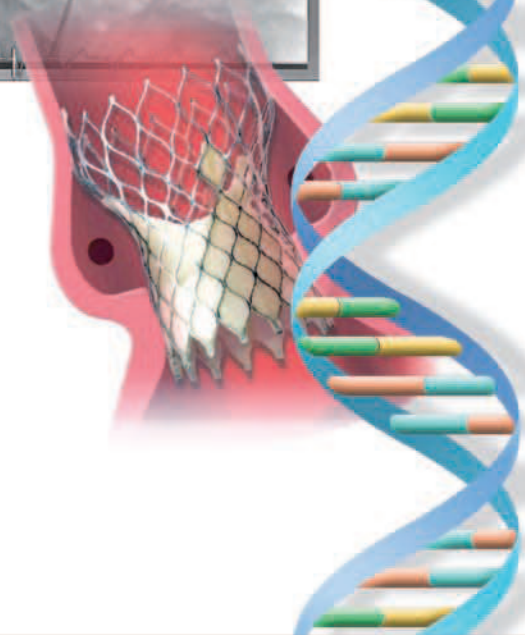


Annual Report 2008

Department of Medicine



Director: Prof. Thomas Münzel, MD



Our Expertise for Your Health



UNIVERSITÄTS**medizin.**

MAINZ

ANNUAL REPORT 2008

Department of Medicine



Prof. Thomas Münzel, MD

Department of Medicine 2
Johannes Gutenberg University Mainz Medical Center
Langenbeckstr. 1
55131 Mainz
Germany

Phone: +49-6131 / 17-7251
Fax: +49-6131 / 17-6615
E-mail address: tmuenzel@uni-mainz.de

Artwork:

Margot Neuser

Photos:

Peter Pulkowski

Production

DINGES & FRICK GmbH
Greifstraße 4
65199 Wiesbaden
Germany
Phone: +49-611 / 39699-0
Fax: +49-611 / 39699-30
E-mail address: df@dinges-frick.de
www.dinges-frick.de

We would like to thank all authors and contributors, particularly Ms. Barbara Reinke, for their collaboration in this Annual Report 2008. Any patient(s) recognizable in the photos have given their informed consent.

Foreword	4
Staff News	6
Honors, Promotions and Habilitations	10
Prof. Christine Espinola-Klein, MD	10
Assistant Prof. Ascan Warnholtz, MD	10
Assistant Prof. Ulrich Hink, MD	10
Assistant Prof. Marc von Mach, MD	10
Scientific Staff Members in Profile	11
Tommaso Gori, MD	11
Renate Schnabel, MD	12
Dissertations 2008	13
Case Management – Discharge Management in Profile	14
News from the Field:	17
How Do Heart Attacks Develop?	17
New Study Techniques in the Cardiac Catheter Lab	19
– Pressure Wire Studies	19
– Intravascular Ultrasound	20
Heart Valve Replacement	21
Cardiac Arrhythmia Treatment	25
Chest Pain Unit - Certification	27
Emergency Department	28
Intensive Care Unit	29
Presentation of the New Thrombosis Service	30
Gutenberg Heart Study Update 2008	32
Research	34
Clinical Research/Endothelial Function Group	34
Clinical Trials Center	35
Preclinical Experimental Research/Vascular Biology	36
Molecular Cardiology – Sponsored Projects	38
Department Performance in Numbers	39
Mainz Heart Network	40
Department Events in 2008	42
Department Award 2008 –	
Nomination of the Department of Medicine 2 for “Best Marketing Concept 2008”	44
Department of Medicine 2 in the Media	45
Foundation Heart of Mainz	47
Margarete Waitz Foundation Award and Paul Schölmerich Award	49
Publications 2008	51



Prof. Thomas Münzel, MD

Dear All,

On behalf of the Department of Medicine 2, I am pleased to be able to present to you the Annual Report 2008 so quickly after the Annual Report 2004-2007.

As in the years before, we have been very successful in 2008 and have continued the positive trend seen in 2004-2007. We have been able to bolster our strong showing in the area of cardiology, in particular by extending our **heart network** accompanied by finalizing cooperation agreements with other hospitals and large private cardiological practices. Now all hospitals and private practices in Mainz have accepted our **Chest Pain Unit** as the first place to turn to when confronted with chest pain patients. Our greatest competitor in Mainz, CardioPraxis near the central train station, has relocated its emergency clinic to the University Medical Center down the hall from the Chest Pain Unit. This **dovetailing** of hospital treatment with outpatient care is unique in Germany. Our department plays a vital role nationwide in establishing chest pain units since we chair the commission certifying these units.

We have established new diagnostic techniques in the **cardiac catheter lab** which will help to improve the assessment of coronary narrowing (plaques). In close cooperation with cardiac surgery, we were the first hospital department in the state of Rheinland-Pfalz to have started **heart valve replacement via the groin approach**. In an attempt to improve the care of patients under oral anticoagulation with Marcumar (phenprocoumon) our department in Mainz has established, along the lines of the Dutch example, the first **thrombosis service** in Germany, which will optimize the dosing of anticoagulants, particularly in patients with atrial fibrillation or artificial heart valves.

All these efforts to improve patient care and networking were rewarded last year at the Congress for Innovative Hospital Communications in Cologne, Germany, by being **nominated for “Best Marketing Concept 2008”**.

Our largest research effort, the **Gutenberg Heart Study**, has enrolled more than 7,000 participants, and by the summer of 2009 we are expecting preliminary results on the causes of cardiac infarction in the population of Mainz and its surrounding areas.

The year 2008 has also been successful for us in economic terms. The department has continued its positive development by increasing the number of admissions, case mix points and revenues. Sponsored research and publication output continued at the high level of previous years. In addition, we are still in the running for sponsorship of the **Mainz Thrombosis Center** by the Federal Department of Education and Research, involving a possible Euro 50 million, a feat which we already regard as a major success.

Starting this year we would like to present in somewhat more detail those members of our team who have excelled in patient care and research and who have added to the standing of the department. This year, those members meriting special mention are **Tommaso Gori, MD**, who relocated from Siena, Italy, to Mainz and **Ms Renate Schnabel, MD** who has successfully completed her research sabbatical in Framingham, Massachusetts, USA, sponsored by the German Cardiac Society and has returned to her clinical research work here in Mainz. With the help of our **foundations** (Margarete Waitz Foundation and Foundation Heart of Mainz) we have financed research stays of our staff members in outstanding research labs throughout the world and will continue to do so.

I would like to take this opportunity to encourage people to join the Friends of Foundation Heart of Mainz so that our department can continue advancing progress in patient care and research.

With this annual report we would like to thank the people of Mainz, our colleagues in private practice and the referring hospitals for their continued support.



Prof. Thomas Münzel, MD
Head of Department

Head of Departement and Staff Members



Deputy Head of Department:
Prof. Stefan Blankenberg, MD
Board certified in internal medicine,
cardiology



Head of Department:
Prof. Thomas Münzel, MD



Clinical Manager:
Felix Post, MD
Board certified in internal medicine,
cardiology, intensive care medicine

Senoir Fellows:



Stephan von Bardeleben, MD
Board certified in internal
medicine, cardiology



Prof. Christine Espinola-Klein, MD
Board certified in internal medicine,
cardiology, angiology



Assistant Prof. Sabine Genth-Zotz, MD
Board certified in internal medicine,
cardiology, intensive care medicine



Prof. Ewald Himmrich, MD
Board certified in internal medicine,
cardiology



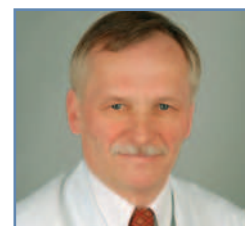
Assistant Prof. Ulrich Hink, MD
Board certified in internal
medicine, cardiology



Klaus Kettering, MD
Board certified in internal
medicine, cardiology



Savvas Savvidis, MD
Board certified in internal
medicine, angiology



Prof. Helmut Schinzel, MD
Board certified in internal
medicine, angiology



Assistant Prof. Ascan Warnholtz, MD
Board certified in internal medicine, cardiology

Senior Staff:



Ludmila Himmrich, MD
Echocardiography



Joachim Kaes, MD
Intensive Care Unit



Dirk Mertens, MD
Pulmonary hypertension
clinic



Hanke Mollnau, MD
Electrophysiology

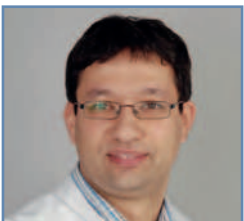


Barbara Nalenz, MD
Ultrasound



Margit Niethammer, MD
Clinical trials cardiac
catheter lab

Staff:



Nico Abegunewardene, MD



Maryam Ayati, MD



Amelie Biedenkopf, MD



Frank Breuckmann, MD



Christiane Buhr, MD



Meike Coldewey, MD



Ewa Czyn, MD



Christoph Dommke, MD



Jörn Dopheide, MD



Frauke Dumstorff, MD



Tommaso Gori, MD



Felix Gramley, MD



Stephanie Herkenhoff, MD



Alexander Jabs, MD



Annika Jagodzinski, MD



Kristina Kaiser, MD



Denise Kämpfner, MD



Susanne Karbach, MD



Till Keller, MD



Arne Klett, MD



Maike Knorr, MD



Edith Lubos, MD



Philipp Nikolai, MD



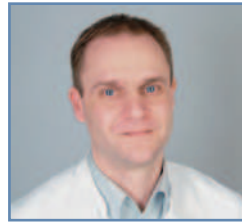
Mir Abolfazl Ostad, MD



Karin Pfirrmann, MD



Ingo Sagoschen, MD



Oliver Sauer, MD



Frank Schmidt, MD



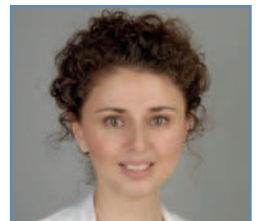
Kai-Helge Schmidt, MD



Renate Schnabel, MD



Eberhard Schulz, MD



Selviye Seta, MD



Christoph Sinning, MD



Sebastian Sonnenschein, MD



Kathrin Stelzer, MD



Cathrin Theis, MD



Nicole Toussaint, MD



Stergios Tzikas, MD



Markus Vosseler, MD



Gerhard Weißer, MD



Philip Wenzel, MD

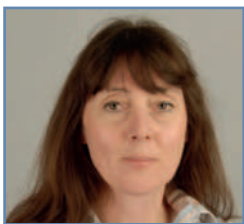


Philipp Wild, MD

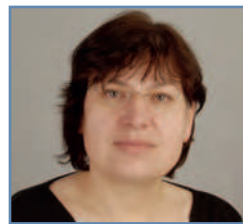


Heide Zellerhoff, MD

Nursing Management Team:



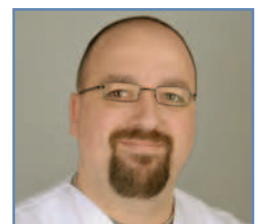
Gabriele Maas
Head Nurse, wards 4A, 4B, 4C
and outpatient department
Leader, case management



Vera Jaresova
Deputy Head Nurse
Wards 4A, 4B and 4C



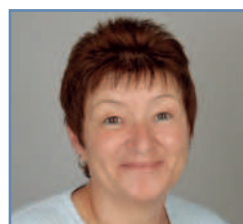
Bianca Steinheimer
Deputy Head Nurse
Wards 4A, 4B and 4C



Mike Böbel
Ward manager
Emergency department



Heike Eich
Deputy Head Nurse
Intensive Care Unit



Annette Möhlenhoff
Deputy Head Nurse
Intensive Care Unit



Silvio Kittlaß
Ward manager
Cardiac cath lab

No photo: Anne-Kathrin Breu, deputy ward manager, emergency department
Angela Frese, deputy ward manager, cardiac cath lab



10 STAFF NEWS

> Honors and Promotions

- **Dr. Thomas Jansen, MD** was honored with the **Margarete Waitz Research Award** 2008, endowed with Euro 36,000 per year for a period of two years at Emory University in Atlanta, Georgia, USA. During his stay at the renowned laboratory of Prof. David G. Harrison, Dr. Jansen's research will primarily focus on the role of inflammatory cells in the pathogenesis of atherosclerosis.

- **Prof. Andreas Daiber, MD** was honored with the **Robert Müller Research Award** 2008 for two of his papers: "Nebivolol Inhibits Superoxide Formation by NADPH Oxidase and Endothelial Dysfunction in Angiotensin II-Treated Rats" and "Role of Reduced Lipoic Acid in the Redox Regulation of Mitochondrial Aldehyde Dehydrogenase (ALDH-2) Activity".

- **Medea Sophia Eleftheriadis** was awarded a scholarship by the **Robert Müller Foundation** for her doctoral thesis "Genome-wide analysis for cardiovascular risk stratification within the context of the Gutenberg Heart Study - validation and functional studies".

- **Peter Schlindwein, MD** und **Katja Weisbrod** were honored with the **Dissertation Award** 2008 of the **Margarete Waitz Foundation**. They share the prize money of Euro 3,000. Dr. Schlindwein submitted an outstanding study of the differentiated intra-individual variability in vascular pathophysiology. The exploratory data analysis of Dr. Weisbrod's thesis has made it possible to come up with a qualified prediction of the actual poisonous potential of plants and to inaugurate a scoring system for herbal hazards.

- **Prof. Christine Espinola-Klein, MD** has been honored with the Euro 10,000 "2008 Teaching Award of Rheinland-Pfalz". With this award the state government honored the vascular specialist for her outstanding teaching performance at Johannes Gutenberg University Mainz Medical Center.

In addition, the German Society of Angiology honored her with the Schwarz-Mohnheim Award for her paper "Different Calculations of ABI and their Impact on Cardiovascular Risk Prediction". In this paper she demonstrated that more patients at risk are detected if the lower rather than higher ankle pressure is used for calculating the ankle brachial index.

- Prof. Christine Espinola-Klein, MD will become **Associate Professor (W2) of Internal Medicine and Angiology** in 2009. She completed her habilitation in 2003 with a study on "Pathogenetic and prognostic aspects of atherosclerosis at various regions of the vascular tree" Her research primarily focuses on the manifestation, diagnosis and treatment of atherosclerosis.

As a member of numerous medical societies Prof. Espinola-Klein is active as chair and organizer of scientific meetings and CME events. In March 2008, she declined the offer of an Associate Professorship in Angiology at the Carl Gustav Carus University Dresden Medical Center.



Inaugural lectures



Assistant Prof. Ascan Warnholtz, MD:

Inaugural lecture on 19 May 2008

Subject: Pathophysiology and diagnostics of mitral valve disease



Assistant Prof. Ulrich Hink, MD:

Inaugural lecture on 9 December 2008

Subject: Aortic valve disease



Assistant Prof. Marc von Mach, MD:

Inaugural lecture on 5 June 2008

Subject : Examination of the abdomen



> Scientific Staff Members in Profile: Tommaso Gori, MD



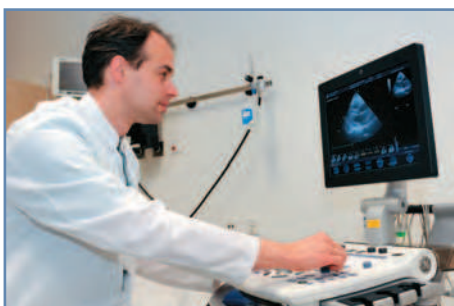
— **Dr. Tommaso Gori** is a board certified cardiologist with the Department of Medicine 2 at Mainz University Medical Center. Born in Italy, he is also a cardiologist with Siena University in Italy and holds an honorary professorship at Siena University Medical School. In addition, he holds a PhD from the University of Toronto in Canada.

Dr. Gori has studied at the universities of Siena in Italy, Toronto in Canada and Mainz in Germany and obtained his doctoral degree in 1998. During his career to date he was awarded six scholarships and fellowships and has been the recipient of 18 international awards. 2001 saw him accomplish the outstanding feat of being awarded two prestigious prizes: **“Young Investigator’s Award of the American College of Cardiology”** and **“Young Investigator Award of the American Heart Association”**. This had never been accomplished before!

His outstanding research covers various areas. His publications have already reached an astounding impact factor of 255 points. He also reviews for 22 international journals and three international guidelines and lectures at many well known international institutions and scientific meetings. As a member of the leading international cardiac societies Dr. Gori is active there in various committees.

Why, then, would an Italian leave beautiful Siena to come to Mainz? The main reason for Dr. Gori’s move to the capital of Rheinland-Pfalz was the outstanding research opportunities offered to him there. “The Department of Medicine 2 offers excellent research opportunities: a large medical department, molecular cardiology lab plus the cooperation with other great scientists”, explains Dr. Gori. One essential aspect in his decision for Mainz and the Department of Medicine 2 was the mutual personal and scientific respect between Prof. Münzel and himself.

The decision to make Mainz their new home was, and still is, a challenge for Dr. Gori and his family. “The start was rather rocky: new environment, major differences in professional practice and the present working conditions, and in particular learning German”. There are still some hurdles to overcome, but as Dr. Gori says: “I relish my new life and that’s what’s most important. You cannot have improvement without change.” This characterizes his attitude which is complemented by his positive thinking and the value he places on honesty, industriousness and integrity.



> Scientific Staff Members in Profile: Renate Schnabel, MD



— Renate Schnabel, MD, MSc has been on the scientific staff of the Department of Medicine 2 since December 2002 and collaborates with the Gutenberg Heart Study.

Awarded a scholarship by the German National Academic Foundation, Ms. Schnabel attended Johannes Gutenberg University Mainz Medical School and in 2002 completed her doctoral thesis on “Quantitative analysis of regional endocardial motility disorders in patients with coronary heart disease by stress echocardiographic color kinesis” in the Department of Medicine 2. Impressed by the excellent training and teaching conditions she found in the department, she did all her internship and residency with us. In 2007, she was awarded an invitational fellowship as research fellow with the Framingham Heart Study, the most important epidemiological trial in the United States. She worked there from 2007 to 2008 as a postdoc and fellow of the German Research Foundation. During her stay Dr. Schnabel also obtained an additional academic qualification, Master of Science in Epidemiology, from the prestigious Boston University School of Public

Health which has graduated many of the most eminent epidemiologists and statisticians in the US.

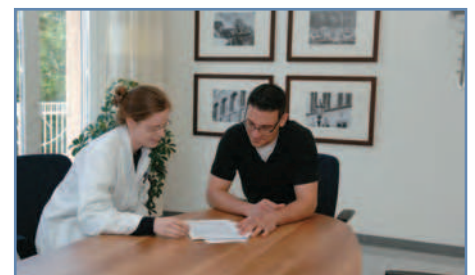
Dr. Schnabel has benefitted immensely from her stay in the United States: “Working right at the cutting edge of cardiovascular science and cooperating with international research groups was one of the highlights of my scientific career to date. Boston offered me an extremely stimulating setting.” But Ms. Schnabel also gained valuable experience outside the realms of science. She will always treasure the “American way of life with its determined optimism no matter what the circumstances” and this sense of hope fired by the presidential election campaign.

Back in Mainz with the Department of Medicine 2 at Johannes Gutenberg University Mainz Medical Center after her primarily theoretical work she is glad to return to the more clinical side of medicine

while helping to expand epidemiological and clinical research at Mainz. For Dr. Schnabel Mainz is a rather promising center of science and research, at the same time offering attractive working conditions: “I see enormous potential in the Department of Medicine 2 to translate epidemiological and clinical research at the highest level. The Gutenberg Heart Study offers the best conditions for cutting edge research. After just two years for the main trial, the volume and quality of the data analyzed has already been recognized internationally. The tie-in with the Department of Medicine 2 makes directly translating the results into clinical epidemiology and trials become a reality. Working for the Department of Medicine 2 I have come to appreciate the open mindedness for scientific concepts and ideas in all areas and the constant effort for efficient workflow and optimizing the working conditions for the clinical and scientific staff.”

Dr. Schnabel has been awarded the following prizes and honors:

- 2006** Benjamin Franklin Contest of the Charité Berlin, Campus Benjamin Franklin, Berlin, Germany
- 2006** “Dagmar Eißner Prize for Promising Young Investigators”, Johannes Gutenberg University, Mainz
- 2007** “Young Investigator Award in Clinical Science” of the European Society of Cardiology
- 2008** “Best Science Award”, Scientific Sessions Poster Competition, American Heart Association
- 2008** Scholarship, Boston University School of Public Health
- 2008** Habilitation scholarship of the Kalkhof-Rose Foundation
- 2008** “Elisabeth-Barrett-Connor Award for Young Investigators”, finalist, American Heart Association



> Dissertations 2008

Aksakal, Devrim	magna cum laude	Assistant Prof. Michael Buerke, MD Assistant Prof. Diethard Prüfer, MD	The impact of genisteine and geldamycin on neointimal hyperplasia after PTA of the iliac artery in rabbits
Bönner, Florian Alfred	summa cum laude	Assistant Prof. Georg Horstick, MD Prof. Oliver Kempfski, MD	Complement-C5a receptor inhibition affects left ventricular remodeling in the ischemia-reperfusion rat myocardial infarction model
Cordier, Tim Christoph	magna cum laude	Assistant Prof. Georg Horstick, MD Prof. Ludwig Sacha Weilemann, MD	Marking of endothelial progenitor cells for histological and nuclear magnetic resonance studies
Danko, Tim	cum laude	Prof. Thomas Münzel, MD Assistant Prof. Sabine Genth-Zotz, MD	Long-term outcome of acute intervention in ST-elevation myocardial infarction (pPCI versus rescue PCI)
Elsner, Veronika Kriemhilde	magna cum laude	Assistant Prof. Ascan Heinrich Warnholtz, MD Prof. Stefan Blankenberg, MD	The effect of a 12-week oral niacin treatment on endothelial function in patients with coronary heart disease
Färber, Julie	cum laude	Assistant Prof. Christian Weiß, MD Prof. Hans-Jürgen Rupprecht, MD	The impact of anticoagulation and/or platelet inhibition on event-free survival in patients with atrial fibrillation after percutaneous coronary intervention
Geimer, Marc Nico	magna cum laude	Assistant Prof. Stephan Lindemann, MD Prof. Stefan Blankenberg, MD	Differential protein synthesis in activated platelets
Gräber, Katharina Viktoria	magna cum laude	Prof. Stefan Blankenberg, MD Prof. Christine Espinola-Klein, MD	Hormonal resistin as risk predictor in patients with coronary heart disease – the AtheroGene Trial
Klages, Matthias	magna cum laude	Prof. Harald Darius, MD Assistant Prof. Sabine Genth-Zotz	The effect of prostacycline and nitric oxide on platelet adhesion in vitro
Mägdefessel, Lars	magna cum laude	Prof. Hans-Jürgen Rupprecht, MD Prof. Manfred Dahm, MD	In vitro comparison of unfractionated heparin with low molecular weight heparin and the pentasaccharide fondaparinux in preventing thrombus formation on artificial heart valves in the thrombosis tester
Sagoschen, Ingo	cum laude	Prof. Ludwig Sacha Weilemann, MD Prof. Helmut Schinzel, MD	High-frequency oscillation ventilation as one treatment option in acute adult respiratory failure
Schmerer, Marten	cum laude	Prof. Christine Espinola-Klein, MD Prof. Stefan Blankenberg, MD	The reliability of combined duplex sonography and NMR angiography in the diagnostic work-up of stenotic extracranial vessels of the neck. Comparison with conventional angiography
Schneider, Manuela	cum laude	Prof. Stefan Blankenberg, MD Prof. Christine Espinola-Klein, MD	Plasma levels of placental growth factor as risk predictor in patients with coronary heart disease and for future cardiovascular death and nonfatal myocardial infarction – the AtheroGene Trial
Weber, Carola Beate	cum laude	Prof. Ludwig Sacha Weilemann, MD Prof. Helmut Schinzel, MD	Analysis of patients with suspected intoxication in one emergency department over a one-year period
Wittenberg, Christiane Nadine	cum laude	Prof. Thomas Münzel, MD Assistant Prof. Sabine Genth-Zotz, MD	Coronary intervention in main artery stenosis

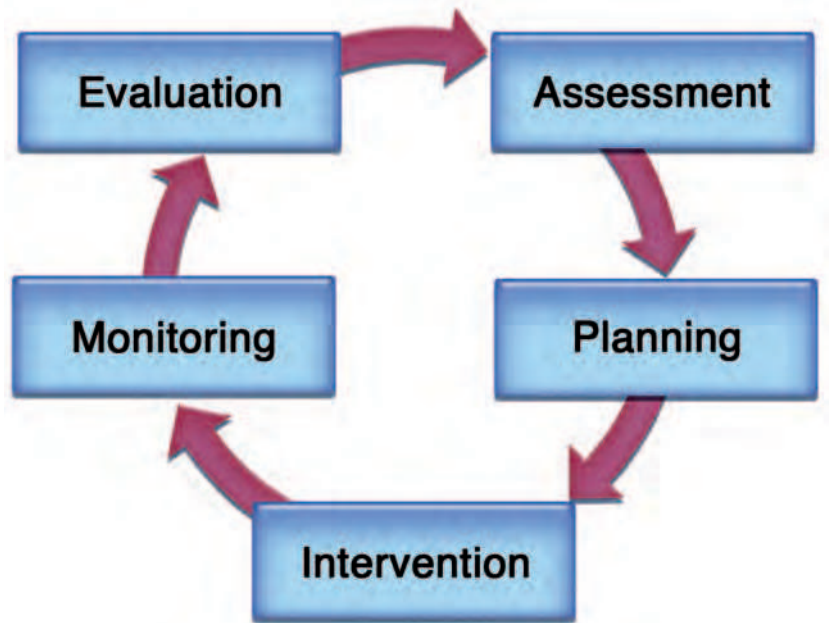
Case Management in the Department of Medicine 2

The Department of Medicine 2 is setting the standard in nursing as well

— In the Department of Medicine 2, state-of-the-art research results and highly advanced concepts and techniques are implemented not only in medical applications but also in the nursing care of our patients. In 2006, we started applying the US concept of case management.

The term “case management” refers to planning and coordinating individualized health services for each patient. At the patient level, clinical case management follows a concept with five tiers and comprises the planning and coordination of all processes, from hospital admission to care on the wards and ultimately discharge. This method generates the necessary organization at the system level (such as a referral concept). Process control and process responsibility is assumed by our experts who attend the patients of the Department of Medicine 2 during all phases of their individual processes.

The overall goal of case management is to improve efficiency. With the dramatic changes in the health care system this has become of paramount importance. Patient care, and the Department of Medicine 2, increasingly finds itself torn between business considerations, gains in



Case management control loop

productivity and patient centrality. Our department has been able to demonstrate the innovative strength needed today while at the same time upholding, and improving even further, the high level of patient care. And the patient is still viewed as a human being rather than a problem to be solved.

Admission management was successfully implemented in 2006.

Phase II, implementation of discharge management, was planned for 2008.



Sonja Köbel, Admission Management



Robert König, Admission Management

Discharge Management in the Department of Medicine 2

— Massive demographic and societal changes, in combination with new types of reimbursement in the health care system, have meant that more and more patients require continued care and support after being discharged from hospital. With its discharge management the Department of Medicine 2 ensures that this increased need for continued care is met.

This process starts on the day of admission: When planning the continued best possible care of the patient, the initial step in this individualized planning process is personal dialog between the patient and our expert staff. From then on our experts determine the individual level of care needed, initiate any rehabilitation measures, coordinate the care providers and advise the patients psychosocially as well as in social security aspects. The spectrum covered by our discharge management also includes all coordination with the other professionals involved in the care of this patient as well as the care of patients in the emergency department who are to be admitted to the Department of Medicine 2. This is where all information comes together and where the entire workflow is coordinated.

The objective of these service measures is to improve not only patient – and therefore customer – satisfaction but also the satisfaction of the department staff and all

other care providers, and to protect the economic interests of the Department of Medicine 2.

Quite soon after its introduction, the benefits generated by the discharge management of the Department of Medicine 2 were evident for all involved.

Patients and their family members can now rely on the fact that treatment and care will be ensured beyond hospital discharge; this puts their mind at ease and makes them more satisfied. In addition, a smooth transition from hospitalization to outpatient status has an extremely positive effect on the overall process of recovery.

Since the newly implemented discharge management is run by staff responsible solely for this special mission, patients and the institutions subsequently caring for them are always able to communicate with the central contact staff. Therefore, when faced with these kinds of questions doctors and nurses can refer the questioner to our experienced and expert discharge management specialists and are relieved of administrative work. This also helps to assure the quality of service we provide.

Discharge management has a positive impact on the economic performance of the Department of Medicine 2 as well. We were able to reduce the mean length of

stay while still increasing the number of cases. And at the same time we avoided the so-called “revolving door” effect.

In real numbers:

Between March and December 2008, discharge management cared for a total of 719 hospitalized patients, 687 patients of which were discharged as planned. Only 23 patients were discharged without previous planning. 301 patients were discharged to rehabilitation programmes, 196 patients were transferred within the medical center or to institutions outside, while 199 patients were discharged home.

Discharge management cared for a total of 284 patients in the emergency department. Of these, 198 were admitted to the Department of Medicine 2 while the others were either discharged home or referred to outside institutions.

During the entire stay staff members of the discharge management team on the average spent 0.47 days with the patient.

Implementation of the discharge management was made possible by innovative leadership of the department and by highly competent staff members.



Sofia Colicelli, Discharge Management



Christine Frank, Discharge Management



Nurses, Ms. Becker and Ms. Kunze

**News from case management:
Service and assistant pool**

In recent years, due to increasing general work load and a rising number of critically ill patients, nursing staff have come under enormous pressure. Medical progress and the German DRG system require highly specialized nursing care. In our department this is ensured by matching staff qualification with the problem at hand.

Workflow analysis of our general wards demonstrated that the nursing staff spent about 20% of their time on activities which stopped them from pursuing their prime work. To allow nursing staff on our general wards to once again concentrate 100% on their core areas of expertise we instituted a pool of service staff and nursing assistants who carry out the work delegated to them by the nurses. This pool, comprising

five members with different levels of nursing qualifications, was created by reassigning nursing staff from the three wards. The members of the service staff and nursing assistant pool work five days a week in early and late shifts and together are responsible for the needs of all three general wards. On wards 4A, 4B and 4C they serve food, take away the dishes, do the beds, dispose of materials, prepare the workroom and restock the nursing cabinets.

Success came quickly with this innovative approach to nursing. The members of our nursing staff are much happier with their work now, peak work loads were reduced and the patients, too, have readily accepted this new service.

Outlook to 2009

The year 2009 will see even further development in the case management of the Department of Medicine 2.

In the coming year the focus will be on workflow control. A professional medical coder will help us realize potential savings and matched funding for optimizing workflow.

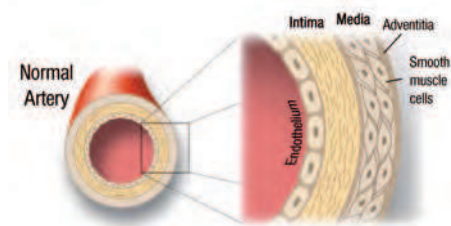
In addition, in close cooperation with the Executive Board of Mainz University Medical Center we will continue to improve our portfolio, and in particular the aspect of patient transportation.



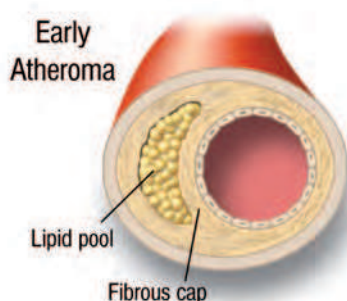
How do Heart Attacks develop?

— To provide you with a better understanding of study techniques such as pressure wire and intravascular ultrasound, it is best to first explain the mechanisms resulting in myocardial infarction. This will be followed by an explanation of the new study techniques.

The following figures detail in schematic fashion the changes in the blood vessels which ultimately result in acute myocardial infarction.



Normally, the artery comprises several layers with the innermost layer, the so-called endothelium, playing the most prominent role in the initial changes of the vascular structure. You will find a more detailed discussion of the impact of risk factors on endothelial function in the section “Preclinical Research”.



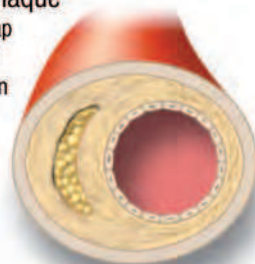
Should the risk factors persist a so-called **early atheroma** evolves. Interestingly enough, the vessel takes on an elliptical shape while the lumen does not change at all (so-called Glago effect).

A lipid core and a cover plate are the most characteristic features of these early changes. In this case, the cover plate consists of connective tissue and is primarily responsible for the structural integrity of this plaque. The size of the lipid core is primarily determined by the serum lipid level. Therefore, a significant elevation in the serum cholesterol level will always result in a large lipid core. This in turn implies that the plaque can burst when the cover plate becomes thinner, thereby promoting myocardial infarction.

In principle, there are two ways in which the early changes may develop.

“Stabilized” Plaque

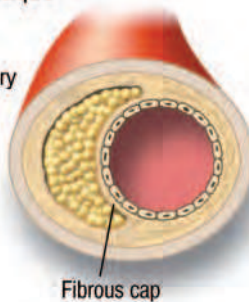
- Thick fibrous cap
- Small lipid pool
- Preserved lumen



Either we manage to get the risk factors, such as elevated cholesterol levels, under control by changing our eating habits, doing more sports or taking appropriate medication, in which case the vessel will become stabilized with a shrinking lipid core and thickening cover plate (**stable plaque**). As a result, the latter cannot tear anymore, reducing the risk of myocardial infarction.

"Vulnerable" Plaque

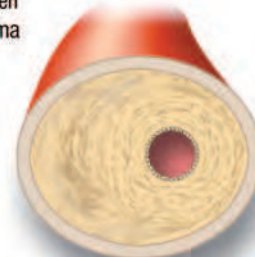
- Thin fibrous cap
- Large lipid pool
- Many inflammatory cells



Should the risk factors continue to persist, the lipid core will thicken while the cover plate is thinning out; this increases the danger that the cover plate will tear which in turn raises the risk of myocardial infarction dramatically (**unstable plaque**).

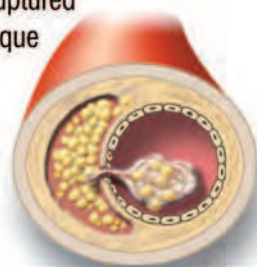
Healed Ruptured Plaque

- Narrow lumen
- Fibrous intima



Generally speaking there are two alternatives. Either this injury heals with the sequela of a severe stenosis at this site of the vessel (**healed plaque rupture**). Subsequently, these patients do not suffer any complaints when resting, but will always develop functional angina pectoris symptoms since there is insufficient oxygen supply to the heart.

Thrombosis of a Ruptured Plaque



Once an unstable plaque tears, its lipid core will all but empty itself into the lumen of the vessel (**plaque rupture**). In turn, this accumulation of lipids will drastically activate the coagulation system meaning that the ruptured plaque may become thrombosed within minutes.

The other alternative results in acute occlusion of the coronary artery and therefore myocardial infarction. In these cases it is absolutely vital to call the medical emergency number (phone 112) for the emergency doctor; this will ensure that once hospitalized the patient will undergo a cath lab study as fast as possible in order to reopen the occluded vessel, so that coronary insufficiency will be as short as possible and therefore limit the extent of the infarction.

Acute Myocardial Infarction



New Study Techniques in the Cardiac Catheter Lab

> Ultrasound of the Coronary Arteries

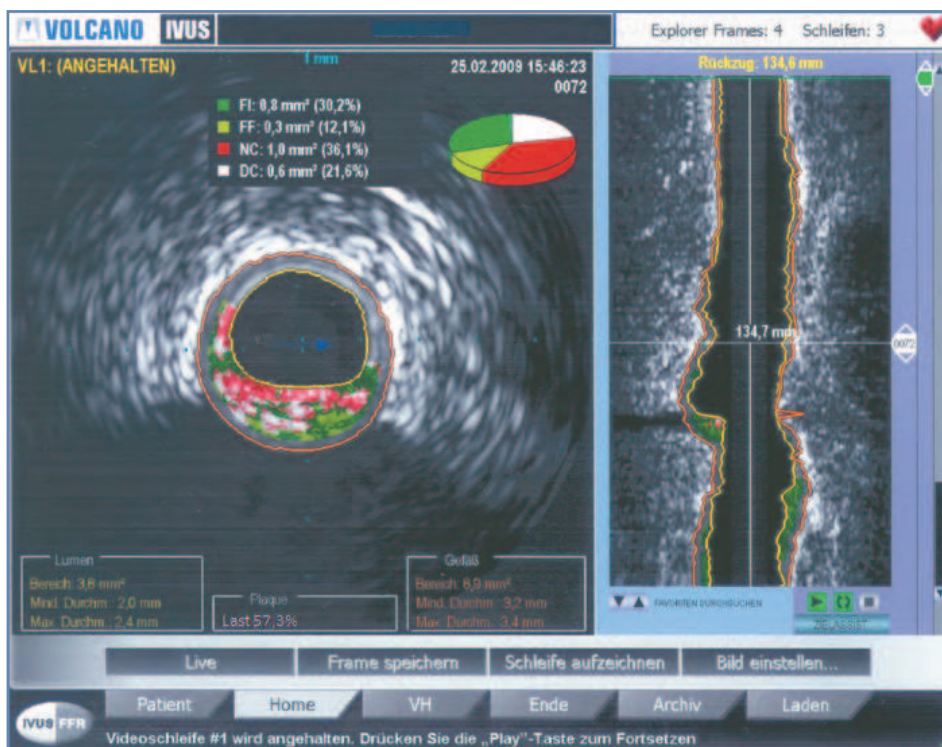
Standard cardiac catheter studies only offer information on the inside (lumen) of the coronaries. It is not possible to visualize the structure of the coronary wall or calcified areas (plaques). In 2008, we obtained a new unit for intravascular ultrasound (IVUS) studies of the coronaries; it allows us to depict as greyscale image not only the detailed structure of the arterial wall but also the structure of calcified areas (virtual histology). This is important since a differentiation has to be made between stable stenoses (stable plaques) and unstable narrowing (unstable plaques).

Particularly in the case of unstable plaques, there is the danger of rupture with subsequent acute myocardial infarction.

In virtual histology the plaque is classified into four categories which are differentiated by color: dark green for fibrous plaques and therefore stability; light green for fibrolipid plaques (more of a marker for an unstable plaque); red for cellular death (more of a marker for an unstable plaque); and white for dense calcium (more of a

marker for stability). When retracting the wire in measured fashion, allowing plaque length definition, not only the quality of the plaque but also the volume of the plaque load can be determined. Apart from identifying plaque characteristics, IVUS is a valuable tool for optimizing coronary stenting. This can be invaluable, particularly today with the increasing advent of drug eluting stents and coronary interventions on the left main artery or on bifurcations.

Intravascular Ultrasound (IVUS)



> The Highlight 2008:

Catheter Assisted Cardiac Valve Replacement

— Since July 2008, Mainz University Medical Center has offered catheter assisted replacement of stenosed aortic valves. The medical team comprises doctors and nurses from cardiology (Department of Medicine 2), heart surgery (Department of Cardiovascular and Thoracic Surgery) and cardio-anesthesiology (Department of Anesthesiology). The cardiac valve replacement team at Mainz was the first group from Rheinland-Pfalz to have implemented this new technique.

Internationally, the technique of percutaneous (i.e., through the skin) replacement of the aortic valve is a true cutting-edge procedure. Compared to standard open heart valve surgery this procedure limits tissue damage with its minimum access concept. By damaging the tissue as little as possible this type of operation will avoid secondary healing and scar formation and will also speed up postoperative patient recovery. Accordingly, for older patients (>75 years) with severe concomitant disease this procedure is a rather promising alternative to standard open heart surgery.

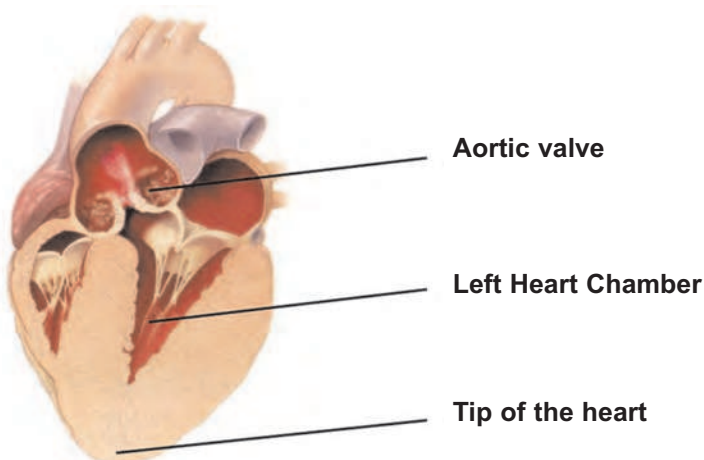
The indication for this type of treatment requires the definite diagnosis of severe narrowing of the aortic valve (aortic valve stenosis) which may be accompanied by symptoms such as dizziness (in particular when exercising); fainting; shortness of breath; feeling of tightness in the chest (angina pectoris); and heart failure (“water in the lungs”).

Aortic valve stenosis

Aortic valve stenosis describes an abnormal narrowing of the aortic valve, the latter acting as non-return valve between the left chamber of the heart and the main artery of the body (aorta).

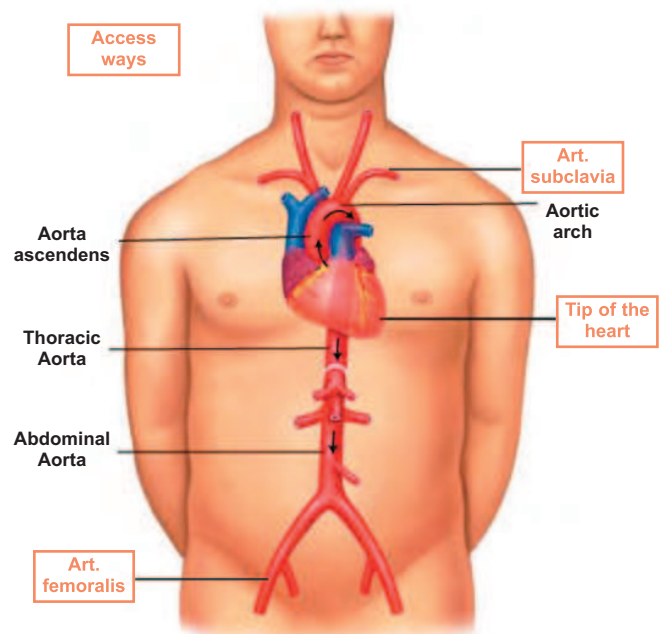
When this valve narrows this means that the muscle of the heart must exert more pressure, and therefore more work, to

expel the blood from the heart. On the one hand, this results in the heart muscle thickening and therefore in a relative lack of oxygen supply, which becomes noticeable as angina pectoris or shortness of breath; on the other hand, aortic valve stenosis may impair the blood supply to the brain, resulting in dizziness and fainting spells. Usually, while the blood is being expelled the opened aortic valve has an area of about 3cm². If this opening area covers less than 1cm² the stenosis of the aortic valve is regarded as severe. With increasing age this disease becomes more and more common and affects more than 3% of all those older than 80 years. Apart from the often severely curtailed quality of life of those affected, aortic valve stenosis has a mean life expectancy of only two years once there are symptoms such as heart failure.



Schematic longitudinal cross-section through the human heart with aortic valve stenosis

Source: Adapted from “Patienteninformation der Fa. CoreValve”



Possible access incatheter based aortic valve replacement

Source: Adapted from “Patienteninformation der Fa. CoreValve”

Surgical treatment of aortic valve stenosis

Open heart surgery is still the standard treatment option in aortic valve stenosis. In general, this procedure can also be performed with acceptable risk in very old patients. Advances such as aortic valve replacement by minimally invasive surgery have made it possible to downsize the access required for implantation of the aortic valve through miniature sternotomy (surgical division of the sternum). This operation on the non-beating heart is still performed under general anesthesia and requires the heart-lung machine.

Catheter assisted aortic valve replacement and aortic valvuloplasty

For quite some time there have been numerous efforts to treat aortic valve stenosis with the help of a catheter. In 1986, Prof. Alain Cribier from Rouen, France, was the first to crack open a narrowed aortic valve by means of an inflatable balloon (aortic valvuloplasty). After the initial euphoria about the clinical benefit for the patients had died down, unfortunately it became evident that the patients did not benefit in terms of life expectancy

since the leaflets of the valve “stuck” to each other again. Again, it was Cribier who in April of 2004 successfully implanted the first collapsible “bio valve”, mounted on a catheter, via the groin. The procedure is always preceded by valvuloplasty of the affected valve which is then pushed aside by the new expanded valve. Two such valve systems have been approved for implantation in people. Depending on the system, either the valve is unfolded by means of a balloon (Edwards Sapien system) or it unfolds all by itself (Medtronic CoreValve system). Although no benefit in terms of survival has been demonstrated for this procedure compared to standard open heart surgery, this new technique offers fundamental benefits such as the principal chance to forego general anesthesia, cardiovascular support systems (heart-lung machine), and the need to split open the sternum with its subsequent scar formation. Particularly when treating elderly high risk patients, these aspects may be of decisive advantage since fast ambulation of the patients after the procedure is of paramount importance.

Generally, the diseased valve may be accessed via the artery at the groin (femoral artery) or below the clavicle (subclavicular artery). Both systems described above are suited for either access route. The Edwards Sapien System also offers the option to implant the new valve under general anesthesia via minimum access surgery forcing apart the ribs of the left chest wall over the tip of the heart. This type of procedure is used primarily in those patients whose arteries either are too tortuous or calcified and therefore do not lend themselves as access routes.

Both current valve models are so-called “bio valves”; in other words, just as the valves implanted during open heart surgery the leaflets of these valves are made of preprocessed biological material from cattle or pigs which is sutured to a collapsible metal frame. These valves are anchored to the cardiac wall at the level of the diseased original valve by means of balloon dilation or their own power of self-expansion and start to function immediately upon deployment.



CoreValve bio valve (left: longitudinal view, right: top view) comprising a metal scaffold (nitinol) and sutured valve pockets (porcine pericardium), Source: in-house

Preparation of catheter assisted aortic valve replacement

Once a patient is diagnosed with severe aortic valve stenosis work-up is needed to see if he/she can undergo a catheter assisted procedure. In general, the patient should be older than 65 years and/or run a high surgical risk because of the concomitant disease (logistical EuroScore >20% according to <http://www.euroscore.org>). Pertinent concomitant disease includes heart and kidney disorders; previous open heart surgery; vascular disorders; neurological disorders; and pulmonary hypertension. Once these conditions are met, usually our admissions management (phone +49-6131-17-2633 or -3290) will plan for a three to four day admission for work-up. This work-up includes admission consultation with the doctor; informed consent; physical examination; ECG; lab tests; abdominal sonography and cardiac ultrasound with transesophageal echocardiography; cardiac cath study with pulmonary blood pressure measurement; and additional imaging of the possible access arteries by computerized tomography (CT) and ultrasound scanning. Unfortunately, these numerous studies are needed for detailed planning of the procedure and keeping the possible complications as low as possible.

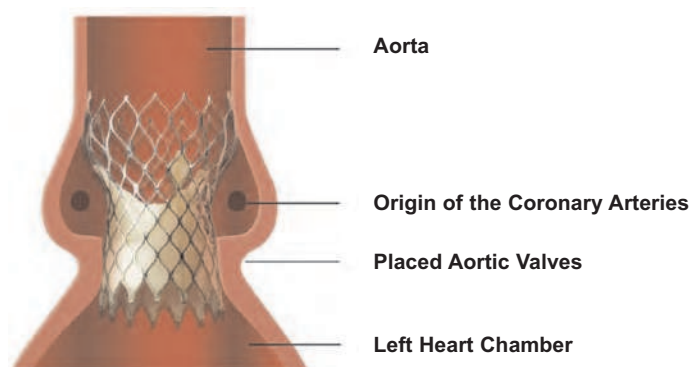
The findings are discussed first by our “valve team” between heart surgeons, cardiologists and cardio-anesthesiologists, and then with the patients and his/her family members. Depending on the findings and symptoms the individual procedure is mapped out. This covers the whole gamut – from the catheter assisted procedure via one of the access routes noted above to open heart surgery in standard fashion or as minimum access aortic valve replacement and also aortic valvuloplasty for temporal relief until definite therapy.

Catheter assisted aortic valve replacement

The patient is admitted one or two days before the actual procedure. Any anticoagulants should have been withdrawn before then. The patient is prepared just as for open heart surgery and informed consent is obtained by the anesthesiologist and the physician in charge of the ward. In the case of concomitant narrowing of the coronaries (coronary heart disease) these stenoses may be stented while indwelling venous catheters for drug delivery and patient monitoring are being placed. For instance, this may be performed on the day before the actual procedure. During the actual procedure our patients are deeply sedated, preferably with ventilation

support (larynx mask) in order to stress the patient as little as possible. Catheter access is gained under local anesthesia, usually via the groin. Under fluoroscopy a wire is advanced from the groin through the aorta into the heart and finally to the stenosed aortic valve. Under rapid stimulation with an external temporary pacemaker a short cardiac arrest is triggered while at the same time dilating the narrowed aortic valve (valvuloplasty).

In case of the self-expanding CoreValve implant, which is collapsed into a deployment unit on a catheter, the new valve is advanced over the guidewire to the level of the heart valves. Once the best possible position has been reached the protective sleeve is retracted, thereby deploying in place the leaflet-bearing metal frame (CoreValve) by self-expansion and pushing the diseased aortic valve into the wall of the aorta. The CoreValve is anchored down by its own elasticity and starts functioning immediately. The puncture site in the groin is closed with a special suture system (ProStar). After the procedure has been completed, the awake patient is transferred to the intensive care unit and later to the monitoring ward. Since the artificial valve exerts pressure on the surrounding tissue there is the immediate risk of arrhythmic heart action. Therefore, the temporary pacemaker is left in place for at least two days while the patient is being monitored for at least five days. In about 20% of cases it becomes necessary to implant a permanent pacemaker under the skin, a minor procedure which can be carried out under local anesthesia. After the hospital stay the patient should undergo rehabilitation and be on anticoagulation (ASA and clopidogrel for six months, followed by life-long ASA). The patients are followed up six and twelve months after the procedure as part of our aortic valve clinic (phone +49-6131-17-7267).



Optimum position of the CoreValve implant at the transition between the left ventricle and the aorta

Source: Adapted from “Patienteninformation der Fa. CoreValve“

The “Valve Team”

Our team comprises interventional cardiologists, heart surgeons and cardio-anesthesiologists. One unique feature of our center is the fact that all members have to agree on the individual approach to each patient and that they follow up all patients

together. This multidisciplinary approach of our specialized unit represents a unique integrated treatment regimen, combining individual patient centered care with innovative treatment modalities.



Ass. Prof. Ulrich Hink, MD (senior fellow, Department of Medicine 2 – Cardiology)
Jens Karmrodt, MD (senior fellow, anesthesiology)
Nalan Kayhan, MD, (senior fellow, Department of Cardiovascular and Thoracic Surgery)
Ass. Prof. Ali-Ashgar Peivandi, MD (senior fellow, Dep. of Cardiovascular and Thoracic Surgery)
Felix Post, MD, (senior fellow, Department of Medicine 2 – Cardiology)
Alexander Jabs, MD, (staff, Department of Medicine 2 – Cardiology)
Irene Tzanova, MD (senior fellow, anesthesiology)
Markus Vosseler, MD, (staff, Department of Medicine 2 – Cardiology)
Prof. Christian-Friedrich Vahl, MD (head, Department of Cardiovascular and Thoracic Surgery)
Prof. Thomas Münzel, MD (head, Department of Medicine 2 – Cardiology)

Contact

Cardiology/Aortic Valve Clinic (Ass. Prof. U. Hink, MD): phone +49-6131-17-7267
Heart surgery (N. Kayhan, MD, senior fellow, Department of Cardiovascular and Thoracic Surgery):
phone +49-6131-17-2106

News from the Field of Cardiac Arrhythmias

— Cardiac arrhythmias may cause numerous symptoms. Apart from the characteristic rapid or irregular heart beat, arrhythmia may also manifest as sudden fainting or dizziness. It may intensify shortness of breath or impair cardiopulmonary capacity. The electrophysiological focus of our Department of Cardiology primarily deals with the diagnosis and treatment of such arrhythmias. For diagnosis we can draw on Holter ECG (1-7 days); event recording; ergometry; tilt table testing; and invasive electrophysiological studies.

While some arrhythmias need not be treated, others may require medication. Today, many arrhythmias may be cured permanently by so-called catheter ablation (sclerotherapy either by heat or cold). Until recently the classic indications for catheter ablation were atrial flutter, AV node reentry tachycardia and WPW syndrome. But now an increasing number of patients with ventricular tachycardia and intermittent or persistent atrial fibrillation are treated by this technique as well. This is one of the areas in which our department specializes. Today, it is assumed that it is primarily triggering extrasystoles from the pulmonary veins which irritate the left atrium and thereby set in motion atrial fibrillation. Primary objective of catheter ablation is therefore electrical isolation of the pulmonary veins from the atrium and to modify the electrical characteristics of the left atrium in particular.

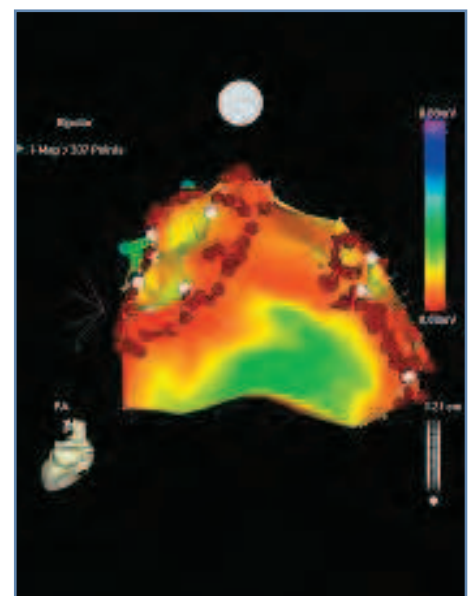
Such catheter ablations are carried out in a specially equipped cath lab unit. This unit is equipped with a special electrophysiological workstation (for ECG recording and analysis), a so-called mapping system (CARTO) and technical equipment for applying energy (ablation generator (high-frequency current) and equipment for cryoenergy). Electrical isolation of the pulmonary veins is the prime focus when treating intermittent atrial fibrillation. One technique used for this purpose is cryoablation (application of cold) which is performed with a special cryo balloon.



Treatment of atrial fibrillation with the cryo-balloon
Source: Courtesy of CryoCath Co.

Alternatively, another strategy may be pursued when treating patients with intermittent atrial fibrillation and in particular persistent atrial fibrillation. The geometry of the left atrium is delineated with a so-called mapping system which is also used to mark the location of the pulmonary veins, and by applying high-frequency current electrical isolation of the pulmonary veins is attempted. In many cases this complex treatment can completely cure the patients of any symptoms.

Another focus of the Department of Medicine 2 is pacemaker and AICD therapy. Patients with bradycardia (abnormally slow heart beat) can be implanted a pacemaker for one or both chambers. In patients with life-threatening rapid arrhythmia originating in the chambers of the heart, however, a so-called AICD (automatic implantable cardioverter defibrillator) may be implanted which can stop these potentially life-threatening arrhythmias by applying electrical shocks.



Application of the CARTO mapping system in the treatment of atrial fibrillation

Another new treatment option is cardiac resynchronisation therapy by biventricular stimulation. In this procedure not only the usual electrodes are placed in the right atrium and right chamber but also a third electrode in the coronary sinus stimulating the left chamber. This can compensate the asynchronism in patients with left bundle branch block. This is particularly beneficial in patients with severely impaired cardiac capacity and poor left ventricular function.



Electrophysiology team
 (Dr. Felix Gramley, Angela Frese RN,
 Dr. Hanke Mollnau, Dr. Cathrin Theis,
 Dr. Klaus Kettering, Prof. Ewald Himmrich)

In our special pacemaker and AICD clinic (phone +49-6131-17-2548 and -70589) we regularly follow up more than 4,000 patients. Today, patients with implanted pacemakers and AICD's not living close to Mainz University Medical Center may be followed up simply via telemetry. Telemonitoring the patients via the internet helps to cut down on the number of monitoring appointments in the department, as long as the patients adhere to their regular telemetry schedule.

Range of services (noninvasive):

- standard ECG, exercise ECG, Holter ECG (up to 7 days)
- tilt-table testing
- event recording (external and internal systems)
- pacemaker and AICD checks

Range of services (invasive):

- invasive diagnostic electrophysiological study (EPS)
- catheter ablation (via high-frequency current or cryo application), in complex arrhythmia, possibly aided by a 3D mapping system (CARTO)
- pacemaker implantation
- AICD implantation
- implantation of biventricular pacemaker/ AICD systems.

Outpatient services:

- pacemaker clinic
- AICD clinic
- special arrhythmia clinic

Table: Electrophysiological activity in numbers

Procedure	2004	2005	2006	2007	2008
Catheter ablations	74	81	117	138	255
Diagnostic EPS	25	25	39	33	41
EPS/ abl. overall	99	106	156	171	296
PM implants de novo	91	102	89	124	140
PM replacements and revisions	51	87	86	86	63
PM procedures overall	142	189	175	210	203
AICD implants de novo	56	66	75	80	95
AICD replacements and revisions	11	37	17	48	55
Biventricular AICD implants de novo	3	14	10	13	14
AICD procedures overall	70	117	97	143	150



In our last annual report we presented the organization of our Chest Pain Unit (CPU), preliminary statistics and the awareness campaign with the 1. FSV Mainz 05 soccer club.

In 2008, 1,960 patients were treated on the CPU representing an increase of almost 20% over the previous year.

We are aware that in the United States the establishment of Chest Pain Units has significantly increased the survival rate after myocardial infarction. Dr. Till Keller from our department has compared the data from more than 1,200 patients who came to the Mainz CPU with those from 550 patients admitted to the emergency department with suspected myocardial infarction.

The analysis clearly demonstrates that the patients do benefit from being treated on the Mainz CPU. Within two years, the establishment of the CPU with its guideline based rapid patient care significantly reduced the combined target outcome of mortality and the rate of reinfarction and

stroke in patients with acute coronary syndrome.



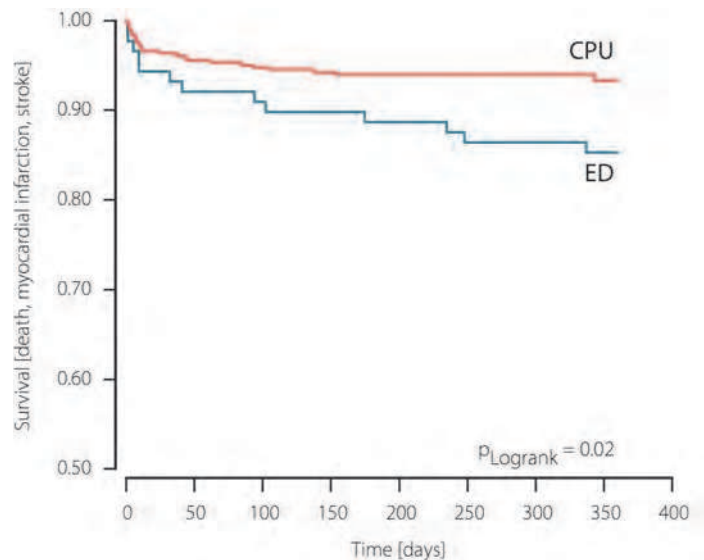
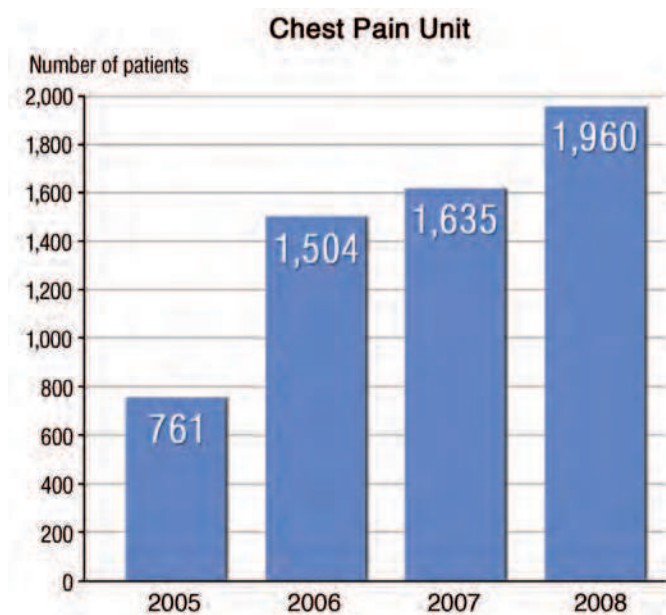
Certified CPU Mainz

Mainz Chest Pain Unit – one of the first to be certified in Germany:

The last few years have seen a rapid rise in the number of chest pain units in Germany. Following the American and British example the objective was – and still is – to improve the care of patients with acute chest pain.

Both of these countries were able to demonstrate that establishing these types of CPU's improved prognosis. However, the rapid rise in the number of CPU's has led to somewhat of a rank growth. The German Cardiac Society (Deutsche Gesellschaft für Kardiologie – Herz- und Kreislaufforschung e. V.) has therefore published recommendations on the quality of chest pain units. German CPU's can now be certified based on these quality guidelines. The process of certification was laid down by Dr. Felix Post from our department and a colleague from Essen, Germany. In the end a total of 300–400 CPU's with monitored quality are likely to be established to cover all of Germany. The care of patients with chest pain demands an ambitious organizational concept. Chest pain units are a very good solution to this problem. Last year the Mainz Chest Pain Unit was one of the first to be certified in Germany.

For 2009, we plan to increase the capacity of the CPU from the present six to eight beds and to rekindle the awareness and information campaign with 1. FSV Mainz 05 soccer club.



Better prognosis in patients with an acute myocardial infarction when treated in the CPU compared to the emergency department

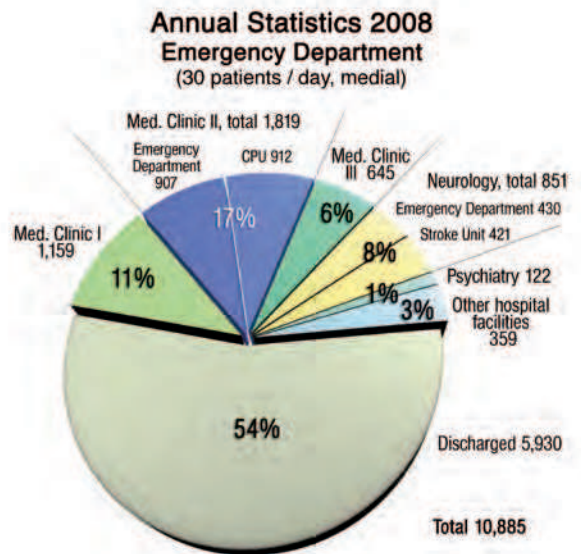
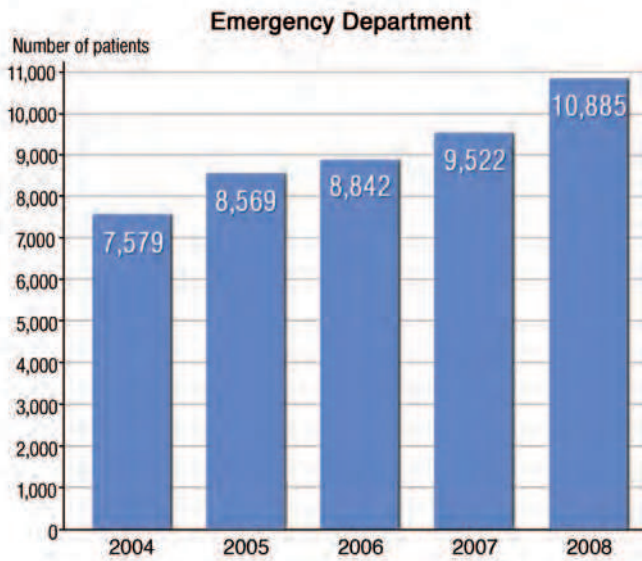
News from the emergency department

As in the years before, the emergency department cared for far more patients than ever before.

While 7,579 patients were treated in 2004, by 2008 this number has risen to 10,885 cases. This represents an increase of 45% seen by the same number of nursing staff and physicians as in 2004, demonstrating the heavy increase in workload for this section of the department. When looking at the distribution of patients admitted by the Departments of Internal Medicine,

most of them are admitted to the 1st Department of Internal Medicine while our department admits not only patients from the emergency department but also the Chest Pain Unit.

Due to the dramatic rise in patient numbers in this section, restructuring is planned here for 2009 aiming to improve patient care in the emergency department.



News from the Intensive Care Unit

— Our ICU patients are cared for by a team of physicians comprising one senior fellow plus ten staff members and the nursing team. The latter currently comprises 45 experienced nurses, with most of them being board certified in “intensive care”. All physicians have ample experience on the ICU, some already holding board certification (internal medicine, cardiology) and subspecialization in “special internal intensive care medicine”. In addition, the care of our patients also includes physiotherapy. The ICU is directed by Professor Sacha Weilemann, MD and Assistant Professor Sabine Genth-Zotz, MD. In 2009, senior fellow Felix Post, MD and senior staff member Joachim Kaes, MD will be in charge of this unit. Dr. Post is accredited for fellowship training in “special internal intensive care medicine”.

As for many other areas, internal intensive care is deeply involved in the changes and optimization taking place in the Department of Medicine 2. In 2009, this service section will be enlarged. We will report on this in the annual report for 2009.



Members of the ICU team



Presentation of the New Thrombosis Service

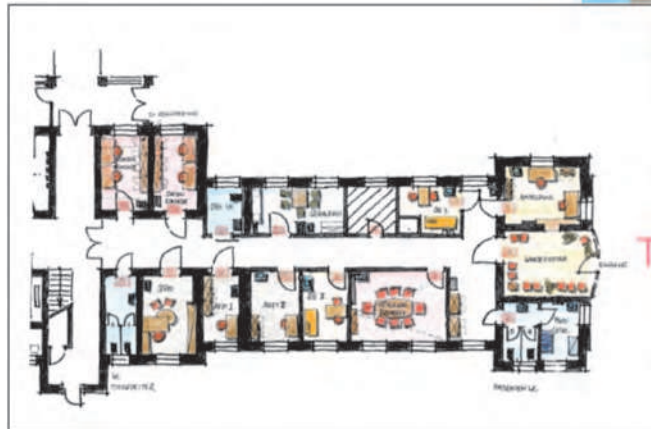
— One of our key projects striving to improve health care in the Mainz region has been the establishment of the first thrombosis service in Germany caring for patients taking the anticoagulant Marcumar (phenprocoumon). To this end, the Executive Board of the medical center has provided ample space in building 403.

Why does this type of thrombosis service make sense?

More than 900,000 patients in Germany are currently on long-term oral anticoagulation (drugs used for blood thinning). The most common indications for these drugs are atrial fibrillation, artificial heart valves and secondary prevention of thromboembolic events. In the coming years, the number of patients with the indication for anticoagulation will be increasing, since life expectancy and the percentage of the elderly in the population will be rising even further.

In 1948, the Netherlands began establishing so-called thrombosis services, with full nationwide coverage for the last 12 years. These are specialized facilities caring for patients on oral anticoagulants. This specialized care assures high treatment efficacy and a high treatment rate for the patients. **In the Netherlands, roughly 2.2% of the population is treated with oral anticoagulants, while in Germany this percentage is about 1.1%, in other words a difference of 50%.** However, there are some countries with even higher treatment rates: for instance, in the US this percentage is at 3.6% of the total population. **These numbers emphasize that there might be a high number of unreported cases in Germany who actually need this important treatment, but do not receive it for various reasons. The most common complications of oral anticoagulants are overdosage induced hemorrhage and underdosage related thromboembolic events, in particular a stroke.** In countries where

Building 403, ground floor



these patients are cared for by specialized services, the **complication rates for hemorrhage and embolism are significantly lower.**

The Dutch numbers are particularly useful since in this country thrombosis services provide nationwide care coverage for these patients. Not only does this guarantee best possible indication for oral anticoagulation,

but the **outstanding infrastructure** also ensures that a **large percentage of patients (>80%) is well dosed**, their lab tests being within the therapeutic range. The success of the thrombosis centers in the Netherlands speaks for itself: **The thromboembolic complication rate is at roughly 1.5% and the incidence of hemorrhage at about 2.0%. While there is no definite data for Germany,**

Indication	# of pts.	% of population OAC
Overall	800-900,000	1%
Atrial fibrillation	400,000	0.5% (about 50% of pts. OAC)
Deep venous thrombosis	200,000	0.25%
Artificial heart valves	80-90,000	0.1%
Others	175,000	0.2%

(OAC – Oral anticoagulated patients in response to phenprocoumon)

estimates of both complication rates assume much higher values.

Accordingly, Germany is starting to establish thrombosis services along the lines of the Dutch example. Mainz will be the first German site for this care model sponsored by the EU, and as reference center it will support the roll-out in Germany.

How does the thrombosis service work?

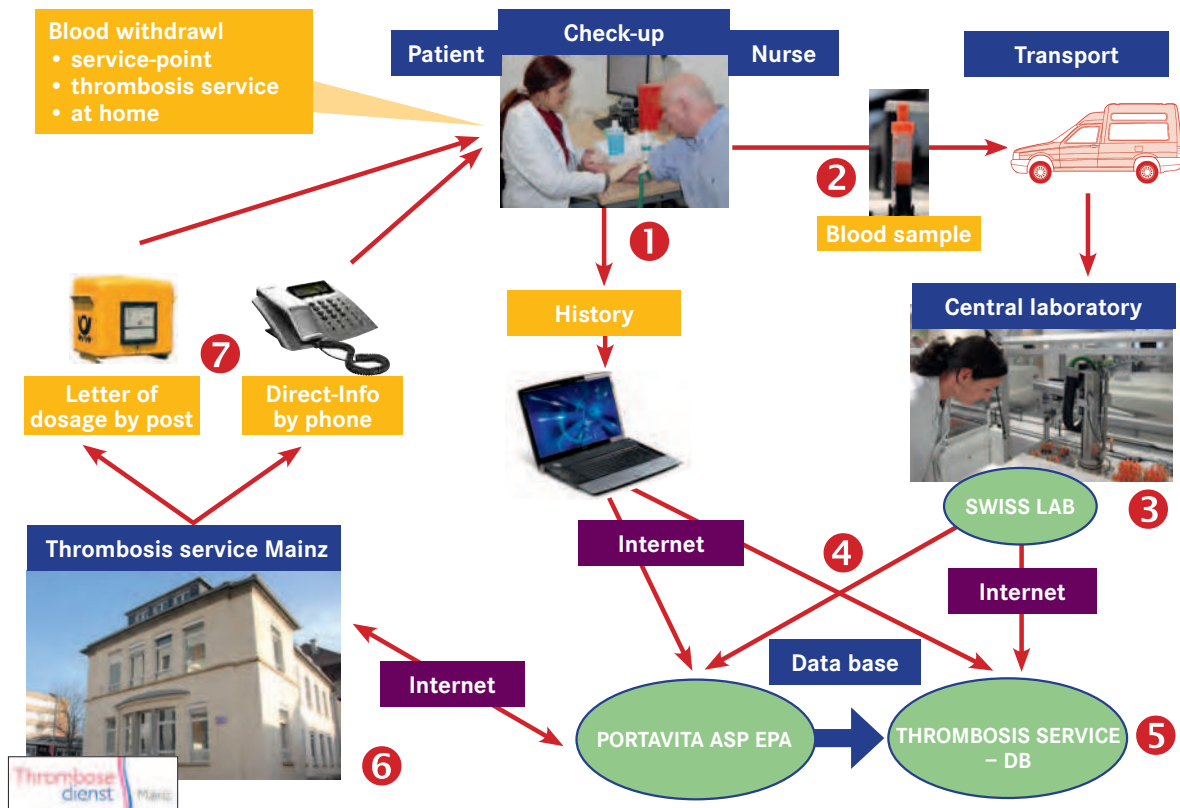
After blood has been drawn (1) it will be sent to the central lab at Mainz University Medical Center (2). The results are fed into a database (3) and then communicated to the thrombosis service via internet (4-5). The test results are analyzed and assessed by a computer program at the thrombosis

service (6). Based on this analysis a dosage for the next few weeks is suggested and mailed to the patient who then will be informed about his/her Marcumar dose within 24 hours after blood has been drawn. If the test results fall outside the desired target range, the patient will be informed personally by a staff physician on the thrombosis service.

Apart from these regular patients, the thrombosis service will also care for **self-monitoring patients**, in other words patients who have their own unit for anti-coagulation testing (INR). After the test has been completed these patients can log into their own patient record via their computer at home and enter the test result. If the latter falls outside the therapeutic range the thrombosis service will be

informed automatically. In turn, the service would contact the patient immediately and attempt to ascertain why the therapeutic range has been exceeded.

The following German health insurance providers are actively participating in this contract for integrated care: DAK, GEK and HMK. Negotiations with other health insurance providers are underway. This health care model was established by the Rheinland-Pfalz Department of Labor, Social Security, Women Affairs and Health and will continue to receive huge support.

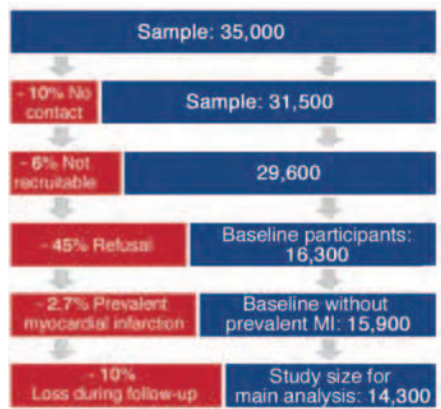


Gutenberg Heart Study



> Update 2008

The Gutenberg Heart Study is a population based prospective cohort trial which has enrolled a random sample of 35,000 people living within the city of Mainz and the district of Mainz-Bingen. Of these, about 14,300 will be entered into the core analysis.



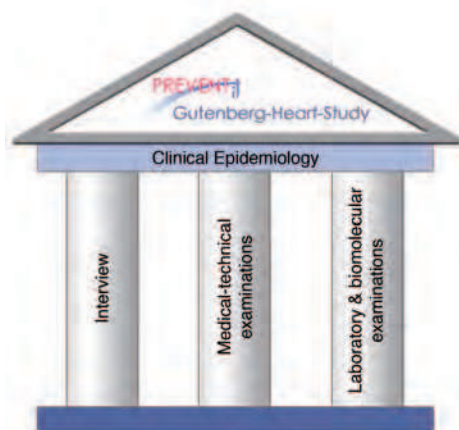
Planned inclusion numbers of the study

The participants are between 35 and 74 years old and are recruited for the study on a male:female basis of 1:1. The primary objective of the Gutenberg Heart Study is to define a score which can reliably predict cardiovascular risk, while taking into account, in addition to any standard risk factors present, psychosocial conditions, environmental and life-style aspects, extent of subclinical atherosclerosis already present as well as blood test based phenotype and genetic phenotype. Since it was launched on 10 April 2007, 7,063 participants have been enrolled in this study.

Directed by Prof. Blankenberg, MD and the university steering committee (comprising Prof. Münzel, MD, Department of Medicine 2; Prof. Lackner, MD, Department of Clinical Chemistry and Laboratory Medicine; Prof. Pfeiffer, Department of Ophthalmology, Prof. Blettner PhD, Department of Medical Biometrics, Epidemiology and Information Science;

and Prof. Beutel, MD, Department of Psychosomatic Medicine and Psychotherapy), this trial integrating different specialties is a beacon of the university. Daily work is coordinated by the study manager, Philipp Wild, MD, supported by a team of investigators comprising Andreas Bender, MD, Stephanie Herkenhoff, MD and Christoph Sinning, MD.

The organization of the Gutenberg Heart Study is an integrated component of the studies carried out. The diagram below illustrates the pillar concept of the trial. The first follow-up phase of the Gutenberg Heart Study, initially reestablishing contact with the participants just by phone, will start at the end of 2009. Starting October 2011, all approx. 15,000 participants until then will be invited once again to undergo reassessment.



Concept of the GHS

On a global level, coronary heart disease (CHD) is the leading cause of cardiac death. Although in recent years cardiovascular mortality has decreased in most developed nations, the rates for coronary heart disease have remained constant in the western world. In contrast, the traditional factors of cardiovascular risk keep rising, resulting in a steady increase in

diabetes mellitus, hyperlipoproteinemia and hypertension, the triad mostly responsible for the risk of myocardial infarction.

The objective of prospective epidemiological trials is to identify and highlight these risk factors. These trials observe a well defined population over a certain amount of time and record disease related events during this period, such as myocardial infarction, stroke and cardiovascular death. This design of the study makes it possible to identify a large number of risk factors. However, this design can still be improved if the trial delineates earlier end-points, applying the latest genetic and proteomic techniques, since this would let us describe events still evolving.

The prospective population based Gutenberg Heart Study (GHS) was initiated at Johannes Gutenberg University Mainz Medical Center to study and gain a better understanding of the origin of atherosclerosis and coronary heart disease. The trial covers three different data aspects. First, there is epidemiological data obtained from questionnaires and computer assisted personal interviews; secondly, other data yielded by measuring subclinical atherosclerosis; and thirdly, establishment of a biological database permitting prospective genomic and proteomic research.



Gutenberg Heart Study Team

The research network of the Gutenberg Heart Study will gather detailed information on the following major research areas:

- provision of the degree of strain tied into psychosocial and environmental factors as well as daily work;
- quantitation of early subclinical atherosclerosis;
- identification of protein patterns related to atherosclerosis;
- identification of genetic patterns related to atherosclerosis and application of genome-wide association (GWA) studies and RNA expression analysis;
- provision of information on the extent of subclinical disease;
- provision of endpoint data related to fatal and non-fatal disorders.

In conjunction with the population based Gutenberg Heart Study other trials were established at the study center which will study the acute coronary syndrome. One focus is to delineate the role of genetic information in the development and expression of disease. Therefore, the

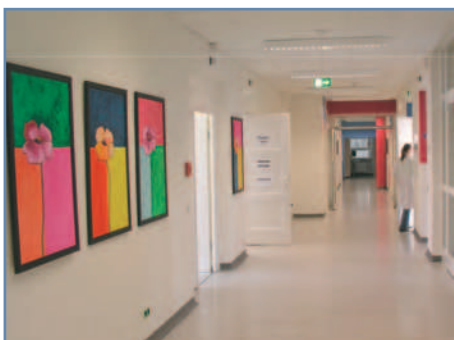
Gutenberg Heart Study was complemented by establishing the Gutenberg HerzINFARKT Study and the Gutenberg Tako Tsubo Trial.

The Gutenberg HerzINFARKT Study researches the genetic background of acute coronary syndrome. This is a case control trial with retrospective enrolment of patients, aged 18-50 years, into the sample investigated. Three months after the acute event the patients are asked to participate in the study. This ensures stable conditions for scar formation as well as for biomarker levels and genetic studies. The trial has been running on the study ward of the Gutenberg Heart Study since June 2008 with a current enrolment of 233 patients. The study center for cardiovascular prevention at Johannes Gutenberg University Mainz Medical Center has its scientific focus on the study of cardiovascular disorders. The Gutenberg HerzINFARKT Study is being conducted to gain a better understanding of the origins of myocardial infarction in young patients. Not all cases can be adequately explained

by traditional risk factors such as hypertension, smoking, high cholesterol levels and diabetes, implying that genetic disposition probably plays an important role as well. The study is recruiting patients who have suffered myocardial infarction below the age of 50; these patients come from the Mainz University Medical Center, GPR Hospital in Rüsselsheim and Armed Forces Medical Center in Koblenz. The patients are identified by the hospitals where they are treated and contacted by mail. Upon enrolment in the trial they undergo detailed examination at the study center, the focus being on the cardiovascular system.

Cardiovascular diseases are the most common cause of morbidity and mortality in the developed nations of the West. According to the data of the German Federal Office of Statistics, in 2005 about 368,400 men and women died of cardiovascular disorders; in other words, these diseases caused almost every other death. Each year almost 300,000 patients suffer myocardial infarction. In recent years the incidence of cardiovascular disease has increased significantly and therefore makes additional research vital.

The Gutenberg Heart Study currently employs almost 70 people and has an annual budget of almost Euro 1.5 million.



Rooms where the GHS takes place



Johannes Gutenberg University Mainz
 Medical Center
 Building 406, Floor 1
 Langenbeckstr. 1
 55131 Mainz, Germany
 Phone: +49-6131-17 5926
 Fax: +49-6131-17 3403

Clinical Research

> Endothelial Function Group

Group topic

The group is researching the pharmacological influence on endothelial dysfunction in patients with coronary heart disease. Randomized unicenter controlled double blind and investigator initiated clinical trials fulfilling the German Pharmaceuticals Act study the effect of various drugs on endothelial function, the latter quantified as flow-mediated dilation of the brachial artery. For this investigation into the mechanisms of endothelial dysfunction markers for inflammation, oxidative stress and platelet function are measured. According to the requirements of modern investigator initiated clinical trials, the studies are implemented in close cooperation with the Interdisciplinary Center for Clinical Studies (IZKS; headed by M. Seibert-Grafe, MD).

The trials are carried out within the context of intradepartmental cooperation (e.g., INEF study in cooperation with the Gutenberg Heart Study) and interdepartmental cooperation (Department of Clinical Chemistry and Laboratory Medicine; headed by Prof. K. Lackner, MD; Medical Center Pharmacy, headed by I. Krämer, MD). The studies are either financed by industry sponsors or departmental resources from the budget for research and teaching.



Endothelial Function team

(Mir Abolfazl Ostad, MD, Seyed Ebrahim Ostad, Hannelore Seiler, Boris Schnorbus, Robert Schiewe, Assistant Prof. Ascan Warnholtz, MD)

Working group staff organization

Head:

Assistant Prof. Ascan Warnholtz, MD

Medical coordinator: Mir Abolfazl Ostad, MD

Study nurse: Hannelore Seiler

IT support and statistics:

Seyed Ebrahim Ostad

Project specific medical doctoral students:

Boris Schnorbus, Robert Schiewe

Projects:

Topic: Sponsor: Sponsored budget: Time frame:	The effect of pentaerithryltetranitrate on endothelial function in patients with coronary heart disease (PENTA trial) Actavis GmbH & Co. KG, Langenfeld Euro 180,000 2006 - 2008
Topic: Sponsor: Sponsored budget: Time frame:	Evaluation of the effect clopidogrel termination one year after drug eluting stenting has on inflammation markers (DECADES trial). Bristol Myers Squibb Euro 20,000 2007-2008
Topic: Sponsor: Sponsored budget: Time frame:	Evaluation of the effect dalcetrapib has on endothelial function in patients with stable CHD or risk factors for CHD Multicenter study. Roche 2008-2011



Clinical Trials Center team

(Susanne Wüst; Gabriele Gebel, Dr. Frauke Dumstorff, Assistant Prof. Sabine Genth-Zotz, MD, Ute Junker-Sopart, Dr. Margit Niethammer, Bärbel Kaesberger, Ulrike Rady-Pizarro, Dr. Amelie Biedenkopf, Heike Braun)

— The last two decades have seen major progress in the care of heart disease, particularly in the treatment of myocardial infarction and heart failure. Apart from the development of new medications and medical devices by industrial research, this progress also grew out of the implementation of extensive clinical trials. Patients participating in these studies have made a major contribution to medical progress to date. The patients themselves benefit significantly by participating in this type of trial since not only are they given the chance to be treated with the latest drugs but they also obtain more intense medical care from the study team.

Within this context, we partner major international pharmaceutical companies and administer phase II-IV trials. In the cath lab the focus of our studies is on treating acute coronary syndrome and investigating into anticoagulation after balloon angioplasty (PTCA) and stenting. In addition, we put particular emphasis on studies of new types of drug eluting stents. Furthermore, we provide long-term care for patients with chronic heart failure or cardiac arrhythmia.

The Clinical Trials Center is directed by Assistant Professor Genth-Zotz, MD and Dr. Niethammer, MD acting as deputy head. Dr. Biedenkopf, MD is staff member, while the studies are coordinated by Ms. Braun who is responsible for the invasive

trials, together with Ms. Käsberger and Ms. Wüst. The trials on heart failure and cardiac arrhythmia are administered by Ms. Junker-Sopart and Ms. Rady-Pizarro.

In 2008, the Clinical Trails Center was involved in carrying out 19 clinical studies. 273 patients were enrolled in running trials

Clinical Trial Center

and more than 430 patients overall were cared for by our center during their studies.

The recruitment numbers listed in the table prove that Ass. Prof. Genth-Zotz, MD and her group have been successful in enrolling patients in studies already running.

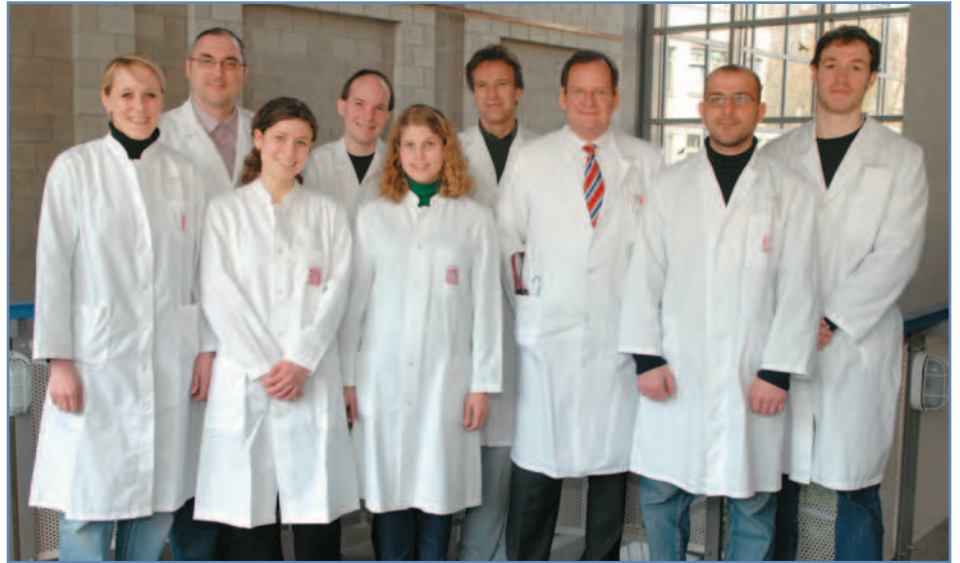
At this point we would like to thank all patients who were willing to participate in these trials.

Successful implementation of clinical trials in the future requires the continued cooperation of patients and we therefore appreciate any and each participant in these studies. Only together will we secure future medical progress.

Study designation	pts. enrolled 2008	overall enrolled patients 2008
Averroes	3	3
Certify	13	16
Champion	6	6
Cogent	21	21
Crescendo	2	35
Improve IT	22	24
Current	96	102
I-Preserve	recruiting terminated	15
Olympia	recruiting terminated	12
Plato	11	35
Proency	79	79
Rely	recruiting terminated	32
Rocket	2	2
Red-HF	2	7
Sepia	5	5
Shift	5	6
Spirit Women	6	6
Transcent	recruiting terminated	16
Zomaxx	recruiting terminated	14
	273	436

Preclinical Experimental Research

> Vascular Biology/Molecular Cardiology Lab



Preclinical Research team

(Dipl.-Biol. Swenja Schumacher, Prof. Andreas Daiber, Merle Götz, Jörg Schreiner, Nicole Schramm, Dr. Matthias Oelze, Prof. Thomas Münzel, Mohammed Alhamdani, Moritz Brandt)

— The preclinical studies primarily focus on those mechanisms resulting in impaired endothelial function. The endothelium is a single layer of cells lining the inside of vessels and stopping blood components from penetrating into or through the wall.

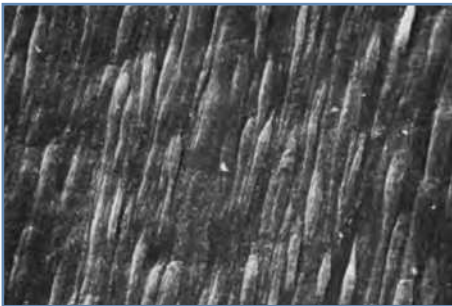
Because of the large number of cells (5×10^{13}), mass (1.5kg) and surface area ($1,000\text{m}^2$) the endothelium plays a pivotal role in vascular homeostasis, and due to its marked metabolism it may justly be regarded as the biggest organ of the body. Its surface area is as big as a football field.

The endothelium produces substances which may dilate or constrict vessels, stop or accelerate the process of vascular calcification.

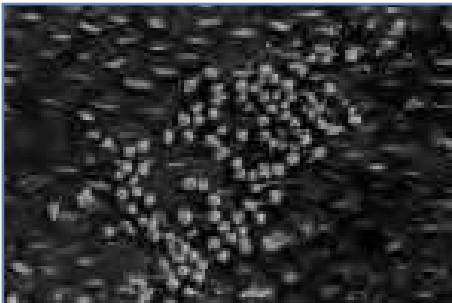
The possible course of vascular calcification is determined not only by risk factors such as smoking, hypertension, diabetes and excessively elevated cholesterol levels, but also by the individual genetic disposition.

Functional impairment of the endothelium is known as endothelial dysfunction and is important for clinicians, as this dysfunction is the first clinically noticeable marker for evolving atherosclerosis which can be measured. This in turn permits the early recommendation of preventive measures such as a change in lifestyle or drug regimen in order to prevent full blown atherosclerosis which often develops into fatal complication of acute myocardial infarction.

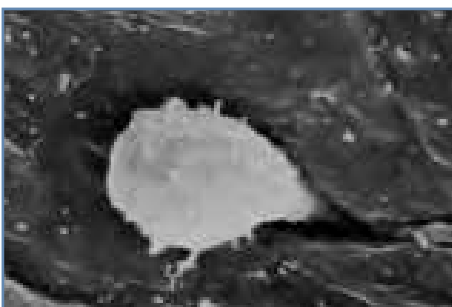
The early vascular changes will be explained briefly using the following images obtained by electron microscopy:



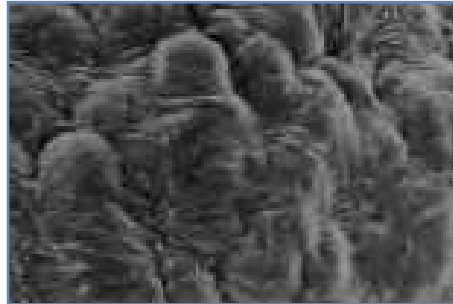
In healthy vessels the endothelial cells are aligned uniformly and parallel to the direction of the blood flow. The surface appears smooth and based on this electromicrograph good endothelial function may be assumed.



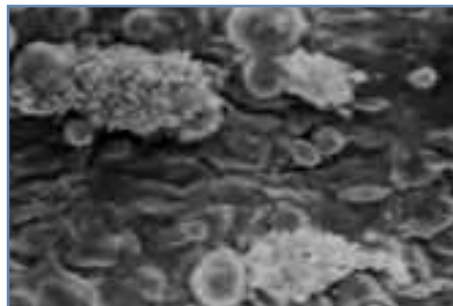
Once risk factors come into play, inflammatory cells, in this case white blood cells, stick to the endothelium.



They are also capable of slipping through the endothelial cell layer.



With the deposition of blood lipids the surface becomes more irregular and the platelets will clot more easily. This will also release growth factors. The latter will facilitate the growth of changes in the wall and may ultimately result in the vessel narrowing, e.g., coronary stenosis.



This in turn will impair the blood supply of the heart and produce the pain known as angina pectoris. It is important that these electron micrographs depict early stages of vascular changes (endothelial dysfunction) which may regress by appropriate diet or physical exercise. This is the reason why in the Department of Medicine 2 endothelial function is determined in almost all patients and for each participant in the Gutenberg Heart Study this vascular function is measured by three different techniques.

During the last year our experimental lab has pursued different projects promoting the development of endothelial dysfunction.

- age,
- diabetic metabolism and
- implantation of drug eluting stents.

Quite interesting are the results of studies identifying new mechanisms which help medication such as lipid reducing drugs (statines) or angiotensin receptor blockers (sartanes) improve vascular function in animals with induced diabetes.

We have also made significant progress in analyzing the different modes of action of organic nitrates such as nitroglycerin and PETN (Pentalong®).

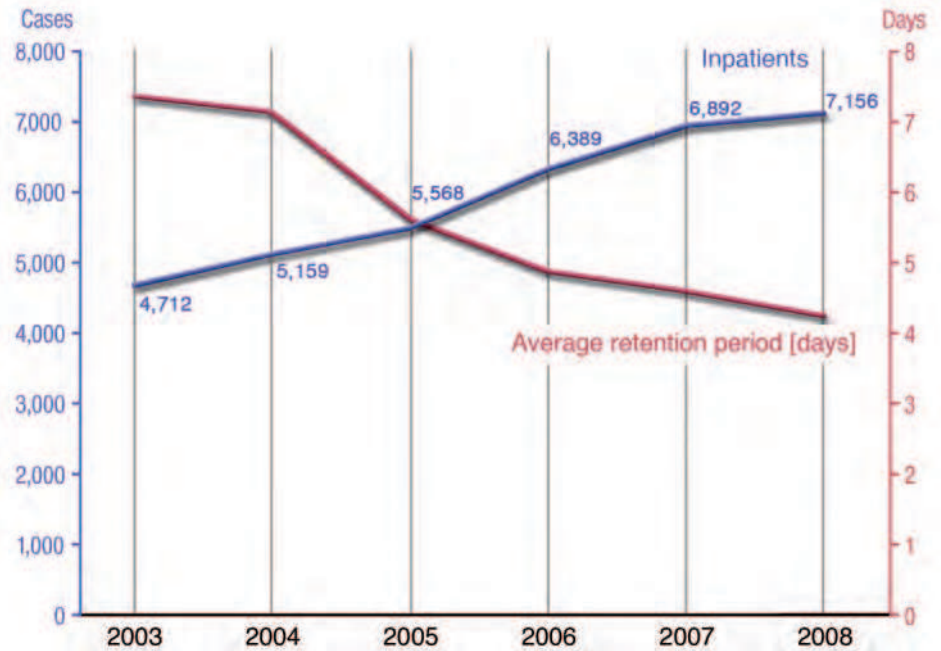
> Molecular Cardiology – Sponsored Projects 2008-2009

Project	Supervisor	Financial support	Publications
The effect of pentaerithryltetranitrate (PETN) treatment on angiotensin II induced endothelial dysfunction and hypertension	Daiber Münzel	ACTAVIS Robert Müller Foundation (scholarship)	Schuhmacher et al., submitted
A new class of organic nitrates: Studies on bioactivation, tolerance and cross-tolerance phenomena.	Daiber	Development funds 2008 + SMRC resources (8851284)	Schuhmacher et al., Br. J. Pharmacol. 2009
The role of ALDH-2 in the development of nitrate tolerance following the acute application of organic nitrates: patient study based on monocyte ALDH-2 activity and other blood parameters	Daiber Wenzel Schulz	Development funds 2008 + Science and Medicine Research Center resources (8851284)	Wenzel et al., J. Pharmacol. Exp. Ther. 2009
The role of mitochondrial and NADH oxidase mediated superoxide sources in the development of nitrate tolerance	Daiber Wenzel	Collab Res Center 553 and remaining MAIFOR funds	Wenzel et al., Antiox. Redox. Signal. 2008
The effect of in vivo treatment with telmisartan on streptococin induced diabetes mellitus (IDDM) in Wistar rats	Daiber Wenzel	Boehringer Ingelheim	Wenzel et al., Free Radic Biol Med 2008
The effect of AMP-mediated protein kinase activation on endothelial function, hypertension, septic shock and nitrate tolerance in vivo	Schulz	German Research Foundation (DFG)	Schulz et al., Circulation 2008 and Schuhmacher et al., being revised
The critical role of cardiac NADPH oxidases as superoxide sources in the development of alcoholic cardiomyopathy: studies of a murine model of acetaldehyde overload	Wenzel	German Heart Foundation	Being prepared
Aging and endothelial dysfunction	Wenzel Daiber	Robert Müller Foundation	Wenzel et al., Cardiovasc Res 2008
Nitros(yl)ating species in the nitric oxide – superoxide – peroxynitrite system: evidence of the essential role of peroxynitrite in physiological nitros(yl)ating reactions	Daiber	JGU development funds 2008 + Science and Medicine Research Center resources (8851284)	Daiber et al., Free Radic. Biol. Med.
Causes of endothelial dysfunction induced by drug eluting stents	Jabs	Cordis	Jabs et al., J Am Coll Cardiol 2008
The effect of atorvastatin on STC induced insulin dependent diabetes mellitus	Wenzel Daiber Oelze	Pfizer	Wenzel et al., Atherosclerosis 2008
The role of isolated reducing of the heart rate with ivabradin on the progression of atherosclerosis in the murine model	Schulz Münzel	Servier	Schuhmacher et al., submitted
The role of biliverdin reductase as antioxidative system in increased oxidative stress	Jansen Daiber	JGU development funds 2008 + SMRCenter res (8851284)	Being prepared
Recovery of endothelial dysfunction and vascular oxidative stress in rats with streptococin induced insulin dependent diabetes mellitus through treatment with pentaerithryltetranitrate	Daiber Münzel	ACTAVIS	Being prepared
The effect of immune cells from the blood stream on endothelial dysfunction in an experimental hypertension model	Wenzel Münzel		Trial was started
The effect of telmisartane on vascular formation of reactive oxygen species and vascular dysfunction in an experimental nitrate tolerance model	Daiber Münzel	Boehringer Ingelheim	Trial was started
Mechanisms of nebivolol-mediated protection of endothelial function in various animal models	Daiber Wenzel Münzel	Forest Research Institute	Trial was started
Crosstalk between reactive oxygen species from the mitochondria and NADPH oxidases	Daiber	Development funds 2008 + Sc and Med Research Center resources (8851284)	Trial was started

Department Performance in Numbers

Through the restructuring described above and additional optimization in admission and discharge management, once again we have been able to increase our admissions and therefore our revenues.

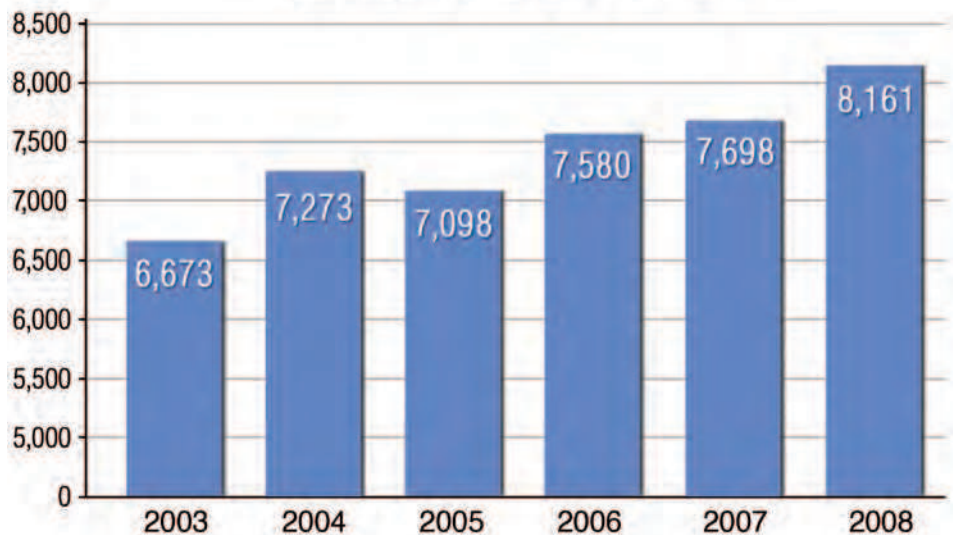
We have now passed the level of 7,000 patient per year, and the forecast for this year indicates that we are rapidly approaching 7,500 admissions per year. There has been a corresponding decrease in the mean length of stay to just above four days.



Regarding the accumulated casemix points we have seen a dramatic increase of almost 500 points.

Multiplied with the going base rate of almost Euro 2,900, this represents an increase in revenues of about Euro 1.4 million (source: internal budgeting).

Cumulative Case Mix Points



Mainz Heart Network

As far as the treatment of cardiovascular disease in the Rhein-Main area is concerned, there are quite a number of competitors. The mission is to increase the number of cardiovascular cases is therefore a major challenge. On the next few pages we would like to concentrate on describing the organization of our Mainz Heart Network and its effect on patient flow in the highly competitive Rhein-Main area.

Initial situation in 2004:

Starting 1 January 2004, all hospitalized patients in Germany were to be billed according to the German DRG system (G-DRG – diagnosis related groups). Supposedly the DRG system allows better economic assessment of the cases, will reduce length of stay and help cut costs by reducing the number of hospital beds. In this context it is interesting to note the computed comparison of 2003 between the medical centers of the universities of Mainz and Heidelberg. Despite a comparable number of hospital beds the number of admissions, and therefore revenues, in Mainz was significantly lower than in Heidelberg. In addition, by 2003 Heidelberg had already introduced a chest pain unit (CPU) in an attempt to improve care of patients with acute myocardial infarction.

	Mainz	Heidelberg
Admissions	4700	7500
# of beds	117	110
Primary revenues	19 mill.	33 mill.
Chest Pain Unit	no	yes

The Department of Medicine 2 never wavered from its goal to optimize the regional quality of care for patients with cardiac symptoms.

Until recently the path of chest pain patients in Mainz was not clearly defined, resulting in a significant loss of valuable time which made the situation of these patients even worse, especially if the chest pain was due to myocardial infarction.

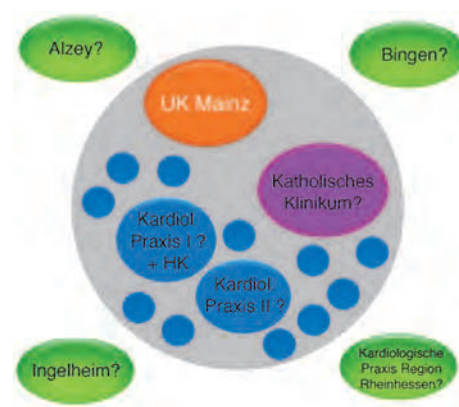
Patients with chest pain either contacted one of the private cardiological practices (e.g., CARDIOACUT), the family physician or Mainz University Medical Center. After initial assessment ruling out or confirming possible myocardial infarction, the patient was then referred back to the family physician or referring physician or admitted to the University Medical Center. Consistent rules for Mainz were almost nonexistent. Due to the special experience of the head of department, Prof. Münzel, MD, gained in the highly competitive cardiological situ-



Situation before the Mainz Heart Network was founded

ation in Hamburg, it was evident that in Mainz networking and not lone action was called for; in other words, not only should the care offered by the university be scrutinized, but also the overall situation in the region in an attempt to create cardiological networks. The following figure illustrates the possible cooperating partners of this type of heart network.

In mid-2004 corresponding discussions were held with private cardiological practices, the Mainz Catholic Medical Center, health insurance providers and the Rheinland-Pfalz Department of Health. The overall objective was to improve the emer-



gency treatment of patients with chest pain by establishing a specialized chest pain unit. After rather brief preparation the Mainz University Chest Pain Unit was established in 2005 (see Annual Report 2004-2007).

At the same time Mainz Catholic Medical Center (KKM) decided to establish a cardiac cath lab. Use of this cath lab was of some interest for private cardiological practices as well as Mainz University Medical Center.

In the summer of 2007 Mainz University Medical Center was able to sign a contract of cooperation with KKM for a period of eight years. The lab was opened and blessed in a ceremony officiated by Monsignore Eberhardt.



In an effort to improve the care of chest pain patients even further, subsequent discussions were held with the CARDIOPRAXIS. As a result, a seamless interface was created between outpatient and hospitalized care of patients with chest pain at the Mainz University Medical Center. This interface was unique in all of Germany.

In an attempt to improve the care of patients with chest pain, the CARDIOPRAXIS has relocated its emergency clinic (**CARDIO ACUT**) to the Mainz University Medical Center. The rooms of **CARDIO ACUT** are now right next door to the chest pain unit (figure).

Once **CARDIO ACUT** has diagnosed a chest pain patient as having myocardial infarction, he/she is immediately referred to the chest pain unit next door. This ensures rapid and efficient treatment of the infarction. On the other hand, patients admitted to the Mainz University Medical Center with suspected myocardial infarction will be referred back to the Cardiopraxis once infarction has been ruled out.

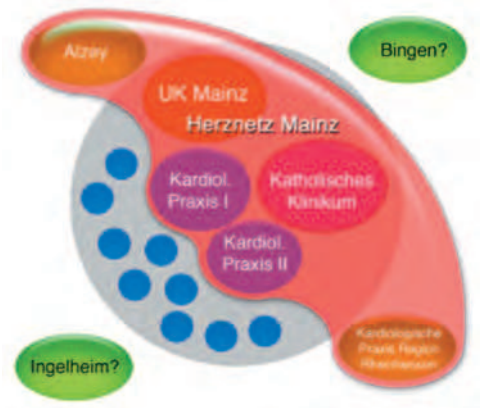


Situation after the Mainz Heart Network had been founded

In both 2007 and 2008, our Mainz Heart Network was expanded further by finalizing cooperation agreements with the private cardiological practices of **Rittgen/Katsaros** (Mainz) and **Hauser** (Bad Kreuznach).

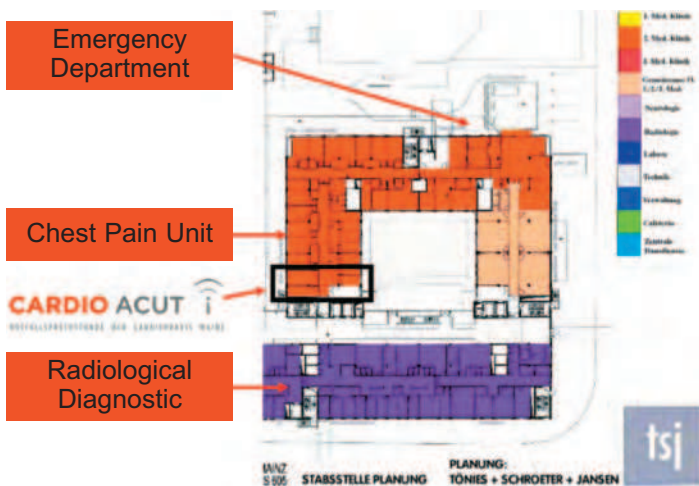
The benefit of this type of cooperation with private cardiological practices is the fact that patients treated by physicians in these offices may be catheterized by them at the cath lab of the Medical Center, with the latter providing maximum expertise and best possible emergency management.

Our heart network with its objective of optimizing the care of patients with coronary heart disease has developed accordingly.



The exciting question is to what extent these measures have impacted on the performance numbers of the Department of Medicine 2. As illustrated by the table there was a definite increase in the number of admissions and revenue level with a concomitant reduction in the number of beds provided. At least part of this development is a direct result of establishing the chest pain unit.

	Mainz 2004	Mainz 2008
Admissions	4725	7156
# of beds	118	110
Primary revenues	19 Mio	~30 Mio
Chest Pain Unit	no	yes



Department Events in 2008

Date	Event	Presentations
16 January 2008	Hot topics in cardiology and heart surgery	<ul style="list-style-type: none"> ■ “Pill in the Pocket” concept in atrial fibrillation ■ current heart valve surgery ■ percutaneous heart valve replacement ■ Renin-angiotensin system in cardiovascular risk patients
12 March 2008	Symposium Cooperative care of cardiological emergencies in the Mainz Heart Network Sponsored by Pfizer	<ul style="list-style-type: none"> ■ Cardiac emergency: Who should be hospitalized and what happens? ■ Cardiac emergency: What is the role of the private cardiological practice? ■ Where is the place of the family physician in the Mainz Heart Network? ■ Integrated care as a model of cooperation
09 April 2008	ONTARGET – results forum Sponsored by Boehringer Ingelheim	<ul style="list-style-type: none"> ■ Sudden cardiac death ■ HOPE and ONTARGET – trial review and rationale ■ ONTARGET – study results in cardiovascular prevention ■ Discussion forum for results and their pertinence to practical work
25-26 April 2008	BNK satellite symposium Mainz – Atlanta, USA Innovations 2008 Interventional strategies: Coronary heart disease and heart valves supported by numerous sponsors	<ul style="list-style-type: none"> ■ Diagnosis and therapy 2008 ■ Valvular disorders ■ New quantitation in echocardiography
11 June 2008	1 st network event: Success through cooperation - Rheinhessen healthcare region	<ul style="list-style-type: none"> ■ Network potentials: Rheinhessen healthcare region initiative ■ Expectations of the leaders for the participants ■ Expectations of the participants for the healthcare region ■ Future course / milestones
06 August 2008	Symposium Thrombosis service – integrated care in oral anticoagulation	<ul style="list-style-type: none"> ■ Oral anticoagulation in Germany – situation analysis ■ Patient care through the Mainz Thrombosis Service ■ The thrombosis service as an integrated care project
03 September 2008	Symposium Secondary prevention of stroke supported by numerous sponsors	<ul style="list-style-type: none"> ■ What is new in secondary medical stroke prevention? ■ Which embolic sources must I remember? ■ What to do in patent foramen ovale (PFO)?
10 October 2008	Hypertension Symposium: Aspects in diabetology, cardiology and nephrology	<ul style="list-style-type: none"> ■ Hypertension: Special aspects in cardiac patients ■ Hypertension: Special aspects in renal patients ■ Hypertension: Special aspects in diabetic patients ■ CardioAcute – initial experience, preliminary results

<p>24 October 2008</p>	<p>Symposium: IBISCUS Imaging School for Contrast-Enhanced Ultrasound</p> <p>International course on contrast echocardiography in cardiac imaging</p> <p>Hosted by the German Cardiac Society – Herz- und Kreislaufforschung e.V.</p> <p>Sponsored by Bracco</p>	<ul style="list-style-type: none"> ■ Technical and physiological principles in contrast echocardiography ■ Clinical benefit of contrast enhancement in resting and exercise echocardiography ■ Assessment of global and regional systolic function. Current data and initial experience from a 3D study. ■ Live study in contrast echocardiography (live coverage from the echo lab) <ul style="list-style-type: none"> – Assessment of global and regional function (dobutamine stress echocardiography) – Ischemia detection (vasodilator stress echocardiography) ■ interspersed with interactive case presentations (televoting) ■ Report from clinical research: <ul style="list-style-type: none"> Vitality assessment after myocardial infarction ■ Myocardial contrast echocardiography: <ul style="list-style-type: none"> Technical aspects and clinical significance
<p>29 October 2008</p>	<p>Symposium: Cardiology update – heart rate and CHD</p> <p>Organized by Servier</p>	<ul style="list-style-type: none"> ■ Heart rate as cardiovascular risk factor ■ Sole heart rate reduction in the treatment of cardiovascular disease ■ News from CHD: The Beautiful trial – reduce heart rate and live longer?
<p>28 November 2008</p>	<p>Evening topic for patients</p> <p>“Heart valve disease, valve surgery, anticoagulation”.</p> <p>In cooperation with the German Heart Foundation</p>	<ul style="list-style-type: none"> ■ Latest results from the American Heart Congress 2008 ■ The new thrombosis service in Mainz ■ Implanting heart valves through the groin: Preliminary results from Mainz
<p>29 November 2008</p>	<p>Workshop: Diagnosis and treatment of early stage atherosclerosis</p> <p>In cooperation with Berlin-Chemie</p>	<ul style="list-style-type: none"> ■ Prognostic significance and pharmacological modification of endothelial function ■ Measuring the thickness of intima and media: when, how and why? ■ Workshop <ul style="list-style-type: none"> – endothelial function – intima-media thickness ■ Antiatherosclerotic effects of renin-angiotensin receptor blockers ■ New types of healthcare provision – the rules have changed: Health care system requirements

“Mainz Heart Network”

> nominated for the Hospital Award 2008



— With its innovative “Mainz Heart Network” project the Department of Medicine 2 was nominated for the best referral concept of the 4th Congress on Hospital Communications. Among the 80 contenders for this award it was voted one of the top four concepts.

The jury emphasized the distinctive concept of restructuring the regional health-care market through the “Mainz Heart Network”. Established under the directorship of Felix Post, MD of the Department of Medicine 2, the “Mainz Heart Network” rests on cooperation between urban and regional hospitals and private cardiological practices in providing acute care for patients with cardiac complaints in the Mainz and Rheinhessen regions. The common cooperative care of cardiac emergencies not only helped to prevent the establishment of expensive parallel pathways but improved all other economic parameters as well – while at the same time improving quality of care and patient satisfaction.

The Hospital Award is given to the best concepts and managers in the area of hospital communications. The awards for “Best Marketing Concept”, “Best Referral Concept”, “Best Website” and “Manager of the Year” were presented 27-30 October 2008 during the 4th Congress on Hospital Communications in Cologne. The topics of this congress hosted by Rotthaus Medical GmbH are hospital communications, hospital marketing and public relations.

Department of Medicine 2 in the Media

Thrombose im Blickpunkt

Herz-Kreislauferkrankungen sind die häufigste Todesursache in Deutschland. Einem Herzinfarkt folgt die Thrombose als zweithäufigste Todesursache. Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein.

Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein. Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein.

Meiner Zeitung

Von Diabetes bis Thrombose

Substitutionsbehandlung (Schnell- und Langzeitinsulin) ist ein zentraler Bestandteil der Diabetesbehandlung. Die Substitutionsbehandlung ist ein zentraler Bestandteil der Diabetesbehandlung. Die Substitutionsbehandlung ist ein zentraler Bestandteil der Diabetesbehandlung.

Gesundheit ist für viele Herzessache

Auftrag bei Gesundheitsfragen auf flächendeckende Patientenaufklärung: Patienten können sich schützen.

Die flächendeckende Patientenaufklärung ist ein zentraler Bestandteil der Gesundheitsversorgung. Die flächendeckende Patientenaufklärung ist ein zentraler Bestandteil der Gesundheitsversorgung. Die flächendeckende Patientenaufklärung ist ein zentraler Bestandteil der Gesundheitsversorgung.

Herzkappen-OP mit Katheter

Herz-Kreislauferkrankungen sind die häufigste Todesursache in Deutschland. Einem Herzinfarkt folgt die Thrombose als zweithäufigste Todesursache. Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein.

Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein. Die Thrombose ist eine Gefäßerkrankung, bei der sich Blutgerinnsel bilden, die das Gefäß verstopfen können. Dies führt zu einer Durchblutungsstörung und kann lebensbedrohlich sein.

Herzinfarkt

Herzinfarkt ist eine der häufigsten Todesursachen in Deutschland. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Gutenbergs-Herzstudie

Prof. Thomas Münzel (Bild) und seine Mitarbeiter an der Mainzer Universitätsklinik haben über einen Zeitraum von zehn Jahren Daten von rund 17.000 Personen unter die Lupe gefasst.

Die Gutenbergs-Herzstudie ist eine groß angelegte Kohortenstudie, die die Entwicklung von Herz-Kreislauferkrankungen über einen Zeitraum von zehn Jahren untersucht. Die Gutenbergs-Herzstudie ist eine groß angelegte Kohortenstudie, die die Entwicklung von Herz-Kreislauferkrankungen über einen Zeitraum von zehn Jahren untersucht.

Retningsinsel für Herzranke: CPU

Herzranke sind eine der häufigsten Todesursachen in Deutschland. Eine Retningsinsel ist eine kleine Insel im Herzen, die die Durchblutung verbessert und das Risiko für Herzranke senkt.

Die Retningsinsel ist eine kleine Insel im Herzen, die die Durchblutung verbessert und das Risiko für Herzranke senkt. Die Retningsinsel ist eine kleine Insel im Herzen, die die Durchblutung verbessert und das Risiko für Herzranke senkt.

Was das Herz schlägt

Das Herz schlägt etwa 100.000 Mal pro Tag. Die Herzschlagfrequenz wird durch verschiedene Faktoren beeinflusst, darunter Stress, Bewegung und Alter.

Die Herzschlagfrequenz wird durch verschiedene Faktoren beeinflusst, darunter Stress, Bewegung und Alter. Die Herzschlagfrequenz wird durch verschiedene Faktoren beeinflusst, darunter Stress, Bewegung und Alter.

Herzinfarkt

Herzinfarkt ist eine der häufigsten Todesursachen in Deutschland. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Herzinfarkt

Herzinfarkt ist eine der häufigsten Todesursachen in Deutschland. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Herzinfarkt

Herzinfarkt ist eine der häufigsten Todesursachen in Deutschland. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Herzinfarkt

Herzinfarkt ist eine der häufigsten Todesursachen in Deutschland. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen. Ein Herzinfarkt tritt ein, wenn ein Teil des Herzmuskels absterbt, weil er nicht genügend Sauerstoff bekommt. Dies kann zu bleibenden Schäden am Herzen und zu Herzschwäche führen.

Die Experten der Herzen

Die Experten der Herzen sind Spezialisten für die Diagnose und Behandlung von Herz-Kreislauferkrankungen. Sie arbeiten in spezialisierten Kliniken und sind für die Versorgung von Patienten mit Herz-Kreislauferkrankungen verantwortlich.

Die Experten der Herzen sind Spezialisten für die Diagnose und Behandlung von Herz-Kreislauferkrankungen. Sie arbeiten in spezialisierten Kliniken und sind für die Versorgung von Patienten mit Herz-Kreislauferkrankungen verantwortlich. Die Experten der Herzen sind Spezialisten für die Diagnose und Behandlung von Herz-Kreislauferkrankungen.

Ein Mammutprojekt im Dienste der Herz-Vorsorge

Ein Mammutprojekt im Dienste der Herz-Vorsorge ist ein groß angelegtes Projekt zur Früherkennung von Herz-Kreislauferkrankungen. Es umfasst die Untersuchung von Millionen von Menschen auf Herz-Kreislauferkrankungen.

Das Mammutprojekt im Dienste der Herz-Vorsorge ist ein groß angelegtes Projekt zur Früherkennung von Herz-Kreislauferkrankungen. Es umfasst die Untersuchung von Millionen von Menschen auf Herz-Kreislauferkrankungen. Das Mammutprojekt im Dienste der Herz-Vorsorge ist ein groß angelegtes Projekt zur Früherkennung von Herz-Kreislauferkrankungen.

Kostenlose Tickets für die Forschung

Kostenlose Tickets für die Forschung sind eine Initiative zur Unterstützung von wissenschaftlichen Projekten. Die Tickets sind kostenlos und können für die Finanzierung von Forschungsvorhaben verwendet werden.

Die kostenlosen Tickets für die Forschung sind eine Initiative zur Unterstützung von wissenschaftlichen Projekten. Die Tickets sind kostenlos und können für die Finanzierung von Forschungsvorhaben verwendet werden. Die kostenlosen Tickets für die Forschung sind eine Initiative zur Unterstützung von wissenschaftlichen Projekten.

Stark gegen Brustschmerz

Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen.

Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen. Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen.

Stark gegen Brustschmerz

Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen.

Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen. Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen.

Stark gegen Brustschmerz

Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen.

Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen. Die Initiative umfasst die Bereitstellung von Informationen und Unterstützung für Patienten mit Brustschmerzen. Die Initiative Stark gegen Brustschmerz ist eine Initiative zur Unterstützung von Patienten mit Brustschmerzen.

Publication Highlights 2008

Vol. 51, No. 22, 2008
ISSN 0735-3997/08/44-46
doi:10.1093/ajph.2008.01.058

Journal of the American College of Cardiology
© 2008 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vascular Medicine

Different Calculations of Ankle-Brachial Index and Their Impact on Cardiovascular Risk Prediction

Christine Espinola-Klein, MD; Hans J. Rupprecht, MD; Christoph Bickel, MD; Karl Lackner, MD; Savvas Stavridis, MD; Claudia M. Messow; Thomas Münzel, MD; Stefan Blankenberg, MD; for the AtheroGene Investigators

ANTIOXIDANTS & REDOX SIGNALING
Volume 11, Number 22, 2008
DOI: 10.1093/ajph.2008.01.058

Sirolium-Induced Vascular Dysfunction

Increased Mitochondrial and Nicotinamide Adenosine Dinucleotide Phosphate Oxidase-Dependent Superoxide Production and Decreased Vascular Nitric Oxide Formation

Alexander Jahn, MD, Sebastian Göbel, MS, Philip Wenzel, MD, Andrei L. Kleschyov, PhD, Marcus Hortsmann, MS, Matthias Oelze, PhD, Andreas Daiber, PhD, Thomas Münzel, MD Mainz, Germany

B-type natriuretic peptide as a marker for sepsis-induced myocardial depression in intensive care patients*

Felix Post, MD; Ludwig S. Weilemann, MD; Claudia-Martina Messow; Christoph Sinning, MD; Thomas Münzel, MD

Suppression of the JNK Pathway by Induction of a Metabolic Stress Response Prevents Vascular Injury and Dysfunction

Eberhard Schulz, MD¹; Jörn Dopfke, MD²; Swenja Schützmeier, BS; Shane R. Thomas, PhD; Kai Chen, MD, PhD; Andreas Daiber, PhD; Philip Wenzel, MD; Thomas Münzel, MD; John F. Keane, Jr, MD

Background—Oxidative injury and dysfunction of the vascular endothelium are early and causal features of many vascular diseases. Single antioxidant strategies to prevent vascular injury have not with mixed results.

Methods and Results—Here, we report that induction of a metabolic stress response with adenosine monophosphate kinase (AMPK) prevents oxidative endothelial cell injury. This response is characterized by stabilization of the mitochondria and increased mitochondrial biogenesis, resulting in attenuation of oxidative c-Jun N-terminal kinase (JNK) activation. We report that peroxisome proliferator coactivator 1 α is a key downstream target of AMPK that is both necessary and sufficient for the metabolic stress response and JNK attenuation. Moreover, induction of the metabolic stress response in vivo attenuates reactive oxygen species-mediated JNK activation and endothelial dysfunction in response to angiotensin II in wild-type mice but not in animals lacking either the endothelial isoform of AMPK, or peroxisome proliferator coactivator 1 α .

Conclusions—These data highlight AMPK and peroxisome proliferator coactivator 1 α as potential therapeutic targets for the amelioration of endothelial dysfunction and, as a consequence, vascular disease. (Circulation. 2008;118:1347-1357.)

Key Words: angiotensin ■ endothelium ■ hypertensive ■ metabolism

Original Research Communication

First Evidence for a Crosstalk Between Mitochondrial and NADPH Oxidase-Derived Reactive Oxygen Species in Nitroglycerin-Triggered Vascular Dysfunction

PHILIP WENZEL,^{1,6} HANKE MOLLNAU,^{1,6} MATTHIAS OELZE,¹ EBERHARD SCHULZ,¹



Circulation Heart Journal 2008; 118:44-47
doi:10.1161/CIRCULATIONAHA.107.709990

CLINICAL RESEARCH
Prevention and Epidemiology

Association of adiponectin with adverse outcome in coronary artery disease patients: results from the AtheroGene study

Renate Schnabel¹, Claudia M. Messow², Edith Lubos¹, Christine Espinola-Klein¹, Hans J. Rupprecht¹, Christoph Bickel¹, Christoph Sinning¹, Steggos Trikas³, Till Keller⁴, Sabine Genth-Zorn¹, Karl J. Lackner⁵, Thomas F. Münzel¹, and Stefan Blankenberg¹

Effects of oral niacin on endothelial dysfunction in patients with coronary artery disease: Results of the randomized, double-blind, placebo-controlled INEF study

Ascan Warmholtz^{1,2,3}, Philipp Wild^{4,5}, Mir-Abolqazl Ostad⁶, Veronika Elsner⁶, Fabian Stieber⁴, Reinhard Schinzel⁶, Ulrich Walter⁶, Dirk Peetz⁴, Karl Lackner^{4,5}, Stefan Blankenberg¹, Thomas Münzel¹

¹Department of Medicine II, Johannes Gutenberg University Mainz, Mainz, Germany

²Department of Internal Medicine, Johannes Gutenberg University Mainz, Mainz, Germany

³Department of Internal Medicine, Johannes Gutenberg University Mainz, Mainz, Germany

⁴Department of Clinical Chemistry and Laboratory Medicine, Johannes Gutenberg University Mainz, Mainz, Germany

⁵Department of Internal Medicine, Johannes Gutenberg University Mainz, Mainz, Germany

⁶Department of Internal Medicine, Johannes Gutenberg University Mainz, Mainz, Germany

Foundation Heart of Mainz

www.herzstiftung-mainzer-herz.de

Foundation Heart of Mainz – Objective of the foundation

The objective of the Foundation Heart of Mainz is the early detection and effective treatment of myocardial infarction and the early stages of other heart diseases in order to counteract the predicted increase in these disorders. About 300,000 patients in Germany currently experience myocardial infarction, with roughly 65,000 patients dying from it. Experts estimate that this rate will double by 2025.

The foundation, founded in 2007, supports research and teaching and continuous improvement of patient care at the Department of Medicine 2. Foundation work focuses on prevention, diagnosis and treatment of cardiovascular shock, interventional therapy of coronary heart disease (CHD), diagnosis and interventional treatment of cardiac arrhythmias and the treatment of peripheral vascular disorders.

The Mainzer Volksbank donated a total of Euro 35,000 for the “Foundation Heart of Mainz”.



Hans-Werner Diehl presenting his donation of Euro 25,000 to Prof. Thomas Münzel

The Mainzer Volksbank supported the Foundation Heart of Mainz with Euro 10,000

in June 2008 and another donation of Euro 25,000 in October 2008. “Our commitment is geared towards saving lives and contributing to research and patient care, as well as improving the quality of life for these patients”, said Hans-Werner Diehl, CEO of the MVB, on presenting the first cheque to Prof. Münzel, Head of the Department of Medicine 2 and initiator of the Foundation Heart of Mainz, and Hermann Becker, member of the board of trustees of the foundation. According to Prof. Münzel all steps taken by the Foundation Heart of Mainz follow one common goal: to always keep cardiological diagnosis and treatment state-of-the-art so as to ensure best possible care for all patients.

“Every euro donated to the foundation will help save lives. And this is why we are very pleased about the generous donation from Mainzer Volksbank”, added Prof. Münzel. The money for the second donation was collected by Hans-Werner Diehl, the former CEO of Mainzer Volksbank, at his retirement festivities.

Big support for foundation Foundation Heart of Mainz says thank you to its patrons

Institutions, banks and companies from Rhineland-Pfalz have been supporting the Foundation Heart of Mainz since its incep-



Secretary Doris Ahnen and Prof. Thomas Münzel at a meeting with the sponsors of the Foundation Heart of Mainz (Peter Ditsch, Jürgen Dietz, Prof. Thomas Münzel, Peter Geipel, Secretary Doris Ahnen, Deputy Speaker of the State Parliament and Chairman, Foundation Heart of Mainz, Hans-Artur Bauckhage, Hans-Joachim Metternich, and Uwe Abel)

Ditsch and Jürgen Dietz, businessmen from Mainz.

At the same time, Prof. Münzel expressed his hope that commerce and industry will continue to lend their support in the future. Due to the predicted doubling of the annual number of deaths from acute myocardial infarction, the effort in research and prevention must be continued at this level, pleaded Prof. Münzel. Doris Ahnen, Secretary of Science, who used this opportunity to emphasize the importance of foundations for the common good in Rheinland-Pfalz.

“Foundations offer enormous benefits for society. The long-term commitment of foundations make them important partners when it comes to fulfilling civic responsibilities.” This is why she is glad that the Rheinland-Pfalz Foundation Act is a role model nationwide. “Our state offers the best possible conditions for founders. With our transparent foundation laws we let you work effectively and with a minimum of red tape, thereby supporting civic commitment,” said Secretary Ahnen.

Q and A evening for patients on heart valve disorders, valve surgery and anticoagulation

As part of its activity, the Foundation Heart of Mainz cooperates with national and international universities and the German Heart Foundation. As part of a nationwide information campaign in November of 2008, both foundations offered a joint Q & A evening for patients on heart valve disorders, valve surgery and anticoagulation. The audience was able to gain an insight into the latest research results and to see for themselves the innovative power of the Department of Medicine 2.



Joint event of the Foundation Heart of Mainz and German Heart Foundation

Margarete Waitz Foundation

www.margarete-waitz-stiftung.de

> Margarete Waitz Foundation awards doctoral prizes and research scholarship Outstanding young medical investigators honored

— As laid down in its charter, the Margarete Waitz Foundation awarded its annual prize for outstanding scientific doctoral theses from students in the Department of Medicine 2.

Honored in 2008 were Peter Schlindwein, MD and Katja Weisbrod, MD. They shared the Euro 3,000 doctoral thesis award for their theses, both of which were given highest marks with magna cum laude.

In his excellent thesis Dr. Schlindwein presented the results of his morphometric analysis of various vessels after percutaneous transluminal angioplasty in the large animal model. The results definitely indicated a heterogeneous reaction of individual vascular segments to identical dilation stimuli and therefore demonstrated that results for vascular control may not simply be transferred from one vessel to another. Dr. Schlindwein has submitted an outstanding study of the differentiated intra-individual variability in vascular pathophysiology.

For her thesis, Dr. Weisbrod has studied more than 27,000 plant poisonings documented from 1995 to 2004 at the Mainz Poison Information Center. The exploratory data analysis of Dr. Weisbrod's thesis has made it possible to come up with a qualified prediction of the actual poisonous potential of plants and to inaugurate a scoring system for herbal hazards. This is helpful to avoid overtreatment, in particular since most of the time the actual symptoms of poisoning due to ingested fruits, leaves and blossoms are less serious than reported in the literature.

The 2008 research fellowship of the Margarete Waitz Foundation in the amount of Euro 36,000 for one year was awarded to Thomas Jansen, MD for his work on a

research project within the context of basic immunological and cardiological research.

Dr. Jansen will spend one year in the United States at Emory University, Atlanta, with Prof. D. Harrison in his Laboratory of Molecular Cardiology. In October, Prof. Harrison and his group were able to demonstrate a new association between oxidative stress, inflammation, vascular dysfunction and hypertension. RAG-1 (-/-) mice lacking T and B lymphocytes display a markedly muted hypertensive response to intravenous administration of angiotensin II. This effect was compensated by the administration of donor T lymphocytes, but not donor B lymphocytes. This process involves various receptor-ligand interactions (CCR5/RANTES). During his stay in the United States Dr. Jansen will work on this project, being part of basic research in immunology and cardiovascular science.

The Margarete Waitz Foundation was established on 1 May 2004 after Ms. Margarete Waitz made out her will that her estate be used to establish a foundation

sponsoring nonprofit activities of the Department of Medicine 2, in particular the training of young medical professionals. The foundation is endowed with Euro 1.4 million and according to its statutes can allocate a sum of Euro 50,000 each year. Winners of the award must have completed their doctoral thesis with the Department of Medicine 2 and made a significant contribution to research in science and medicine. At the time of the research award the scholars must be members of the Department of Medicine 2. The Margarete Waitz Foundation is a nonprofit entity under civil law registered in Mainz.



Jan Kanty Fibich, Thomas Jansen, MD, Peter Schlindwein, MD, Prof. Thomas Münzel, MD

Paul Schölmerich Award

> for internal Medicine 2008

— During the annual meeting of the German Society of Internal Medicine in late March 2008, Dr. Konstantinos Stellos, 27, from Tübingen University Medical Center was honored with the Paul Schölmerich Award for Internal Medicine. Dr. Stellos was awarded this prize for his work on “Platelet-derived stromal cell derived factor-1 regulates adhesion and promotes differentiation of human CD34+ cells to endothelial progenitor cells”. Prof. Münzel, Chair of the Section of Medicine and Science of the German-Romanian Academy, presented the award endowed with Euro 10,000. In his tribute Prof. Münzel pointed out “that the work of Dr. Stellos helps to explain in particular the role of platelets in vascular and myocardial regeneration”. Once again, the award was supported by Actavis Deutschland GmbH, Langenfeld.

Second place went to Dr. Philipp Bahrmann, 40, from the Jena University Medical Center.

Dr. Bahrmann presented a paper on CHD patients undergoing an intracoronary duplex study during coronary intervention. The study was able to demonstrate the presence of microemboli, particularly after stenting and also while the balloon was passing over the guidewire.

Dr. Michael Lauterbach, 35, from Mainz University Medical Center was awarded third place. He studied the functional consequences of C1 esterase inhibition during occlusion of the superior mesenteric artery employing intravital microscopy.

Second and third place are endowed with Euro 1,000 each.

German-Romanian Academy intensified Contacts with Romania
The German-Romanian Academy is an international forum on science, ethics, theology, literature and arts registered in Mainz. This nonprofit organization supports science, culture and international understanding and fosters the establishment of scientific, cultural and intellectual ties between Germany and Romania. With the Paul Schölmerich Award, the Section of Medicine and Science of the German-Romanian Academy, chaired by Prof. Münzel, MD, honors clinical and experimental studies in the area of internal medicine, particularly in intensive care medicine. The first award was presented in 2007.



Dr. Dirk Stalleicken (Actavis), Dr. Philipp Bahrmann, Prof. Thomas Münzel, MD, Emeritus Prof. Paul Schölmerich, MD, Dr. Michael Lauterbach, Dr. Konstantinos Stellos, Prof. Hans-Rüdiger Vogel, MD

Publications 2008

1. *Bartoli G, Menegaz G, Lisi M, Di Stolfo G, Dragoni S, Gori T*
Departmental authors: *Gori T*
Model-based analysis of flow-mediated dilation and intima-media thickness. *Int J Biomed Imaging* 2008; 2008: 738545
2. *Daiber A, Harrison DG, Munzel T*
Departmental authors: *Daiber A, Munzel T*
Doubt about an essential role for constitutive nitric oxide synthase in nitroglycerin-mediated vasodilation. *Proc Natl Acad Sci U S A* 2008; 105 (47): E92; author reply E93
3. *Daiber A, Wenzel P, Oelze M, Schuhmacher S, Jansen T, Münzel T*
Departmental authors: *Daiber A, Wenzel P, Oelze M, Münzel T*
Mitochondrial aldehyde dehydrogenase (ALDH-2)-Maker of and marker for nitrate tolerance in response to nitroglycerin treatment. *Chem Biol Interact* 2008; 178: 40-47
4. *Daiber A, Wenzel P, Oelze M, Munzel T*
Departmental authors: *Daiber A, Wenzel P, Oelze M, Munzel T*
New insights into bioactivation of organic nitrates, nitrate tolerance and cross-tolerance. *Clin Res Cardiol* 2008; 97 (1): 12-20
5. *Daiber A, Shoun H, Ullrich V*
Departmental authors: *Daiber A*
Nitric Oxide Reductase (P450nor) from *Fusarium oxysporum*.. Contribution in: The smallest biomolecules – diatomics and their interactions with heme proteins. Editor: Abhik Ghosh, Elsevier Amsterdam, 2008, S.54-77
6. *Daiber A, Wenzel P, Oelze M, Seeling A, Coldeway M, Steinhoff L, Lehmann J, Münzel T*
Departmental authors: *Daiber A, Wenzel P, Oelze M, Coldeway M, Münzel T*
Oxidativer Stress und antioxidative Funktionen – Vergleich von Pentaerithryltetranitrat und Nitroglycerin. *Herz* 2008; 33: 8-12
7. *Daiber A, Gori T*
Departmental authors: *Daiber A, Gori T*
Vascular tolerance to nitroglycerin in ascorbate deficiency: results are in favour of an important role of oxidative stress in nitrate tolerance. *Cardiovasc Res* 2008; 79 (4): 722-3; author reply 724
8. *Denk K, Albers J, Kayhan N, Ister D, Hakami L, Mehlhorn U, Peivandi AA, Werner C, Münzel T*
Departmental authors: *Münzel T*
Geschlechtsspezifische negative inotrope Wirkung von Übergewicht *Z Herz, Thorax Gefäßchir* 2008; 22: 1
9. *Espinola-Klein C, Rupprecht HJ, Bickel C, Lackner K, Savvidis S, Messow CM, Münzel T, Blankenberg S*
Departmental authors: *Espinola-Klein C, Savvidis S, Münzel T, Blankenberg S*
Different calculations of ankle-brachial index and their impact on cardiovascular risk prediction. *Circulation* 2008; 118 (9): 961-967
10. *Espinola-Klein C, Rupprecht HJ, Bickel C, Lackner K, Genth-Zotz S, Post F, Münzel T, Blankenberg S*
Departmental authors: *Espinola-Klein C, Genth-Zotz S, Post F, Münzel T, Blankenberg S*
Impact of inflammatory markers on cardiovascular mortality in patients with metabolic syndrome *Eur J Cardiovasc Prev Rehabil* 2008; 15 (3): 278-284
11. *Espinola-Klein C, Neufang A, Duber C*
Departmental authors: *Espinola-Klein C*
Infrarenales Aortenaneurysma. *Internist (Berl)* 2008; 49 (8): 955-64
12. *Espinola-Klein C, Münzel T*
Departmental authors: *Espinola-Klein C, Münzel T*
Oxidativer Stress und Endothelfunktion: Welche Rolle hat das Geschlecht? *Blickpunkt der Mann* 2008; 6: 29-31
13. *Fineschi M, Bravi A, Gori T*
Departmental authors: *Gori T*
The "slow coronary flow" phenomenon: evidence of preserved coronary flow reserve despite increased resting microvascular resistances. *Int J Cardiol* 2008; 127 (3): 358-61
14. *Fineschi M, Gori T*
Departmental authors: *Gori T*
Very late thrombosis in a bare metal stent: an under-recognized problem. *Can J Cardiol* 2008; 24 (2): e6-7
15. *Gori T, Salerno D, Donati G*
Departmental authors: *Gori T*
'Parachute' accessory mitral leaflet and pulmonary valve stenosis in an asymptomatic 85-year-old man. *Eur Heart J* 2008; 29 (2): 223
16. *Gori T, Dragoni S, Lisi M, Di Stolfo G, Sonnati S, Fineschi M, Parker JD*
Departmental authors: *Gori T*
Conduit artery constriction mediated by low flow a novel noninvasive method for the assessment of vascular function. *J Am Coll Cardiol* 2008; 51 (20): 1953-8
17. *Gori T, Münzel T, Daiber A*
Departmental authors: *Gori T, Münzel T, Daiber A*
Nicht-hämodynamische Effekte organischer Nitrate und unterscheidende Charakteristika von Pentaerithrylte-trinitrat. *Arzneimitteltherapie* 2008; 26: 290-298

- 18.** *Gori T, Parker JD*
Departmental authors: *Gori T*
Nitrate-induced toxicity and preconditioning: a rationale for reconsidering the use of these drugs.
J Am Coll Cardiol 2008; 52 (4): 251-4
- 19.** *Gori T, Di Stolfo G, Dragoni S, Lisi M, Leone MC, Forconi S, Parker JD*
Departmental authors: *Gori T*
The mechanism of nitrate-induced preconditioning.
Clin Hemorheol Microcirc 2008; 39 (1-4): 191-6
- 20.** *Grotti S, Gori T*
Departmental authors: *Gori T*
Endothelium, ischemia and the good side of oxygen free radicals.
Clin Hemorheol Microcirc 2008; 39 (1-4): 197-203
- 21.** *Hink U, Alhamdani MS, Munzel T*
Departmental authors: *Hink U, Munzel T*
Nitroglycerin hits the nerve: role for mitochondrial aldehyde dehydrogenase?
J Am Coll Cardiol 2008; 52 (11): 961-3
- 22.** *Horstick G, Bierbach B, Schlindwein P, Abegunewardene N, Vosseler M, Bittinger F, Becker D, Lauterbach M, Lehr HA, Kempfski O*
Departmental authors: *Vosseler M, Becker D*
Resistance of the internal mammary artery to restenosis: a histomorphologic study of various porcine arteries.
J Vasc Res 2008; 45 (1): 45-53
- 23.** *Jabs A, Gobel S, Wenzel P, Kleschyov AL, Hortmann M, Oelze M, Daiber A, Munzel T*
Departmental authors: *Jabs A, Wenzel P, Kleschyov AL, Oelze M, Daiber A, Munzel T*
Sirolimus-induced vascular dysfunction. Increased mitochondrial and nicotinamide adenosine dinucleotide phosphate oxidase-dependent superoxide production and decreased vascular nitric oxide formation.
J Am Coll Cardiol 2008; 51 (22): 2130-8
- 24.** *Kettering K*
Departmental authors: *Kettering K*
Minimally invasive direct coronary artery bypass grafting: a meta-analysis.
J Cardiovasc Surg (Torino) 2008; 49 (6): 793-800
- 25.** *Kettering K, Weig HJ, Busch M, Laszlo R, Schreieck J*
Departmental authors: *Kettering K*
Segmental pulmonary vein ablation: success rates with and without exclusion of areas adjacent to the esophagus.
Pacing Clin Electrophysiol 2008; 31 (6): 652-9
- 26.** *Kreitner KF, Koch K, Steyns F, Abegunewardene N, Todt M, Horstick G, Dueber C*
Departmental authors: *Abegunewardene N*
Value of cardiac magnetic resonance imaging in patients with suspected acute myocarditis with a follow-up period of 1 year
Eur Radiol 2008; 18 (S1): 265
- 27.** *Leone MC, Gori T, Fineschi M*
Departmental authors: *Gori T*
The coronary slow flow phenomenon: a new cardiac "Y" syndrome?
Clin Hemorheol Microcirc 2008; 39 (1-4): 185-90
- 28.** *Li H, Hortmann M, Daiber A, Oelze M, Ostad MA, Schwarz PM, Xu H, Xia N, Kleschyov AL, Mang C, Warnholtz A, Münzel T, Förstermann U*
Departmental authors: *Daiber A, Oelze M, Kleschyov AL, Warnholtz A, Münzel T*
Cyclooxygenase 2-selective and non-selective nonsteroidal anti-inflammatory drugs induce oxidative stress by up-regulating vascular NADPH oxidases.
J Pharmacol Exp Ther 2008; 326 (3): 745-53
- 29.** *Lieb W, Zeller T, Mangino M, Gotz A, Braund P, Wenzel JJ, Horn C, Proust C, Linsel-Nitschke P, Amouyel P, Bruse P, Arveiler D, König IR, Ferrieres J, Ziegler A, Balmforth AJ, Evans A, Ducimetiere P, Cambien F, Hengstenberg C, Stark K, Hall AS, Schunkert H, Blankenberg S, Samani NJ, Erdmann J, Tiret L*
Departmental authors: *Zeller T, Blankenberg S*
Lack of association of genetic variants in the LRP8 gene with familial and sporadic myocardial infarction.
J Mol Med 2008; 86 (10): 1163-70
- 30.** *Maegdefessel L, Schlitt A, Faerber J, Bond SP, Messow CM, Buerke M, Raaz U, Werdan K, Muenzel T, Weiss C*
Departmental authors: *Muenzel T, Weiss C*
Anticoagulant and/or antiplatelet treatment in patients with atrial fibrillation after percutaneous coronary intervention. A single-center experience.
Med Klin (Munich) 2008; 103 (9): 628-32
- 31.** *Morange PE, Tregouet DA, Godefroy T, Saut N, Bickel C, Rupprecht HJ, Lackner K, Barbaux S, Peiretti F, Juhan-Vague I, Blankenberg S, Tiret L*
Departmental authors: *Blankenberg S*
Polymorphisms of the tumor necrosis factor-alpha (TNF) and the TNF-alpha converting enzyme (TACE/ADAM17) genes in relation to cardiovascular mortality: the AtheroGene study.
J Mol Med 2008; 86 (10): 1153-1161
- 32.** *Münzel T*
Departmental authors: *Münzel T*
Bedeutung der Herzfrequenz in der Therapie kardiovaskulärer Erkrankungen
Editor: Prof. Dr. Thomas Münzel, UNI-MED Bremen, 1. Aufl. 2008, 72 Seiten

- 33.** Münzel T, Sinning C, Post F, Warnholtz A, Schulz E
Departmental authors: Münzel T, Sinning C, Post F, Warnholtz A, Schulz E
Pathophysiology, diagnosis and prognostic implications of endothelial dysfunction.
Ann Med 2008; 40 (3): 180-96
- 34.** Münzel T
Departmental authors: Münzel T
Sonderstellung von PETN unter den Nitraten. Keine Toleranzentwicklung, weniger Kopfschmerzen.
Mmw Fortschr Med 2008; 150 (1-2): 41
- 35.** Neufang A, Espinola-Klein C, Dorweiler B, Pitton M, Savvidis S, Schmiedt W, Vahl C
Departmental authors: Espinola-Klein C, Savvidis S
Questionable value of adjuvant arteriovenous fistula in pedal bypass at high risk for early failure.
Ann Vasc Surg 2008; 22 (3): 379-87
- 36.** Niethammer M, Sieber M, von Haehling S, Anker SD, Munzel T, Horstick G, Genth-Zotz S
Departmental authors: Niethammer M, Munzel T, Genth-Zotz S
Inflammatory pathways in patients with heart failure and preserved ejection fraction.
Int J Cardiol 2008; 129 (1): 111-7
- 37.** Post F, Weilemann LS, Messow CM, Sinning C, Münzel T
Departmental authors: Post F, Weilemann LS, Sinning C, Münzel T
B-type natriuretic peptide as a marker for sepsis-induced myocardial depression in intensive care patients.
Crit Care Med 2008; 36 (11): 3030-7
- 38.** Salerno D, Donati G, Forconi S, Gori T
Departmental authors: Gori T
Giant pseudoaneurysm of the mitro-aortic intervalvular fibrosa: incidental diagnosis.
Intern Emerg Med 2008; 3 (3): 279-82
- 39.** Schildknecht S, Daiber A, Ghisla S, Cohen RA, Bachschmid MM
Departmental authors: Daiber A
Acetaminophen inhibits prostanoid synthesis by scavenging the PGHS-activator peroxynitrite.
FASEB J 2008; 22 (1): 215-24
- 40.** Schildknecht S, van der Loo B, Weber K, Tiefenthaler K, Daiber A, Bachschmid MM
Departmental authors: Daiber A
Endogenous peroxynitrite modulates PGHS-1-dependent thromboxane A2 formation and aggregation in human platelets.
Free Radic Biol Med 2008; 45 (4): 512-20
- 41.** Schnabel R, Messow CM, Lubos E, Espinola-Klein C, Rupprecht HJ, Bickel C, Sinning C, Tzikas S, Keller T, Genth-Zotz S, Lackner KJ, Münzel TF, Blankenberg S
Departmental authors: Lubos E, Espinola-Klein C, Sinning C, Tzikas S, Keller T, Genth-Zotz S, Münzel TF, Blankenberg S
Association of adiponectin with adverse outcome in coronary artery disease patients: results from the AtheroGene study
Eur Heart J 2008; 29 (5): 649-657
- 42.** Schnabel R, Lubos E, Messow CM, Sinning CR, Zeller T, Wild PS, Peetz D, Handy DE, Munzel T, Loscalzo J, Lackner KJ, Blankenberg S
Departmental authors: Schnabel R, Lubos E, Sinning CR, Zeller T, Wild PS, Munzel T, Blankenberg S
Selenium supplementation improves antioxidant capacity in vitro and in vivo in patients with coronary artery disease The SElenium Therapy in Coronary Artery disease Patients (SETCAP) Study.
Am Heart J 2008; 156 (6): 1201.e1-11
- 43.** Schnorbus B, Schiewe R, Ostad MA, Ostad SE, Medler C, Seiler H, Münzel T, Warnholtz A
Departmental authors: Schnorbus B, Schiewe R, Ostad MA, Ostad SE, Seiler H, Münzel T, Warnholtz A
Die PENTA-Studie: Wissenschaftlicher Hintergrund und klinische Relevanz
Herz 2008; 33 (2): 31-39
- 44.** Schuetz M, Moenk S, Vollmer J, Kurz S, Mollnau H, Post F, Heinrichs W
Departmental authors: Mollnau H, Post F
High degree of realism in teaching percutaneous coronary interventions by combining a virtual reality trainer with a full scale patient simulator.
Simul Healthc 2008; 3 (4): 242-6
- 45.** Schulz E, Jansen T, Wenzel P, Daiber A, Munzel T
Departmental authors: Schulz E, Wenzel P, Daiber A, Munzel T
Nitric oxide, tetrahydrobiopterin, oxidative stress, and endothelial dysfunction in hypertension.
Antioxid Redox Signal 2008; 10 (6): 1115-26
- 46.** Schulz E, Munzel T
Departmental authors: Schulz E, Munzel T
NOX5, a new "radical" player in human atherosclerosis?
J Am Coll Cardiol 2008; 52 (22): 1810-2
- 47.** Schulz E, Dopheide J, Schuhmacher S, Thomas SR, Chen K, Daiber A, Wenzel P, Münzel T, Keaney JF Jr
Departmental authors: Schulz E, Dopheide J, Daiber A, Wenzel P, Münzel T
Suppression of the JNK pathway by induction of a metabolic stress response prevents vascular injury and dysfunction.
Circulation 2008; 118 (13): 1347-57

- 48.** Schunkert H, Gotz A, Braund P, McGinnis R, Tregouet DA, Mangino M, Linsel-Nitschke P, Cambien F, Hengstenberg C, Stark K, Blankenberg S, Tiret L, Ducimetiere P, Keniry A, Ghorji MJ, Schreiber S, El Mokhtari NE, Hall AS, Dixon RJ, Goodall AH, Liptau H, Pollard H, Schwarz DF, Hothorn LA, Wichmann HE, König IR, Fischer M, Meisinger C, Ouwehand W, Deloukas P, Thompson JR, Erdmann J, Ziegler A, Samani NJ
Departmental authors: Blankenberg S
Repeated replication and a prospective meta-analysis of the association between chromosome 9p21.3 and coronary artery disease. *Circulation* 2008; 117 (13): 1675-84
- 49.** Seiler S, Schlitt A, Jiang XC, Ulrich C, Blankenberg S, Lackner KJ, Girndt M, Werdan K, Fliser D, Heine GH
Departmental authors: Blankenberg S
Cholesteryl ester transfer protein activity and cardiovascular events in patients with chronic kidney disease stage V. *Nephrol Dial Transplant* 2008; 23 (11): 3599-3604
- 50.** Sinning C, Schnabel R, Peacock WF, Blankenberg S
Departmental authors: Sinning C, Schnabel R, Blankenberg S
Up-and-coming markers: myeloperoxidase, a novel biomarker test for heart failure and acute coronary syndrome application? *Congest Heart Fail* 2008; 14 (4 Suppl 1): 46-8
- 51.** Vogt FM, Willinek WA, Campos Coy M, Ogresta F, Salomonowitz E, Sanchez Cortazar J, Kreitner K-F, Stahlke H-J, Voigtländer T, Beresnak A, Rossi S
Departmental authors: Voigtländer T
Intra-individual open-label international multicenter study of magnetic resonance angiography (MRA) with the blood pool contrast agent gadofosveset and conventional extracellular contrast agents with intra-arterial digital subtraction angiography as standard of reference in patients with peripheral artery disease. *Eur Radiol* 2008; 18 (S1): 232
- 52.** Warnholtz A, Ostad MA, Velich N, Trautmann C, Schinzel R, Walter U, Münzel T
Departmental authors: Warnholtz A, Ostad MA, Münzel T
A single loading dose of clopidogrel causes dose-dependent improvement of endothelial dysfunction in patients with stable coronary artery disease: results of a double-blind, randomized study. *Atherosclerosis* 2008; 196 (2): 689-95
- 53.** Weber S, Kronfeld A, Kunz RP, Münnemann K, Horstick G, Kreitner KF, Schreiber LM
Departmental authors: Horstick G
Quantitative myocardial perfusion imaging using different autocalibrated parallel acquisition techniques. *J Magn Reson Imaging* 2008; 28 (1): 51-59
- 54.** Wenzel P, Müller J, Zurmeyer S, Schuhmacher S, Schulz E, Oelze M, Pautz A, Kawamoto T, Wojnowski L, Kleinert H, Münzel T, Daiber A
Departmental authors: Wenzel P, Müller J, Zurmeyer S, Schuhmacher S, Schulz E, Oelze M, Münzel T, Daiber A
ALDH-2 deficiency increases cardiovascular oxidative stress—evidence for indirect antioxidative properties. *Biochem Biophys Res Commun* 2008; 367 (1): 137-43
- 55.** Wenzel P, Schulz E, Oelze M, Müller J, Schuhmacher S, Alhamdani MS, Debrezion J, Hortmann M, Reifenberg K, Fleming I, Munzel T, Daiber A
Departmental authors: Wenzel P, Schulz E, Oelze M, Schuhmacher S, Munzel T, Daiber A
AT1-receptor blockade by telmisartan upregulates GTP-cyclohydrolase I and protects eNOS in diabetic rats. *Free Radic Biol Med* 2008; 45 (5): 619-26
- 56.** Wenzel P, Mollnau H, Oelze M, Schulz E, Wickramanayake JM, Müller J, Schuhmacher S, Hortmann M, Baldus S, Gori T, Brandes RP, Munzel T, Daiber A
Departmental authors: Wenzel P, Mollnau H, Oelze M, Schulz E, Gori T, Munzel T, Daiber A
First evidence for a crosstalk between mitochondrial and NADPH oxidase-derived reactive oxygen species in nitroglycerin-triggered vascular dysfunction. *Antioxid Redox Signal* 2008; 10 (8): 1435-47
- 57.** Wenzel P, Schuhmacher S, Kienhofer J, Müller J, Hortmann M, Oelze M, Schulz E, Treiber N, Kawamoto T, Scharffetter-Kochanek K, Münzel T, Burkle A, Bachschmid MM, Daiber A
Departmental authors: Wenzel P, Schuhmacher S, Oelze M, Schulz E, Münzel T, Daiber A
Manganese superoxide dismutase and aldehyde dehydrogenase deficiency increase mitochondrial oxidative stress and aggravate age-dependent vascular dysfunction. *Cardiovasc Res* 2008; 80 (2): 280-9
- 58.** Wenzel P, Daiber A, Oelze M, Brandt M, Closs E, Xu J, Thum T, Bauersachs J, Ertl G, Zou MH, Förstermann U, Münzel T
Departmental authors: Münzel T
Mechanisms underlying recoupling of eNOS by HMG-CoA reductase inhibition in a rat model of streptozotocin-induced diabetes mellitus. *Atherosclerosis* 2008; 198 (1): 65-76
- 59.** West MJ, Nestel PJ, Kirby AC, Schnabel R, Sullivan D, Simes RJ, Pollicino C, Lubos E, Munzel T, White HD, Tonkin AM, Bickel C, Tiret L, Blankenberg S
Departmental authors: Schnabel R, Lubos E, Munzel T, Blankenberg S
The value of N-terminal fragment of brain natriuretic peptide and tissue inhibitor of metalloproteinase-1 levels as predictors of cardiovascular outcome in the LIPID study. *Eur Heart J* 2008; 29 (7): 923-31

FRIENDS OF THE



FOUNDATION HEART OF MAINZ

By supporting the Friends of the charitable
FOUNDATION HEART OF MAINZ you will have a direct
impact on saving lives and improving the quality
of life for those affected.

Donations account:

FOUNDATION HEART OF MAINZ

Mainzer Volksbank

IBAN: DE38 5519 0000 0006 1610 61

BIC (SWIFT): MVBMD555

Deutsche Bank Mainz

IBAN: DE 46 550 700 400 011099900

BIC (SWIFT): DEUT DE 5MXXX

Please feel free to contact us if you have any
questions.

Contact:

Department of Medicine 2
Mainz University Medical Center
Office of Prof. T. Münzel, MD

Phone: +39-6131-17 57 37 and -17 62 68

E-mail: info@herzstiftung-mainzer-herz.de
www.herzstiftung-mainzer-herz.de

Foundation for
promoting research and
patient health care

At the Department of Medicine 2
University Medical Center
Johannes Gutenberg-University Mainz

We have laid out this form for easy mailing. Just detach along this line, slip into envelope and mail.

To the Friends of the
FOUNDATION HEART OF MAINZ
Office of Prof. T. Münzel, MD
Department of Medicine 2
Mainz University Medical Center
Langenbeckstraße 1
55131 Mainz
Germany

Dear All,

Each year about 300,000 people in Germany will suffer a heart attack and roughly 65,000 of them will die. Experts forecast that this number will double by the year 2025.

The mission of the **FOUNDATION HEART OF MAINZ** is the timely diagnosis and effective treatment of heart attacks and the early stages of other cardiovascular diseases, in order to counteract the projected rise in these diseases.

This begins with the prevention of and screening for these diseases and ends with the optimal care of those who have suffered an acute heart attack.



These goals can only be realized through intensive research, state-of-the-art equipment and the first class education of our medical team. In order to overcome these challenges, we need your financial support.

Please support the **FOUNDATION HEART OF MAINZ** through your donation.

Sincerely

Head, Department of Medicine 2
Mainz University Medical Center

The Friends support the aims of the **FOUNDATION HEART OF MAINZ** both actively and through donations.

The Friends want to

- step up the fight against heart attacks and other cardiovascular disorders right here in Mainz,
- foster research and education,
- support continuous improvement of patient care in the Department of Medicine 2,
- optimize the diagnosis and treatment of coronary heart disease (CHD) and its risk factors, cardiac arrhythmia and peripheral artery occlusive disease (PAOD),
- award prizes for outstanding achievements in the clinical care of our patients and research,
- establish foreign scholarships.

The **FOUNDATION HEART OF MAINZ** offers several orientation events during the year. Please check our website for the actual dates:
www.herzstiftung-mainzer-herz.de

And please also note the bulletin board postings and the announcements in the press!

I would like to support the **FOUNDATION HEART OF MAINZ** with a donation:

Last name, first name _____

Street _____

Zip code, city _____

Phone _____

Fax _____

E-mail: _____

I would like to make a one-time only donation of Euro _____.

I would like to join the Friends of the **FOUNDATION HEART OF MAINZ** and authorize the direct debit of an annual donation

of Euro 100 (individual)

of Euro 1,500 (company)

Please debit the funds from my account below:

Account holder _____

IBAN: _____

BIC _____

Name of bank _____

City, date _____

Signature _____