertension and Target Organ Damage”

Qing Wang, MD, research project leader, Service de Néphrologie et D’Hypertension, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland, and professor (adjunct), Huazhong University of Science and Technology, Wuhan, China, talks to Jennifer Taylor, BSc, MSc, MPhil.

The Pfizer Foundation Award for Research, founded in 1991, promotes basic medical research and the development of new and innovative therapeutic approaches in Switzerland. Four awards of at least 30,000 Swiss Francs (CHF) are given for different research areas, 1 of which is cardiovascular medicine, urology and nephrology. Researchers (or research teams) aged <45 years and of any nationality can apply. Winners present their work at an awards ceremony in February the following year.

Qing Wang, MD, research project leader, Service de Néphrologie et D’Hypertension, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland, and professor (adjunct), Huazhong University of Science and Technology, Wuhan, China, who left a post as assistant professor and chair, Department of Physiology, Guangzhou Medical School, Guangzhou, China, in 1996 to join Hans R. Brunner, MD, and his group at the Division of Hypertension, CHUV, received a Pfizer Foundation Award for Research of 50'000 CHF in 2007. Previously, he had invented an implant providing deoxycorticosterone acetate (DOCA) for 3 months to generate a mouse or rat model of salt-sensitive hypertension and cardiac and renal hypertrophy.1 He also developed a fluid-filled catheter for monitoring left ventricular contractility in mice without the need for general anaesthesia.2

In 2002, in collaboration with Professor Brunner, Professor Jürg Nussberger, MD, and Professor Michel Burnier, MD, at the Division of Hypertension, CHUV, and with Dr Edith Hummler, PhD, and Professor Bernard Rossier, MD, at the Institute of Pharmacology, Lausanne University, Dr Wang went on to describe the impact of the number of renin genes (Ren-1 and Ren-2) on blood pressure and on the cardiac and renal response to salt and DOCA in mice.1 He and his coworkers then studied the interactive role of potassium and sodium in the development of target organ remodeling in hypertensive DOCA/salt mice (2-renin genes) or in mice without hypertension (1-renin gene). They found that correction of hypokalemia and metabolic alkalosis with dietary potassium supplementation prevented cardiac hypertrophy and normalised cardiac function independent of blood pressure in normotensive, 1-renin gene, DOCA/salt mice. In 2-renin gene, DOCA/salt hypertensive mice, potassium supplementation also prevented cardiac hypertrophy and left ventricular dysfunction, but the effect could not be dissociated from the decrease in blood pressure.3 He says, “This observation is important for a dietary approach to prevent hypertension and target organ damage among people with a typical high-sodium and low-potassium modern diet.”

Dr Wang believes that reducing the dietary sodium/potassium ratio may be more important than only reducing sodium intake for preventing hypertension and target organ damage. He has started a potassium salt intervention study in China in collaboration with Professor Lisheng Liu, MD, president, World Hypertension League and Chinese Hypertension League, her colleague, Professor Hongye Zhang, MD, Professor Chunming Chen, MD, senior scientific consultant, Chinese Centre for Disease Control and Prevention, Professor Kean Wang, MD, vice-president, Chinese Preventive Medical Association, and other experts.

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Jennifer Taylor is a freelance medical journalist.
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