

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

## European Perspectives in Cardiology



### Spotlight: Serap Erdine, MD



**Pioneering Research in Hypertension and Playing an Active Role in National, European, and International Hypertension Societies**

**Serap Erdine, professor of medicine at Istanbul University, Istanbul, Turkey, and president of the Turkish Society of Hypertension and Atherosclerosis, talks to Judy Ozkan about her life and work.**

Originally from the Anatolian town of Çankırı, about 150 km from the Turkish capital Ankara, Serap Erdine, MD, was raised in a hard-working and loving family environment that valued and encouraged education. Her mother was a primary school teacher and her father was a physics teacher. She says the family ethos of hard work leading to success has stayed with her through her education and professional life.

Professor Erdine's childhood dream to study medicine came true when she won a place at the Cerrahpaşa Medical School, within Istanbul University, one of Turkey's oldest—currently in its 555th year—and most distinguished seats of learning. This also represented a family reunion of sorts because, at that time, Erdine's elder brother (and only sibling) was studying as an undergraduate in the same medical faculty. This signalled the start of a long association between the Erdine siblings and Cerrahpaşa Medical School.

Professor Erdine describes her brother, Serdar Erdine, MD, who also serves as a professor within the Faculty of Medicine at the University of Istanbul, as “like a mentor, an idol, and one of the biggest influences on my life and work.” She says, “I could see that he worked very hard, and that inspired me, as I loved medicine, and to study in the same medical faculty was a dream come true. Now, we are

not only brother and sister, but friends and colleagues.” Professor Serdar Erdine has the distinction of having developed pain relief into a speciality in Turkey known as “Algology,” and he heads up the Department of Algology at the university. He also serves as president of the European Federation of the International Association for the Study of Pain and as president of the International Society of Pain.

#### **A Full Professor of Medicine at Just 36 Years of Age**

Keen to follow in her brother's footsteps, Professor Erdine graduated from Cerrahpaşa Medical School in 1979 with first-class degree honours, and she gained the university medal for being the most outstanding student in her year. She received a prestigious scholarship from the Turkish Scientific and Technical Research Association.

A residency in the Department of Internal Medicine at Cerrahpaşa Medical School followed graduation and lasted until 1984. Between 1986 and 1993, Professor Erdine undertook a fellowship in clinical cardiology at the Cardiology Research Centre, which led to her becoming an associate professor of medicine in 1987 at the age of 30. She then had a guest fellowship in Germany at the University of Grosshadern–München in 1990. In 1993, she became a full professor of medicine at the age of just 36. Becoming a professor at such a young age represented a

#### **On other pages...**

##### **Spotlight: Bortolo Martini, MD**

Dr Bortolo Martini, director of the cardiovascular unit, Boldrini Hospital, Thiene, Italy, talks about his career in cardiology, including his work on arrhythmias in the 1980s at the University of Padua Medical School, Padua, Italy.

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##### **Spotlight: Javier Díez, MD, PhD**

Professor of vascular medicine and director of the Division of Cardiovascular Sciences at the Centre for Applied Medical Research, University of Navarra, Pamplona, Spain, Javier Díez, talks about his work and his strong underlying work ethos.

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great achievement and a source of great satisfaction, though Professor Erdine now recognises that she felt a great deal of pressure to study and pass examinations much earlier than most people would have done. "At the time, it was very hard because I was working all the time and seemed to be constantly preparing for the next exam, but I didn't think so much about it then."

### Research That Is Enhancing the International Reputation of the University of Istanbul

According to Professor Erdine, hypertension in Turkey represents a highly prevalent public health problem that has received inadequate management and resources during the past few decades. Clearly a broad scope for research and development exists in this area in Turkey, and Istanbul University has played a pivotal role in the advances Professor Erdine has made in this field. Professor Cemi Demiroğlu, rector of the University of Istanbul, has enthusiastically supported Professor Erdine's often pioneering work, much of which has enhanced the international reputation of the university as a centre of excellence.

Other important mentors include Giuseppe Mancina, MD, PhD, of the University of Milan-Bicocca, Milan, Italy, the former European Society of Hypertension (ESH) and International Society of Hypertension (ISH) president and chair of the Guidelines Committee, and John Chalmers, MD, past president of the ISH, from Sydney, Australia. Alberto Zancetti, MD, of the University of Milan, and Jose Rodicio, MD, of the University of Madrid, Madrid, Spain, number among international experts who have served as inspiring colleagues along the way.

Professor Erdine has served as a steering committee member and national coordinator of several major clinical and epidemiological studies on hypertension, such as the INVEST (International Verapamil-Trandolapril Study) hypertension map of Turkey. She particularly enjoys her work on the Scientific Council of the ESH, and she regards the opportunity for sharing ideas on a cross-European basis as important for academics and clinicians to help develop solutions to the growing problem of hypertension in Europe.

### Involvement With Guidelines for the Management of Hypertension, and Many Other Important Roles

One of Professor Erdine's most important roles of the past decades has involved her work on the 1993 World Health Organization-ISH and the ESH and European Society of Cardiology Guidelines for the Management of Hypertension, and she has also participated in the subsequent updates in 2003 and 2007, which have helped to establish important standards for doctors across Europe.

Professor Erdine enjoys the challenge of organising meetings and conferences for international colleagues in Turkey. Teaching, both inside and outside the university, represents another important role that takes Professor Erdine all around Europe and, often, further afield.

Professor Erdine has had many important positions in European and Turkish hypertension and cardiology organisations. Since 1999, she has served as president of the Turkish Society of Hypertension and Atherosclerosis, which she helped found in 1991. The society has become an important and influential body since its establishment, and Professor Erdine believes it has had a positive influence on issues of hypertension in Turkey. She served as vice president of the ESH between 2005 and 2007 and as secretary of the board of ESH for European Hypertension Specialists. In addition, she serves as a representative of the ESH in the European Union of Medical Specialists and the European Board for Accreditation in Cardiology.

Between 2000 and 2002, Professor Erdine served as a board member of the European Society of Cardiology and as vice chair of the Working Group on Hypertension and the Heart of the European Society of Cardiology. For Professor Erdine, being vice president of the European Society of Cardiology represented a career highlight.

Despite the high level of commitment these roles demand, as well as constant travel, Professor Erdine feels happy to take an active rather than a passive role across all aspects of her work. She says, "For me, working hard was like a habit which started in the early years of school life; being educated in this way has helped me achieve success."

### Raising the Profile of Hypertension and Coronary Heart Disease in Turkey

Professor Erdine takes pride in having raised the profile and importance of hypertension and coronary heart disease in Turkey. She says, "Since we started the Turkish Society of Hypertension in 1991, there has been a lot more research and resources made available for hypertension. Many more people have now become involved in studying the problem, and this had led to an improvement in levels of hypertension and coronary heart disease in Turkey." The part that the Turkish Society of Hypertension has played in improving Turkey's hypertension and coronary heart disease problems cannot be underestimated, and Professor Erdine believes that the organisation will prove critical to future public health improvements in this area.

In the near future, Professor Erdine will play a lead role in a major European hypertension trial. Looking at the situation across Europe, Professor Erdine feels optimistic that the efforts of academics and clinicians will soon start to have some effect on hypertension as a public health problem. She says, "I believe that the pathophysiological mechanisms of hypertension will be clarified more precisely, and control and prevention of hypertension will ultimately be achieved."

Away from the office, the clinic, and the lecture theatre, Professor Erdine enjoys being an aunt to her young niece who has just started practising as an architect in London. She also finds time for swimming and sailing around the Turkish coast, and she enjoys reading about Turkey's rich and interesting history.

*Judy Ozkan is a freelance medical journalist.*

## Spotlight: Bortolo Martini, MD



**“Life Has Different Pathways, and Mine Drove Me Home to Help my Population”**

**Dr Bortolo Martini, director of the cardiovascular unit, Boldrini Hospital, Thiene, Italy, tells Lindy van den Berghe, BMedSci, BM, BS, about his career in cardiology, including his “8 wonderful years of clinical work and research” in the 1980s at University of Padua Medical School, Padua, Italy.**

Born in 1953 in a small rural village, Grumolo Pedemonte, Veneto, Italy, at the southern border of the Alps Mountains where his ancestor Giovanni, born in Venice, bought a small farm at the end of the 16th century, Bortolo Martini, MD, is the only doctor in his huge extended family of more than 850 living relatives. At the beginning of the 20th century, his family and relatives began to emigrate all over the world, carving out careers in construction and transportation. His father worked as a distinguished cheese maker, and his uncles paved a large part of central Melbourne, Australia.

### **Inspired by Cardiovascular Researchers in Italy, Australia, and the United Kingdom**

Dr Martini's interest in cardiology started on a Sunday afternoon when, as a medical student at University of Padua Medical School, Padua, Italy, he was hitchhiking to Padua. He was given a lift by a young, inspiring, and enthusiastic doctor, Gaetano Thiene, MD, FESC, who now serves as professor of cardiovascular pathology at University of Padua Medical School. The lectures of Sergio Dalla Volta, professor of cardiology at the University of Padua Medical School, further fuelled Dr Martini's interest.

After graduation in 1978, Dr Martini spent a couple of months at the Royal Victoria Hospital in Melbourne with Graeme Sloman, MB, BS, FRACP, professor of cardiology, who introduced him to a deeper understanding of the electrical properties of the heart. After this, Dr Martini gained admission to the cardiology school in Padua, where he carried out mostly clinical work. At the end of the first year, he went abroad again, to St Bartholomew's Hospital, London, United Kingdom, where John Camm, QHP, MD, BSc, FRCP, FRESA, FACC, FCGC, CStJ, and Antony Nathan, MD, FRCP, increased his interest in arrhythmias.

When Dr Martini returned to Padua, he joined the arrhythmologist group directed by Andrea Nava, MD. Dr Martini says, “Dr Nava is the most brilliant and humble scientist I

have ever known. He has made a huge contribution to the understanding of right ventricular dysplasia/cardiomyopathy and polymorphic ventricular tachycardia. At that time, he (with my dear friend Gianfranco Buja, MD) was studying dual nodal pathway and reentry circuit in atrial flutter, but he never published his original findings outside local medical journals.”

### **“Eight Wonderful Years” at University of Padua Medical School**

After a degree in cardiology, Dr Martini worked for a couple of years in the tertiary hospitals of Camposampiero, Veneto, with Attilio Pantaleoni, MD, and also in the hospitals of Bassano del Grappa, Veneto, with Francesco Cucchini, MD, where he carried out electrophysiological studies, implanted pacemakers, and wrote his first articles on the clinicopathological correlations in patients who suddenly died because of conduction defects. In 1983, Dr Martini became assistant professor at University of Padua Medical School, where he spent “8 wonderful years of clinical work and research in arrhythmology, with excellent and caring colleagues.”

At that time, Professor Thiene, helped by Domenico Corrado, MD, FESC, began researching juvenile sudden death, and the group of arrhythmologists started to look for clinicopathological correlations. Dr Martini says, “We



*Photograph of the Padua Group taken 20 years ago. The group was based at University of Padua Medical School, Padua, Italy, and studied the structural basis of arrhythmias. Left to right: G. Thiene, L. Daliento, M. Valente, medical student, G. Buja, F. Marcus, B. Martini, and A. Nava. Courtesy of Dr Martini.*





The first published electrocardiogram of a patient with the syndrome of “sudden death, right bundle branch block, and ST elevation.” This trace, presented by A. Nava, MD, appeared in the published proceedings of a French–Italian congress on electrovectorcardiography, held in Paris. Reproduced with permission from Nava A, Canciani B, Schiavinato ML, Martini B. *La repolarisation precoce dans le précordiales droites: trouble de la conduction intraventriculaire droite? Correlations de l’electrocardiographie-vectorcardiographie avec l’electro-physiologie.* Mises a Jour Cardiologiques. 1988;17:157–159. Courtesy of Dr Martini.

were mostly looking to preexcitation, but Thiene identified an increasing number of cases of right ventricular cardiomyopathy, and Nava, mainly helped by Bruno Canciani, brightly identified many unknown electrocardiographic features of the disease and its familial distribution. The echo and hemodynamic laboratory with Luciano Daliento [MD, FESC, FACC] had a fundamental role in this cooperative study, identifying many of the well-recognised diagnostic patterns.”

“In those years, we were accused of inaccuracy because of the new evidence on the structural basis of most idiopathic ventricular arrhythmias. Among the group, I was charged to investigate the patients with ventricular arrhythmias originating in the right ventricular outflow tract. I published previously unknown data on structural abnormalities underlying idioventricular rhythms originating in this structure (both slow and fast forms).”<sup>1</sup>

Dr Martini adds, “Nava also asked me to examine our data regarding idiopathic ventricular fibrillation, and, exactly 20 years ago in Florence, we presented abstracts on the syndrome of ‘sudden death, right bundle branch block, and ST elevation,’ now known as Brugada syndrome. Our first (still living) patient with the syndrome was a 42-year-old man with a dynamic electrocardiographic pattern, who suffered aborted sudden death while talking with a post officer on October 2, 1984. Soon after the presentation in

Florence, Nava published the first electrocardiogram at a meeting in France, and, 1 year later, a full description of the syndrome was published in the *American Heart Journal*.<sup>[2]</sup> In our evidence-based opinion, the disorder was rare and familial, and the electrocardiographic pattern was due to a conduction delay at the right ventricular outflow tract and a degenerative pathology both of the right ventricle and the conduction system (as documented in all the published necropsy studies). Another feature was an easily inducible ventricular fibrillation when pacing the right ventricular outflow tract. The same syndrome was then reported by Aihara<sup>[3]</sup> and by the Brugada brothers,<sup>[4]</sup> who did not find evidence for any structural abnormality and who classified the disease as a distinct functional abnormality of repolarisation. The resulting scientific controversy<sup>[5]</sup> has led to the publication of more than 1100 articles worldwide.”

### “Life Has Different Pathways, and Mine Drove Me Home to Help my Population”

For the past 10 years, Dr Martini has directed the cardiac unit of Boldrini Hospital, a tertiary hospital in Thiene, 5 km from the village where he was born and where he now lives with his family. He says, “I miss doing research with Andrea Nava and all the colleagues interested in understanding the structural basis of arrhythmias. We could have achieved much more if we had continued working together, but life has different pathways, and mine drove me home to help my population.” But Dr Martini has been pleased to receive appreciative e-mails about his work from friends around the world.

Dr Martini adds, “I cannot now do any significant research in idiopathic arrhythmias because of the limited number of patients. I and my excellent team are participating in a large epidemiological study involving our population, which is affected by a high rate of cardiovascular disease, probably as a result of a German genetic origin (the old Cimbrians defeated by Caius Marius). We are also looking at the prevention of this cardiovascular disease and taking part in a large European trial, EuroAction.”

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Lindy van den Berghe is managing editor of *Circulation: European Perspectives in Cardiology*.

## Spotlight: Javier Díez, MD, PhD



**It “Is Not Just a Matter of Increasing Knowledge” but Also a “Willingness to Apply This Knowledge,” for Example, in Developing Biomarkers and Therapeutic Targets**

**Javier Díez, professor of vascular medicine and director of the Division of Cardiovascular Sciences at the Centre for Applied Medical Research, University of Navarra, Pamplona, Spain, talks to Mark Nicholls.**

As a teacher, scientist, and clinician, Javier Díez, MD, PhD, professor of vascular medicine and director of the Division of Cardiovascular Sciences at the Centre for Applied Medical Research, University of Navarra, Pamplona, Spain, has carried out significant research in a number of areas, most notably in hypertensive heart disease.

Throughout his career, Professor Díez has retained a strong underlying ethos to his work: to translate research into practice, to ensure that he or his colleagues act on any knowledge gained, and to develop a new generation of cardiologists and doctors. He feels proud of the work he has conducted during the past 2 decades, stressing that it “is not just a matter of increasing knowledge” but also a “willingness to apply this knowledge,” for example, in developing biomarkers and therapeutic targets following the molecular pathways to create innovative diagnostic and therapeutic products. “To do this,” explains Professor Díez, “I have worked hard to teach and train basic and clinical scientists in my country to eliminate intellectual barriers and to develop large and intense multidisciplinary teams of cardiovascular investigation.”

### **Time Spent in France and the United States Led to A Career in Cardiovascular Biology**

Graduating from medical school at the University Autónoma of Madrid, Madrid, Spain, in 1976, Díez became a resident in nephrology and internal medicine at the University Clinic of the University of Navarra, Pamplona, Spain. From an early stage, however, Professor Díez had an interest in the mechanisms underlying arterial hypertension and its associated organ damage, particularly hypertensive heart disease; the direction of his career began to form in the 1980s, at a time, he says, when a “notion was emerging in the field of arterial hypertension” that the way to progress to better care of patients would come through more in-depth research of the molecular aspects responsible for the clinical evolution of the patients.

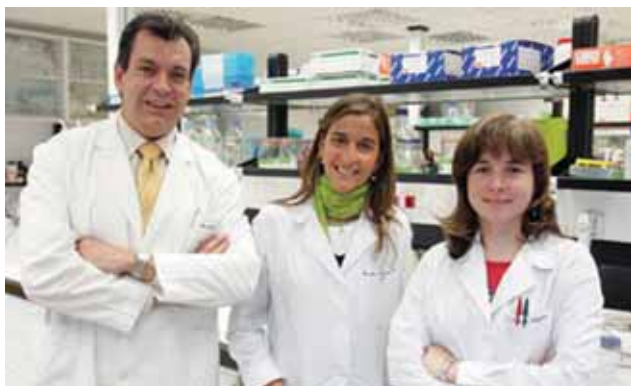
Professor Díez recalls, “I travelled to Paris [France] to an interview with Professor Garay [MD, PhD], who had just described the first alterations in transmembrane ion transport mechanisms potentially involved in both the development and the detrimental consequences of arterial hypertension. I will never forget that his enthusiasm, in combination with his strictness, determined my decision to orientate my career

in the sense of putting the clinical problems under a molecular perspective.” Professor Díez then worked as a research fellow at Necker Hospital, Paris, between 1982 and 1984, and trained in cardiovascular biology at Brigham and Women’s Hospital, Boston, Mass, between 1984 and 1985. In Paris and Boston, he learned the aspects of cardiovascular biology he felt necessary to gain further knowledge of the molecular mechanisms involved in the development of left ventricular hypertrophy and its transition to heart failure in hypertensive patients.

On his return to Spain in 1986, Professor Díez took an appointment as associate professor of medicine and chief of clinical nephrology at the University of Zaragoza, Zaragoza, Spain, later obtaining a tenured position as consultant in the Department of Cardiology at the University Clinic, Navarra. He then became head of a research unit at the university’s Centre of Applied Medical Research and director of the Division of Cardiovascular Sciences in 2001. In 2002, he became full professor of vascular medicine at the School of Medicine; and, from 2005, he has also served as head of the Molecular Cardiology Unit at the University Clinic, Navarra. People who have helped shape his career include Eduardo Ortiz de Landázuri, MD, PhD, and Jesús Prieto, MD, PhD, during his period of clinical training at the University of Navarra; Ricardo Garay, MD, PhD, at Necker Hospital; and Mitzy Canessa, PhD, at Brigham and Women’s Hospital. Professor Díez also cites Edward D. Frolich, MD, from the Alton Ochsner Foundation, New Orleans, La, and Karl T. Weber, MD, from the University of Tennessee, Memphis, Tenn, who played a major role in the translation orientation of his research. He says, “My debt with all of them is not just professional, but also from a human point of view.”

### **A Focus on Translational Research in Arterial Hypertension and Atherothrombosis**

Today, as director of the Division of Cardiovascular Sciences and head of the Molecular Cardiology Unit, Professor Díez’s role involves leading a department of about 50 clinicians and scientists focused on translational research of cardiovascular diseases—namely, arterial hypertension and atherothrombosis. This involves the organisation and development of the scientific work, facilitating the connection between basic and clinical scientists,



Professor Díez (left) with his collaborators Begoña López, PhD, (middle) and Arantxa González, PhD (right). Courtesy of Professor Díez.

and ensuring the availability of required funding. And, as professor of vascular medicine, he takes responsibility for the teaching activities related to the cardiovascular system for students of the School of Medicine and of the educational activities integrated in the programme of continuous medical education that the School of Medicine develops for medical doctor graduates.

Professor Díez's main area of research has focussed on the mechanisms of myocardial remodelling involved in hypertensive heart disease and heart failure, and the work he considers his most important has involved identifying circulating biomarkers of myocardial remodelling;<sup>1</sup> he believes that this has provided new clinical tools for better assessment, diagnosis, and care of patients with hypertensive heart disease. Professor Díez also takes interest in the development of new pharmacological tools in addition to the current antihypertensive treatment to protect the heart in hypertensive patients.<sup>2</sup> In recent years, his interest has also extended to the genetic basis of oxidative stress that makes patients with arterial hypertension prone to develop atherosclerosis.<sup>3</sup>

Professor Díez's work receives 60% funding from the University of Navarra, 30% through public institutions, and 10% from private institutions.

#### Many Awards and Editorial and Advisory Roles

Professor Díez has won a number of awards, including the European Society for Clinical Investigation Pfizer Grant Award for young investigators of the European Society for Clinical Research in 1984, the Parke-Davis Award for achievement in investigation of the Spanish Society of Hypertension in 1995, the Cozaar Angiotensin II Antagonist Investigator Award of the European Society of Hypertension in 2000, and the Mapfre Medicina Award of the Fundación Mapfre, Madrid, Spain, in 2004.

Professor Díez sits on the steering committees of the European Network of Excellence "Integrating Genomics, Clinical Research and Care in Hypertension" and the

Spanish Network of Cardiovascular Research, and he also serves on the Advisory Board of the National Centre for Cardiovascular Research, and he belongs as a member to many other hypertension organisations. In addition he has served as councillor of the European Society of Clinical Investigation and is a past or present member of a variety of editorial boards.

#### "We Live in Promising Times" With "Challenges That, at the Same Time, Can Represent Opportunities"

Professor Díez sees the need to expand research that will lead to better understanding of both the fundamental causes of disease processes and their definitive phenotypic expression, from genomics to environomics. He aims to continue his work in enhancing the understanding of the processes involved in translating research into practice and to "use that understanding to enable improvements in public health and stimulate further scientific discovery." But, challenges lie ahead in the areas of heart failure in hypertension. Professor Díez says, "Appropriate strategies based on new biomarkers of myocardial damage/remodelling must be developed to identify those patients at risk at its asymptomatic stages, or when early structural and functional cardiac abnormalities are identified. In addition, the treatment of hypertensive heart disease must be focussed not just in getting an effective control of blood pressure, but also in achieving the reparation of myocardial structure and the restoration of left ventricular function."

Born in Logroño, La Rioja, Spain, in 1953, Professor Díez lives in Pamplona with his wife, Guadalupe, and they have a son and a daughter. Professor Díez loves Spanish and Latinoamerican poetry, baroque music, and impressionist and Flemish painting. He enjoys basketball and football, and he also jogs, cycles, or swims on most days. And, he remains confident about the future of cardiovascular science. "We live in promising times," he says. "Over the past 2 or 3 decades, we have seen a dramatic decrease in cardiovascular death rates, and the quality of life of patients suffering from these diseases has also been vastly improved."

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