Spotlight: Michael Böhm, MD, FESC

Investigating the Mechanisms of Atrial and Ventricular Remodelling

Michael Böhm, MD, FESC, professor of internal medicine and cardiology and director of Internal Medicine (Cardiology, Angiology, and Intensive Care Medicine) at the University of the Saarland, Homburg, Saarland, Germany, talks to Jennifer Taylor, BSc, MSc, MPhil.

An interest in the social aspects of medicine, together with a scientific interest in research and the life sciences, impelled Michael Böhm, MD, FESC, professor of internal medicine and cardiology and director of internal medicine (cardiology, angiology, and intensive care medicine) at the University of the Saarland, Homburg, Saarland, Germany, to study medicine. There were no doctors in his family previously. His subsequent specialisation in cardiology arose from the influence of good teachers, an interest in pharmacology—which, by chance, was cardiovascular pharmacology—and a good mentor, namely, Hasso Scholz, MD, PhD, who is now retired but at the time was professor and director of the Institute of Pharmacology in Hamburg-Eppendorf, Hamburg, Germany.

Professor Böhm undertook his medical studies at the Medical School of Hannover, Hannover, Germany, from 1977 to 1984. During that time period, he also trained in pharmacology in the Division of Biochemical Pharmacology, and he completed a doctoral thesis on pharmacology. In 1984, he began a 2-year residency in the Division of General Pharmacology at the University Hospital of Eppendorf of the University of Hamburg. He describes it as the place where, at the age of 24, he “took his first steps.” He says, “I did my first experiments there, so I became interested in cardiology and in cardiovascular research.”

It was in Hamburg that Böhm met Professor Scholz, who taught him the basics of pharmacology and experimental techniques. Together they produced many articles, primarily in pharmacology journals. Research into the anti-adrenergic effect of adenosine receptors resulted in an article in the *Journal of Pharmacology and Experimental Therapeutics* in 1984, which showed that adenosine might protect the heart under metabolic stress conditions from overactivity of the sympathetic nervous system.1

Over the years, Professor Böhm’s research has been recognised with a number of awards, the most important being the Theodor Frerichs Award of the German Society of Internal Medicine, which he received in 1989 for the discovery of mechanisms in heart failure. Throughout his career, he has been funded by the Deutsche Forschungsgemeinschaft (German Research Foundation), which awarded him a Heisenberg stipendium named after the German physicist. Today he has a Deutsche Forschungsgemeinschaft Cardiovascular Research Group, which is a network within the Faculty of Medicine that promotes research on cardiac remodelling.

Showing That the Same Mechanisms Are Also at Work Before Heart Failure Has Fully Developed

Professor Böhm moved to Munich, Germany, in 1986, where he started clinical training in the Department of...
Internal Medicine at the University of Munich, which was chaired by Gerhard Riecker, MD. His mentor during this time was Erland Erdmann, MD, professor of medicine and an enthusiastic scientist involved in the development and characterisation of inotropic agents and mechanisms, in particular those of cardiac glycosides. He was the first to describe a Scatchard plot and conduct binding experiments of digitalis receptors. His passion for research meant that he was supportive of conducting experimental research in the clinical setting. Professor Böhm recalls, “He accompanied me in my first steps of clinical cardiology. He was an excellent motivator for science.”

With Professor Erdmann, Böhm studied positive inotropic mechanisms and β-adrenergic desensitisation of the heart. They found that the β-receptors were downregulated independently from the underlying heart disease, and that there was an increase of inhibitory G proteins and an uncoupling of receptors from stimulatory G proteins. The effects occurred in both human heart failure and different models of cardiac hypertrophy and pressure overload. They also discovered the mechanisms of several new inotropic agents. The work produced a number of articles, including one in Circulation Research in 1989, which showed that the adenosine receptors were functionally coupled to adenylate cyclase to inhibit adrenergic effects. The study was performed in explanted human hearts and was the first characterisation of A1 adenosine receptors in the human heart.

An article in Circulation in 1990 revealed that, in addition to β-adrenergic receptors, there was an increase of inhibitory G proteins that directly depressed adenylate cyclase activity and led to reduced inotropy of the failing heart. This occurred while the coupling and effect of inhibitory receptors were unchanged. A second article in Circulation Research, this one published in 1991, showed that even newer inotropic agents, such as phosphodiesterase inhibitors, had reduced effectiveness in the heart because of a reduction in cyclic AMP generation.

In the next phase of Böhm’s research career, he and Professor Erdmann extended their findings to hypertensive cardiac hypertrophy. This research resulted in several articles in Hypertension. In one article, published in 1995, they found that in hypertensive cardiac hypertrophy, irrespective of blood pressure reduction, there was a resensitisation of cyclic AMP formation. Professor Böhm explains, “It showed that, independent of heart failure, the same mechanisms are also at work before heart failure has fully developed. So they precede heart failure in certain cardiac diseases.”

**“This Could Be a Direct Link From Cardiovascular Risk Factors to Vascular Disease”**

Professor Böhm’s move to the University of Cologne in 1993 brought with it the title of assistant professor of cardiology, a post he held until 2000. During this time period, he switched the focus of his research away from myocardial research and towards vascular biology. He and his colleagues investigated the coupling and regulation of the AT1 angiotensin-II receptor and showed that certain cardiovascular risk factors could increase the expression and function of the AT1 receptor. In 1999, this led to the publication of an article in Circulation showing that low-density lipoprotein cholesterol was able to increase the stability of the messenger RNA and protein expression of angiotensin AT1 receptors in both humans and cellular systems. Professor Böhm explains its significance, saying, “This could be a direct link from cardiovascular risk factors to vascular disease.”

The next step was to look at the mechanism of statins, work that was investigated in several articles in collaboration with Georg Nickenig, MD, and Ulrich Lauß, MD, young investigators in Professor Böhm’s laboratory. They found that statins were able to downregulate the AT1 receptors and have an impact on the small G proteins. In 2000, they published the finding that the small G proteins were regulating nitric oxide synthase and that this was related to the maintenance of nitric oxide formation in diseased vessels. Withdrawing statins led to an acute reduction of nitric oxide formation in the vessels, which they speculated might relate to the rebound effect of statins. In addition, the small G proteins were involved in the positive vascular protective effect of statins.

In the same year [2000], Professor Böhm moved to the University of the Saarland and has since broadened his research interests.

**Advocating the Transfer of Experimental Science to Clinical Trials**

In 2007, Professor Böhm’s group was awarded European Society of Hypertension Centre of Excellence status for its work on hypertensive cardiac hypertrophy. In practice, this means that his group has a strong relationship with other centres in Europe and is able to carry out innovative techniques, such as renal artery sympathectomy. The aims are to form networks for producing innovations, to create networks for clinical trials, and to exchange scientists. He strongly supports more transfer of experimental science to clinical trials. Therefore, he has been involved in a number of major clinical trials investigating cardiac remodelling and heart failure, cardiovascular prevention, and new therapies for hypertension: as the national coordinator for the Carvedilol or Metoprolol European Trial (COMET), the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA), the Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (ONTARGET), the Telmisartan Randomized Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease (TRANSCEND), the Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors With Heart Failure (SENIORS), the Studies of Oral Enoximone Therapy in Advanced Heart Failure (ESSENTIAL); as an executive board member of Systolic Heart Failure Treatment With the If Inhibitor Ivabradine Trial (SHIFT); as a member of the Data Safety Monitoring Board of Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycaemia in Diabetes (RECORD); and...
as a steering committee member of CORONA, ONTARGET, TRANSCEND, SENIORS, and ESSENTIAL.

Professor Böhm is furthering his efforts to promote research on cardiovascular disease through his involvement in the German Cardiac Society. He was on the board for 4 years, became president-elect in 2007, and finally became president in April 2009. During his presidency, he has specifically targeted the problem of funding for cardiovascular research in Germany. Epidemiological data on morbidity and mortality trends show “a huge underfunding when comparing cardiovascular research to other fields, such as oncology, stroke, and infectious disease,” he says. Therefore, the Society has begun an initiative to improve funding and possibly to form a cardiovascular research network within Germany. If funding for cardiovascular research is to be balanced with that of other disease areas, Professor Böhm believes this initiative must be accomplished in the next few years. Negotiations are underway with the German government as to how it might fund such a venture, and Professor Böhm is optimistic that the plans will work. He concedes that some centres will feature more prominently in the network, but he adds, “The major goal is to have the most flexible and effective funding to foster interaction and excellence of research.”

“Basic Research Today Is the Clinical Work of Tomorrow”

Professor Böhm is concerned that the current economic climate could spark changes in healthcare systems. “There is a lot of pressure put on university hospitals in particular for reimbursement of cases,” he says. “And there is the fear that in this world of economic pressure, science and innovations might suffer from some shortcomings. The challenge in Germany and elsewhere will be to maintain young people’s enthusiasm for pursuing cardiovascular research. Which comes back to the point of research funding. The optimal research funding would give doctors the liberty to get time off for research in the clinical setting and to give researchers in basic science the opportunity to learn the demands of medical research,” says Professor Böhm. Well-funded, organised research institutions would have a mix of clinical and basic research, and they would be equipped to translate basic research findings into the clinic and bring clinical ideas back into the basic research laboratory.

In addition to his 2 mentors, Professor Böhm has been influenced by his young collaborators, Georg Nickenig; Ulrich Laufs; Christoph Maack, MD; and Sven Wassmann, MD. He says, “They have always been very enthusiastic, and we have an excellent give-and-take way of discussing.” He believes these young collaborators will carry further the idea of combining basic research with clinical science.

His advice for young cardiologists who want to conduct research is to be enthusiastic about research and patient care. “There is no difference between both activities,” he says. “Basic research today is the clinical work of tomorrow because everything we have done in clinical medicine has been physiology and pathophysiology yesterday.”

References


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With 92% of vascular surgical patients presenting with abnormal coronary arteries, cardiology and vascular surgery are closely linked. Olaf Schouten, MD, PhD, surgical resident at Erasmus Medical Centre, Rotterdam, the Netherlands, and Reiner de Graaf Gasthuis, Delft, the Netherlands, became interested in cardiology while conducting research on cardiac complications in vascular surgery patients with Don Poldermans, MD, professor of medicine and head of the section of perioperative cardiac care at Erasmus Medical Centre. Their research has shown that, when both groups are matched for all known cardiac risk factors, patients with peripheral arterial disease who have vascular surgery have a worse outcome than those with coronary artery disease who undergo percutaneous coronary intervention. The worse outcome was partly because patients with peripheral arterial disease received less cardiac medication, including statins and β-blockers, than patients who consulted a cardiologist. “It was quite an eye opener for me to find out that we undertreated our vascular surgery patients,” says Dr Schouten. He adds, “I think that’s one of the problems with vascular surgery patients. Treating physicians are often not fully aware of the generalised problem of vascular disease and focus on just the symptomatic vascular territory such as an occluded peripheral artery. While this affected vessel is treated, less attention is paid to the rest of the patient.” Dr Schouten hopes that their research will stimulate doctors who treat patients with peripheral arterial disease to also treat coronary artery disease. “Doctors who treat patients with peripheral arterial disease should realise that these patients have a high risk for cardiac events and should be treated aggressively in terms of medical treatment with statins and aspirin.”

“β-Blockers and Statins Reduced the Incidence of Perioperative Cardiac Complications”

Dr Schouten studied medicine at Erasmus University Rotterdam between 1995 and 2002, and it was during this period that he got his first taste of research. His project, which he undertook in the Department of Public Health, looked at the parasitology, morbidity, and ultrasound pathology of Schistosoma mansoni in Northern Uganda. His interest in vascular surgery began when he observed the work of Hero van Urk, MD, who at the time was professor and chief of vascular surgery at Erasmus Medical Centre. Dr Schouten secured an extra internship in his department and worked on Vascular Anastomosis (VASCAN), a randomised trial comparing end-to-end with end-to-side distal anastomosis in femoropopliteal bypasses.

A year later, Dr Schouten switched to Professor Poldermans’ group and began his PhD work. The bulk of Dr Schouten’s research has been part of the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo (DECREASE) programme, which is investigating perioperative cardiovascular risk stratification and modification. In DECREASE II, they looked at whether additional cardiac stress testing—including preoperative coronary revascularisation or more intensive medical treatment of patients with stress-induced myocardial ischaemia—would improve risk stratification and cardiac outcome of patients undergoing vascular surgery who had 1 or 2 clinical risk factors for cardiac complications (classified as intermediate risk). They found that performing a stress test preoperatively did not influence outcome, and both groups of patients performed equally well. The Erasmus group has since stopped additional cardiac testing on intermediate risk patients and limits it to the high-risk patients who have 3 or more risk factors. Thus, 25% of patients need additional testing—instead of 75%—and this has produced cost and time savings in the preoperative workup of patients.

DECREASE V was a randomised trial to test whether preoperative coronary revascularisation in patients at high cardiac risk undergoing vascular surgery would reduce the incidence of cardiac events postoperatively. To perform the study, they performed stress tests in all patients with 3 or more risk factors (classified as high risk). Patients with extensive stress-induced myocardial ischaemia—about 10% to 20% of high-risk patients—were randomised to undergo either preoperative coronary revascularisation or best medical treatment only. The pilot study has found that both groups had an incidence of cardiac events of >30% in the perioperative period, and there was no significant
difference between the groups. They found that β-blockers reduced the incidence of perioperative cardiac complications but that statins did not. There was a trend for better outcomes in patients given statins, but it was not significant. Recently the results of the DECREASE III trial, investigating the impact of perioperative statin use in vascular surgery patients, were published. Dr Schouten, first author of this article, is particularly proud of this latest publication, and says, “We found that routine use of statins in the perioperative period can reduce the incidence of perioperative cardiac death and myocardial infarction by half.” The DECREASE programme is ongoing, and funds have just been secured for DECREASE X, which is at the design stage.

“I Knew in Early 2005 What My Career Path Would Be Until 2013”

Dr Schouten attributes his success today to Professor Poldermans, an internal medicine specialist. When the 2 began working together in 2003, the match of internist with prospective surgeon was “something that does not always go very well together,” Dr Schouten. “We knew from earlier studies in the DECREASE programme that patients with extensive stress-induced myocardial ischaemia did not respond well to medical treatment only.”

Dr Schouten’s first article described the design of the DECREASE IV study, which tested whether statins and β-blockers would reduce perioperative cardiac events after noncardiovascular surgery. Dr Schouten and his fellow researchers knew from DECREASE I that patients undergoing vascular surgery benefited from β-blocker therapy and wanted to see whether patients undergoing major noncardiovascular surgery would also benefit from perioperative use of β-blockers and statins. They found that β-blockers reduced the incidence of perioperative cardiac complications but that statins did not. There was a trend for better outcomes in patients given statins, but it was not significant. Recently the results of the DECREASE III trial, investigating the impact of perioperative statin use in vascular surgery patients, were published. Dr Schouten, first author of this article, is particularly proud of this latest publication, and says, “We found that routine use of statins in the perioperative period can reduce the incidence of perioperative cardiac death and myocardial infarction by half.” The DECREASE programme is ongoing, and funds have just been secured for DECREASE X, which is at the design stage.

References

1. Welten GM, Schouten O, Hoeks SE, Chonchol M, Vidakovic R, van Domburg RT, Bax JJ, van Sambeek MR, Poldermans D. Long-term prognosis of patients with peripheral arterial disease: a comparison in patients with coronary artery disease. J Am Coll Cardiol. 2008;51:1588–1596.

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Leading by Example: Attilio Maseri, MD, FRCP, FACC


Professor Attilio Maseri, president of the Italian Heart Care Foundation, Florence, Italy, talks to Lindy van den Berghe, BMedSci, BM, BS, about his passion for extreme sports and his philosophy on living a healthy life.

A pioneer in cardiology, Attilio Maseri, MD, FRCP, FACC, president of the Italian Heart Care Foundation, Florence, Italy, has spent 50 years advancing global understanding of ischaemic heart disease. Now at age 74, he is an example of extreme fitness with a blood pressure of 120/80.

Professor Maseri plays “serious” singles tennis once or twice a week and cycles 30 to 60 km (18 to 38 miles) every weekend for 2 to 3 hours up hills and fast enough to increase his heart rate to 120. He says, “I don’t exercise on a daily basis because it involves too much discipline for me, but I walk briskly, including stairs, and I do some stretching whenever I can. I am rather fit though for 2 reasons. First, I grew up in the countryside and exercise has always been a way of life. When I was a child, it involved running, fishing, and climbing trees. Second, I have continued to enjoy sports throughout my adult life. I like to do sports because it gives me pleasure.” He attributes some of his activity as a child to the lack of television, which didn’t arrive in Italy until 1954. He says of his childhood, “It was a gift, living that way of life.”

In addition to tennis and cycling, Professor Maseri sails, windsurfs, and snowboards. He has sailed since the 1960s. However, it became difficult to sail when he lived in London, United Kingdom, in the 1980s, so he learned to windsurf. He now sails and windsurfs 1 or 2 afternoons every week from late May to early September. He has a boat and a windsurfer based at a “little bay with favourable wind conditions” 100 km (62.5 miles) south of his home in Rome.

Professor Maseri’s most extreme pastime is snowboarding. He learned to snowboard in Cervinia, Italy, in the late 1980s and fell off so many times in the first hour that his instructor became concerned for his health and asked, “Are you sure you’re not going to have a heart attack?” After 1 year of intermittent lessons, Professor Maseri persevered to enjoy snowboarding, which he describes as “very relaxing.”

The one form of exercise that Professor Maseri avoids is jogging. He says, “I don’t like jogging, certainly not on the road. I’ve done it, but cycling is something you can do for longer and with less effort, and it is not so hard on the knees.” He reports no serious injuries during the past 10 years. Before that time, he ruptured his Achilles’ tendon playing tennis. Also thanks to a good surgeon, scars from lacerations on his head from windsurfing are now invisible.

“State of Mind Has a Great Impact on Our Health”

When asked about his diet Professor Maseri says, “I have a Mediterranean diet because I love it. I don’t necessarily focus on fish or meat. I watch my weight and my belt, and I monitor my blood pressure, which is 120/80, so I don’t bother with salt intake. Salt is a pleasure—why deprive your palate when you have a normal blood pressure?” He eats both meat and fish twice a week and says, “I would never deprive myself the enjoyment of eating a fantastic steak.” He adds, “I live now and exercise must be fun. It clears my mind, discharges my toxins, and recharges my batteries. Sports help you look at life with ‘pink glasses’ that focus on the pleasant aspects of life rather than the unpleasant ones, with which the world is full. It is important to keep things in perspective and enjoy a serene state of mind.”

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