Centre of Excellence: Pitié-Salpêtrière Hospital, Paris, France

“Proud of the Interaction That We Have Been Able to Create Among Surgeons, Cardiologists, Intensivists, and Basic Scientists”

Michel Komajda, head of the Department of Cardiology at Pitié-Salpêtrière Hospital and president-elect of the European Society of Cardiology talks to Ingrid Torjesen, BSc.

The Pitié-Salpêtrière Hospital in Paris, France, has a long distinguished history. It was the birthplace of neurology and heart transplantation in Europe, and today it continues to be a centre of expertise in these areas as well as in oncology. “My hospital was the place where neurology was born—Charcot worked here during the 19th century and he is the pioneer of the specialty,” explains Professor Michel Komajda, MD, president-elect of the European Society of Cardiology and head of the Department of Cardiology at Pitié-Salpêtrière Hospital. “It is also where cardiac transplantation was born in Europe. This was the first centre after [Christian] Barnard [MD] in South Africa. Christian Cabrol [MD] immediately followed him here, and we recently celebrated the 40th anniversary of the first heart transplantation in Europe with all the actors who took part in this pioneering intervention.”

The Pitié-Salpêtrière Hospital is one of the oldest in Paris; both La Pitié and La Salpêtrière were founded as separate hospitals at the beginning of the 17th century. La Pitié was originally a beggars’ asylum, and La Salpêtrière was named after an arsenal that had stood before it and was transferred to the Bastille area of Paris.

In the 17th century the hospitals had no obligation to care for the ill, only to shelter the poor, the disabled, the insane, orphans, abandoned children, the destitute elderly, and women of easy virtue. In 1684, a prison was established in the Salpêtrière for female prisoners and prostitutes. This prison was used until the French Revolution. “Interestingly there is a very curious church inside my hospital with several rooms and several altars,” Professor Komajda reveals. “The reason for this is that they wanted to separate men from women who were in jail when they were going to mass, so the architecture of the chapel is absolutely unique because we have 4 or 5 different altars in 1 single church.”

The 2 hospitals became 1 institution in the 1960s and now the 2000-bed Pitié-Salpêtrière Hospital is by far the largest hospital in its health organisation, the Assistance Publique-Hôpitaux de Paris. This organisation provides for the health needs of the 2.2 million people in the city of Paris and its surrounding suburbs, an area that encompasses ≈10 million people. As a tertiary hospital, Pitié-Salpêtrière also treats patients from other regions of France, from former French colonies in Africa and the Antilles, and from a number of other foreign countries.

In addition to the usual patients with coronary heart diseases, valvular heart diseases, arrhythmias, and heart failure, the hospital sees many complex patients (eg, those with severe coronary artery disease, aortic disease, familial arrhythmias, and advanced/end-stage heart failure). It also specialises in the genetics of cardiomyopathies and familial...
arrhythmias, so a concerted recruitment is being undertaken of patients from families with cardiomyopathies or congenital arrhythmias, and the department hosts a “reference centre” recognised by the Ministry of Health. Professor Komajda says, “We see more serious and severe patients than would be seen, say, in a general hospital.”

The hospital’s cardiovascular activities are divided into 3 departments—cardiac surgery, medical cardiology, and an intensive care unit specialising in the treatment of patients in very critical situations, such as cardiogenic shock. All 3 departments are housed in a single purpose-designed building that opened in 2001. The staff includes 12 professors of cardiology or cardiac surgery, 13 consultant-level doctors whose hospital activity is similar to that of the professors but who have no university responsibilities, and 430 nurses.

An Important Heart Transplantation Centre—the Largest in France and the Seventh Largest in the World

The Surgical Department was the first department of cardiovascular surgery in France. Although ≈70 such surgical centres now exist in the country, the Pitié-Salpêtrière Hospital’s Surgical Department remains the largest in terms of activity, performing >2000 procedures annually. In 2007, it carried out 2069 procedures, including 1446 coronary bypasses, 342 valve replacements, and 105 aortic procedures, in which the unit specialises.

The world’s second heart transplantation was performed at the hospital and >2000 more have been performed at the hospital in the subsequent 40 years. The department is an important heart transplantation centre—the largest in France and the seventh largest in the world. In 2007, it carried out 66 heart transplantations.

The Surgical Department recognises the benefits of being at the forefront of developing surgical techniques, and it is a position it seeks to retain. As a result, clinical research is given a very important role within it. Professor Komajda says, “They are also specialised in cardiac assist devices used in end-stage heart failure. They implanted more than 200 assist devices in 2007, and they will develop this in forthcoming years in conjunction with colleagues specialised in heart failure.” In addition to collaborating with the Cardiology Department on heart failure, the Surgical Department is also collaborating with it on the development of percutaneous valve replacement.

“We Are an Active Clinical Department and We Must Strengthen Research Backing This Clinical Activity”

The Medical Cardiology Department was created ≈50 years ago. Its main activities are the management of acute coronary syndromes and heart failure patients in complex situations. The close working arrangements of heart failure specialists, surgeons specialised in heart transplantation and cardiac assistance, and specialists in cardiac resynchronisation therapy promote their collaboration and have real benefits for the treatment of such complex patients.

The department specialises in the treatment of acute coronary syndrome and, in particular, primary percutaneous coronary intervention for acute myocardial infarction, with a team available to perform percutaneous coronary intervention 24 hours a day, 7 days a week. It performs ≈1200 percutaneous coronary interventions every year. Another area of expertise is the management of complex arrhythmias, and >300 ablations are performed every year. Overall, ≈15 000 cardiology patients are seen each year as outpatients and, in 2007, 1700 patients underwent coronary angiography, ≈8000 echocardiography examinations were performed and >400 had pacemakers or defibrillators implanted.

“Because we are a big centre, we have surgeons, cardiologists, and cardiologists specialised in arrhythmias in the same building, so we tend to specialise in highly complex patients and have a very rapid turnover,” Professor Komajda says. And with Pitié-Salpêtrière being a large university hospital, a lot of research is being undertaken on top of the
clinical care of patients. In cardiology, the research ranges from basic or translational research through to clinical trials.

Research activity in the field of thrombosis and atherosclerosis is led by Gilles Montalescot, MD, PhD, and Jean-Philippe Collet, MD. They are using experimental models of thrombosis to test potential new antithrombotic agents and are also interested in biomarkers of thrombosis, particularly biomarkers of platelets.

Professor Komajda is working with Philippe Charron, MD, PhD, and Eric Villard, PhD, on the genetics of cardiomyopathy. Specifically, they are looking at the genetics of hypertrophic and dilated cardiomyopathy, right ventricular dysplasia, and long-QT syndrome. They are searching for new genes and modifier genes, and they are trying to unravel phenotype–genotype relationships. The department is considered to be the national centre of reference in France for hereditary cardiac diseases, and it has established a European collaboration called the EUROGENE Heart Failure Project, led by Richard Isnard, MD, to help identify the genetic factors associated with the development and progression of heart failure.

A new viral technology will also be developed by the department in collaboration with a partner in the United States to enable cDNA with a modified gene to be transferred into patients to regenerate myocardium.

One research team led by Anne Marie Lompré, PhD, specialises in cell signalling and its potential for new therapeutic approaches for cardiovascular diseases. The team is working with a team in Boston, Mass, looking at the role of the calcium ATPase pump of the cytoplasmic reticulum during cardiovascular remodelling.

Another group led by Stéphane Hatem, MD, PhD, is interested in the physiology and pathology of cardiac excitability and is investigating mechanisms that regulate cardiac ion channels. Research is also taking place on percutaneous valves, and it is hoped that in the future more translational research involving arrhythmias will be conducted.

Professor Komajda emphasises, “We are an active clinical department, and my feeling is that we must strengthen research backing this clinical activity.”

“Having All the Expertise in a Single Building Has Considerably Changed the Modality of Care”

The hospital plans to substantially increase the number of dedicated cardiovascular beds and develop a new multimodality imaging centre, incorporating cardiac scanning with magnetic resonance imaging and cardiac computed tomography. This extension will open in 2010. Professor Komajda says, “We are waiting for this new imaging modality to be put in place in our building, but for the rest I think we are covering more or less all the areas of the cardiovascular diseases. In terms of basic science and translational science, we will continue to engage in atherothrombosis, left ventricular assist devices, and heart failure management of complex patients, cardiac heredity diseases, management of cardiogenic shock, and complex arrhythmias, just to mention a few. We are not a centre specialising in hypertension.”

Moving cardiac surgery, cardiology, and the specialist intensive care unit into a single purpose-designed new building in 2001 set the foundations to enable Pitié-Salpêtrière to meet both the research and clinical care demands required of cardiovascular medicine in the 21st century. Professor Komajda says, “Before we moved to this new building we were in separate places, and I must say that having all the expertise in a single building has considerably changed the modality of care. You have a surgeon or someone specialised in arrhythmia or in percutaneous coronary intervention in the right place in 5 minutes. We are specialised in very sick patients, and I think we are proud of the interaction that we have been able to create among surgeons, cardiologists, intensivists, and basic scientists.”

Ingrid Torjesen is a medical writer and health journalist.
Compared with other inner-city university medical teams, ours is relatively small: 4 full-time physicians assisted by medical residents work in the Department of Cardiology of the Avicenne Hospital, which has 552 beds for a range of medical and surgical specialties and a large emergency department; and 1 physician works in the René Muret Hospital, which has 533 beds and caters for older patients. Many of our patients are socially disadvantaged and live on low incomes. As part of the university, our team is also involved in teaching students, and as a result of our clinical and academic responsibilities, we spend much more time reading *Circulation* than writing for it. Clinical trials and basic research require large amounts of funding and many clinical investigators, which we do not have.”

Further research will be driven by the arrhythmia therapy unit (at Avicenne Hospital) and by a collaboration with the Epidemiological Department of Serge Hercberg, MD, PhD, (Inserm, University Paris-13) on the cardiac and vascular changes associated with aging (SUVIMAX-2 [SUPplement en Vitamines et Minéraux AntioXydants] study: 7200 participants in France). This collaboration involves the René Muret Hospital with 575 participants in the cardiovascular substudy, and 344 cardiovascular and ultrasound examinations have already been completed.”

References

Spotlight: Keith Channon, MD, FRCP

“Making Sure That Our Basic Science Is Clinically Relevant”

Keith Channon, professor of cardiovascular medicine and honorary consultant cardiologist, University of Oxford and John Radcliffe Hospital, Oxford, United Kingdom, immediate past chair of the British Atherosclerosis Society, and director of the Oxford Biomedical Research Centre, talks to Mark Nicholls.

In many instances, as their medical careers develop, cardiologists can sense a swing in emphasis with their work. Some continue to focus on their clinical work whereas others are drawn towards a research role. For Keith Channon, MD, FRCP, however, one of the great challenges of his career has been balancing and maintaining both strands. Although at times it may not have been easy, he states, “I would not do one without the other. I think I would find it dull and unstimulating being a busy clinical doctor without any research component, but equally if I spent my entire life working in a research lab—however exciting the research was—I would miss the clinical interaction, the insights, the challenges, and questions that are raised by looking after patients.”

Born in Lincoln, UK, Professor Channon graduated from the University of Manchester Medical School in 1988 and took his first house officer’s job at Manchester Royal Infirmary. He then switched to the North West Cardiothoracic Centre in the city’s Wythenshawe district for his first cardiology role. He was attracted to cardiology as a practical specialty that was strongly evidence-based from clinical trials with interesting and vibrant scientific research aspects.

He moved to Oxford in 1990, attracted by the “excellent medical and academic research” opportunities. He subsequently met many of the people who were to inspire him and shape his career, including Professor John Ledingham, MD, FRCP, Professor David J. Weatherall, MD, FRCP, and Professor Peter Sleight, MD, FACC. He is also grateful for the influence of clinical consultant cardiologists such as David Bennett, MD, FRCP, FACC, FESC. He says, “These were people I enjoyed working with. They also illustrated to me how medicine should be done, how good clinical medicine should be performed, and how it should interact with high quality research.”

Further shaping of his career came from meetings with Professor Sir John Bell, FRSc, PMedSci, who is now Regius Professor of Medicine at Oxford University and one of the top opinion leaders in scientific medicine in the United Kingdom. At the time, Professor Bell was relatively new in Oxford. “He was young, dynamic, and a successful basic scientist,” says Professor Channon. “He shaped my view that it was important to develop the cardiology side of the career with basic science and molecular biology, and he said if I really wanted to reach ‘the next level’ I should take time out to go and do good quality basic science research. I applied for a British Heart Foundation clinical scientist fellowship, and, looking back, this was one of the most privileged opportunities that I had because when I was awarded that, it gave me 7 years of funding, which as a middle-grade doctor is a long time. In other words, the British Heart Foundation gave enough funding to take me all the way through from trainee to consultant level.”

Significantly, this enabled Channon to attend the Duke University Medical Centre, Durham, NC, to study and be a cardiology fellow and a research fellow between 1993 and 1997. Spending time at one of the leading North American cardiac centres proved a formative experience. He studied vascular biology and endothelial function through basic science research and laboratory-based molecular science. He recalls, “That was a very important learning period, and while I could take advantage of US clinical training—I did the North American medical exams—I tried not to get too distracted in clinical work and aimed to really focus on my scientific investigation. As tends to happen in research, you start broadly and focus down on 1 specific area, and for me that became the biology of nitric oxide synthase.”

“Trying to Explain How and Why Abnormalities of Endothelial Function Are Related to Loss of Nitric Oxide Production Within the Vessel Wall”

In 1997, Channon returned to the University of Oxford as a clinical lecturer based at the John Radcliffe Hospital and completed his clinical training. He says, “That gave me an opportunity to have some protected research time. Having been at Duke for 4 years, I could establish my own research interests; I was given the space and time within the Department of Cardiovascular Medicine, supported by Professor Hugh Watkins, MD, PhD, FRCP, the head of department, who had also recently returned from research training in the United States.”

With funding secured from the British Heart Foundation and elsewhere, he employed a research assistant, took on a PhD student, and continued to focus on his interest, developed at Duke, in endothelial function and the importance of endothelial function in the pathogenesis of vascular disease. This topic has continued to be a key part of his research work, with an emphasis recently on the roles of nitric oxide and superoxide in the early endothelial dysfunction characteristic of preatherosclerotic states. He says, “Recently, the most important work has grown out of trying to explain how and why abnormalities of endothelial function are related to...
loss of nitric oxide production within the vessel wall and the importance of reactive oxygen species. From then on, we became very interested on the requirement of nitric oxide synthase for its cofactor, tetrahydrobiopterin.

Professor Channon says that no particular article has had a specific impact on his research work and his thinking, but he has been greatly influenced and inspired by the work of David Harrison, MD, from Emory University, Atlanta, Ga. He says, “He has been able to bring together fundamental observations with the mechanism of vascular biology, using a range of techniques from molecular biology all the way through to clinical studies.”

Much of Professor Channon’s work is funded by the British Heart Foundation, the Wellcome Trust, and the Medical Research Council. Until last year, he was chair of the British Atherosclerosis Society and remains an active member. He is also a member of the British Cardiovascular Society and conducted the Strickland Goodhall Lecture (for the British Cardiovascular Society) in 2007 and the John French Lecture (for the British Atherosclerosis Society) in 2003.

“Making Sure That Our Basic Science Is Clinically Relevant”

The link between treating the patient and the research laboratory underpins Professor Channon’s career philosophy. He says, “Throughout the last 10 years I have continued to work clinically, [under]taking a high volume of coronary intervention, angioplasty, and stenting while my basic science research has focused on the vascular disease of patients with coronary artery disease who are undergoing stenting or coronary bypass surgery. What I have tried to do is be a fully fledged clinical interventional cardiologist who is largely indistinguishable from full-time clinical colleagues at the hospital and to combine that with running a basic and experimental scientific group. This is to maintain an interaction with cardiac surgeons and clinicians to ensure that our basic science is clinically relevant. We can take advantage of the opportunities that patients present for clinical research in a way that is not possible for pure basic scientists because they are not involved in a clinical setting. In the past few years I have emphasised an overarching overlap between clinical work, clinical research, and basic science research.”

Professor Channon remains acutely aware of the value of collaborating with cardiac surgeons during research initiatives and sees this as adding a further dimension to the research. He says, “Some of our most interesting work has come through collaboration with cardiac surgery colleagues. We would not be able to establish those sorts of genuine interactions very easily if we were not clinically involved.”

In the future, Professor Channon sees cardiologists and cardiac surgeons working more closely together. He explains, “We will see a continuing ‘blurring’ of the distinction between cardiology and cardiac surgery; interventional cardiology will become more interventional with more new and quite revolutionary techniques that can be done without a formal operation, and cardiac surgeons will integrate with cardiologists to work as part of a multidisciplinary team.”

“An Opportunity to Influence Research Strategy”

Combining clinical work and research has moved to a new level in the last couple of years, and significantly in recent months, with Professor Channon’s greater role as director of the Oxford Biomedical Research Centre partnership, established under the National Institute for Health Research. As part of the National Health Service (NHS) health research strategy “Best Research for Best Health,” the aim of the centre is to provide a vibrant world-class environment for conducting and using NHS health research. Oxford is 1 of the 5 centres in the United Kingdom, and in April 2007 it was awarded £57.5 million over 5 years to build research partnerships and expertise.

The Oxford Biomedical Research Centre supports translational research, taking research from the bench to the bedside and making it applicable to everyday NHS care. Initially, Professor Channon led the cardiovascular programme before his current role with the Oxford Biomedical Research Centre, which brings together Oxford Radcliffe Hospitals NHS Trust and the University of Oxford in a research role to connect different scientific disciplines, healthcare professionals, and patients to advance medical research and healthcare delivery. Professor Channon sees his role within the organisation as a natural extension of his career ethos of continuing the 2 strands of clinical work and research. Yet it also takes it to a new level. He says, “The challenge there is that it takes you away from the bench and the outpatient clinic but gives you an opportunity to influence research strategy and to put your efforts into building research infrastructure. For me, it is an important illustration of how I can keep the clinical and research aspect of my career going rather than going one way or the other.”

Professor Channon’s commitment as director of the Oxford Biomedical Research Centre is a step up that will occupy more of his time. But he adds, “My aspiration for the future is to take a leadership role in clinical and basic biomedical research, but I will strive hard not to lose my direct contact with my research and with my clinical practice.”

References

Mark Nicholls is a freelance medical journalist.

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