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## Spotlight: The Asklepios Project

### One of the Main Epidemiological Projects of Preclinical Heart Disease Worldwide

**Thierry Gillebert, professor of medicine and cardiology, Ghent University, Ghent, Belgium, talks to Jennifer Taylor, BSc, MSc, MPhil about the Asklepios Project.**

Over the past 5 years, the Asklepios Study Group has published >50 articles describing the results of their epidemiological studies of preclinical heart disease. Supported throughout by Thierry Gillebert, MD, PhD, FESC, professor of medicine and cardiology at Ghent University, Ghent, Belgium, the principal investigator of the Asklepios Project, is Ernst Rietzschel, MD, PhD (see <http://circ.ahajournals.org/cgi/reprint/117/8/f43>), who set up the Asklepios Study Group for his PhD in 2002.

The Asklepios Study Group comprises the Asklepios association of primary care physicians in Erpe-Mere (between Brussels, Belgium, and Ghent) and 4 departments at Ghent University: the Department of Cardiology (Ernst Rietzschel and Marc De Buyzere); the Department of Public Health (Professor Guy de Backer and Professor Dirk De Bacquer); the Department of Biomedical

Technology (Patrick Segers and Pascal Verdonck); and the Department of Molecular Biotechnology (Sofie Bekaert, a specialist in telomere biology).

The Asklepios Project has become one of the main epidemiological projects worldwide, and will lead to more major articles over the next 20 years.

#### **“In a Way It Is an Approach to Vascular Ageing”**

In the first phase of the project, from 2002 to 2004, >2500 healthy subjects between the ages of 35 and 55 were examined.<sup>1</sup> The 2500 datasets, comprising mainly tonometry of the arteries and distensibility of carotid arteries and femoral arteries, were then analysed by the engineers.<sup>2</sup> “We show what happens with age in men and women with all these different parameters,” says Professor Gillebert. “In a way, it is an approach to define successful vascular ageing.”



*Team 2011: The Asklepios Investigators from the University of Ghent, Ghent, Belgium, in front of a research building at the Faculty of Medicine and Health Sciences on March 9, 2011. From left to right: epidemiologist Dirk De Bacquer; clinical chemist Marc De Buyzere; principal investigator and cardiologist Ernst Rietzschel; hypertensive expert Luc Van Bortel; professor of medicine and cardiology Thierry Gillebert; expert in telomere biology Sofie Bekaert; cardiovascular mechanics engineers Sebastian Vermeersch and Patrick Segers. Photograph courtesy of Dries Gaerdelen from the Department of Cardiology.*

**“The First Step Is How Does This Afterload of the Heart Relate to Vascular Morphology and Vascular Function? The Next Step Is How Does This Load on the Heart Impact on Systolic and Diastolic Function?”**

The next stage of the project was to apply previous physiological work on load (wall stress) to the epidemiological dataset. Professor Gillebert explains, “We look at the load in these patients, we reconstruct the afterload of the heart, and we look very carefully at all different aspects of these afterloads.” This is the focus of the PhD thesis of Julio Chirinos, MD, from the University of Pennsylvania, Philadelphia, PA, who works in a department headed by Professor Martin St. John Sutton, MBBS.

Dr Chirinos, whose PhD will be completed later this year, has computed the load on the heart for all Asklepios participants with a wide array of noninvasive tools and looked at the effects of load patterns on diastole and maladaptive remodelling. This is important for understanding the complex interactions between the ageing vascular tree and the heart, for instance, to explain how increased arterial stiffness, pulse wave velocity, and reflected waves impact on cardiac structure and function.

In a *Circulation* article in 2009, Dr Chirinos showed the feasibility of doing a wall stress time curve, which reveals how much load the cardiac muscle faces throughout systole at each moment of systole.<sup>3</sup> “After this proof of concept, he showed that he could do that in >2000 subjects,” says Professor Gillebert. “This is wonderful, and we are using these data to go further. The first step is, how does this afterload of the heart relate to vascular morphology and vascular function? The next step is, how does this load on the heart impact on systolic and diastolic function? And then the circle is closed.”

Dr Chirinos has used the data to construct equations that account for body size and body weight when evaluating the mass of the left ventricle.<sup>4</sup> Left ventricular mass is primarily determined by body size and blood pressure, so to calculate the effect of blood pressure it is necessary to eliminate the effect of body size.

**The Main Goals of the Second Round of the Asklepios Project Are to Look at Successful Vascular and Cardiac Ageing**

The second round of the Asklepios Project beginning on April 1, 2011, will run until 2014.

New ancillary research foci in the second round include pulmonary diseases, sleep apnoea, hormonal influences, early-stage kidney disease, sound and small particle pollution, besides the ongoing interest in epigenetics. The initial 2500 participants will be followed up, after 8 years, and a cohort of 800 new subjects has been added to look for secular trends in parameters.

In the spirit of continuing to combine physiology with epidemiological data, a stress test will be conducted on all subjects. Data on major adverse cardiac events will also be collected. The main goal is to look at successful vascular and cardiac ageing.

Professor Gillebert is currently pursuing European funding for this next phase. He says, “What we showed in the physiological articles is that, with just baseline data, you see just the tip of the iceberg, but if you look at an evolution or an intervention, then you can look at changes, and this is far more powerful from the methodological point of view.” He adds, “You need 10 times more funding for an epidemiological project than you need for a basic science project, and one of the problems we have, at both the university and scientific foundation levels, is that, in the decision-making jury, you always have basic scientists, and basic scientists sometimes do not understand the importance and relevance of epidemiological research. They do not always see that you start similarly with an experimental hypothesis, you try to get the answer in the data, and this is as rigorous as physiological research.”

As epidemiological studies go, the Asklepios Project is not as big or old as the Framingham Heart Study, but it is complementary, and joint work on genetics has been conducted with several other leading international cohorts.

Professor Gillebert is proud of the achievements of the Asklepios Study Group, which have come to fruition through the efforts of people he has coached and collaborated with. He says, “We had to fight for this study, and we had to fight for our careers because when you do something like that, not everyone will go with you. However, on the other hand, it was a very good investment, and everyone presently agrees with that.”

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*Jennifer Taylor is a freelance medical journalist.*

Editor: Christoph Bode, MD, FESC, FACC, FAHA  
Managing Editor: Lindy van den Berghe, BMedSci, BM, BS  
We welcome comments. E-mail: [lindy@circulationjournal.org](mailto:lindy@circulationjournal.org)

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