



# HEART HEALTHY

*For people who are trying to protect their bodies from heart disease, a small daily dosage of aspirin might be lifesaving. We've known that for years. But research indicates that another type of drug might be the "new aspirin," and a William and Mary professor who studies the heart wants to know why.*

BY SYLVIA CORNELIUSSEN

## **HEART DISEASE IS THE NATION'S NUMBER ONE KILLER.**

In 2006 about 1.2 million Americans will have a heart attack, says the American Heart Association (AHA). Slightly less than half of them will die. Chances are high that you or someone you know is at risk.

But take heart. A researcher at your *alma mater* is among the countless scientists studying ways to prevent cardiovascular disease.

Brennan Harris '93, an assistant professor in the College's kinesiology department, has devoted his career to studying cardiovascular physiology with particular emphasis on how exercise protects the heart. Currently, however, he is researching how a drug meant to prevent heart disease in one way also — surprisingly — helps reduce the risk of heart disease in other, unpredicted ways.

About four years ago, while he was still in a postdoctoral position in vascular biology at the Medical College of Georgia, Harris learned of a clinical study in which doctors had administered HMG-CoA reductase inhibitors (commonly known as statins) to patients arriving in the emergency room with symptoms of a heart attack. The mortality rate for these patients was significantly lower than for those who had not been given the drug; health improvements

were seen in a matter of days. As statins were originally developed to lower cholesterol over a period of weeks to months, these results were puzzling.

"It seems to be sort of a wonder drug," Harris says.

The intended purpose of statins — lowering cholesterol levels — has an obvious effect on heart health. The AHA says that high cholesterol is a major risk factor for coronary heart disease. By prescribing statins, such as Lipitor, Zocor or Pravachol, doctors can help bring an at-risk patient's cholesterol down to a healthy level.

"Studies suggest that these drugs may help reduce cardiovascular disease in ways other than their intended purpose, such as lowering blood pressure," explains Harris.

Like cholesterol, the AHA lists low blood pressure as a key factor in preventing heart disease.

Curious to understand why this positive side effect occurs, Harris applied for and received a highly competitive Scientist Development Grant from the AHA. The grant, for which Harris is principal investigator, is officially titled "Mechanisms of eNOS Phosphorylation and Activation by HMG-CoA Reductase Inhibitors." When Harris

## “Studies suggest that these drugs may help reduce cardiovascular disease in ways other than their intended purpose, such as lowering blood pressure.”

accepted his current position at William and Mary in 2004, the study came to Williamsburg with him.

In the Molecular and Cardiovascular Physiology Laboratory, a recently renovated on-campus kinesiology research lab, Harris is working with undergraduate students to examine the short-term effects of statins on an enzyme known as endothelial nitric oxide synthase (eNOS), which helps regulate blood pressure and other cardiovascular events that can ultimately lead to the development of heart disease.

“The best analogy is a garden hose,” explains Harris. “If you squeeze it, the water pressure in the hose goes up. If you relax your grip, the pressure goes down.”

Similarly, blood pressure can be lowered when nitric oxide is released from the endothelium — the cells lining the blood vessels — which causes blood vessels to relax and dilate. Nitric oxide is produced and released by the activation of eNOS through a process called phosphorylation. This process can be instigated by the introduction of statins. Using lab rats and cultured endothelial cells, Harris

and his students have been able to recreate this process and study how and why it works.

Harris has already published some of the results of these studies in the *American Journal of Physiology*. Meanwhile, and for the foreseeable future, he will continue to work with undergraduate William and Mary students in his laboratory. They will evaluate the importance of each of the sites that might be phosphorylated by statins and therefore might help protect the heart.

Scientists have compared the positive side effects of statins to the long-known positive effects a small daily dosage of aspirin has on the heart — even going so far as to call them the “new aspirin.” But Harris points out that the heart-healthy benefit of aspirin — thinning of the blood — is different from the benefits of cholesterol-lowering drugs.

“Ultimately, I hope the results of this study will help us understand how statins can provide protection against cardiovascular disease independent of their cholesterol-lowering effects,” says Harris. “This information may help us develop better drugs for cardiovascular protection or identify new therapeutic uses for statins.” ■

## FOLLOWING HIS HEART

**B**rennan Harris says he made it his goal early on to come back to his *alma mater*. After all, it's where he met (in the choir) and married (in the Wren Chapel) his wife, Terri Hamlet Harris '93.

William and Mary is also where he found academic mentors who have helped him become the teacher and researcher he is today. When Harris left the College following graduation, he went on to pursue a master's at the University of North Carolina at Chapel Hill and a doctorate at the University of Texas at Austin, both in exercise physiology.

At the time, Harris asked one of his mentors — Kenneth Kambis, the professor of kinesiology whose office is now next door to Harris' — what he needed to do to come back to William and Mary.



Assistant Professor of Kinesiology  
Brennan Harris '93

“His advice was to go be the best scientist I could be,” recalls Harris. “He told me that research would really set me up.”

Harris took Kambis' advice to heart — literally — and has focused his career and education on studying the cardiovascular system and ways to protect it.

Statins are not the only way to activate eNOS and thereby reduce your chances of developing coronary heart disease, according to Harris. As a matter of

fact, one of the best ways to instigate the same benefit does not even come in pill form. Similar effects, such as cholesterol lowering and eNOS activation, can actually be produced by exercise.

“Physical inactivity is the most prevalent controllable cause of heart disease,” says Harris. “The reduction in risk occurs when you go from being sedentary — doing nothing — to doing something.”

Harris' research on how exercise protects the heart extends beyond the College's kinesiology department. In spring 2005 he learned that Professor of Modern Languages and Literature George Greenia was leading students on a 500-mile, 30-day pilgrimage across Spain in the summer.

“They were going to be walking five to six hours each day for the 30 days,” says Harris. “That's a real challenge. The energy expenditure for that is equivalent to running a marathon each day for 30 days.”

During his freshman year at the College, Harris had taken a writing-intensive freshman honors course with Greenia and remembered him well. After contacting the professor to discuss the physical impact of the trip, Harris was asked to present to the students on how to train for the long days of walking.

Thanks to a Borgenicht Program Grant from the College, when Greenia leads a similar student trip this summer, Michelle Wolf '07, one of Harris' research students, will be going along to monitor the walkers, studying how the pilgrimage changes their fitness levels and markers for cardiovascular disease risk.

Harris also practices what he preaches — he knows what long-term benefits an active lifestyle will give him and his family. A current Williamsburg resident, he enjoys running, mountain biking and spending time with Terri and their three children, Kayleigh, Sydney and Jake.