Welcome to the Cardiovascular News of Excellence

MCG cardiologists have traditionally been known to be very clinically astute. In the past few years, we have modified our training program, maintaining a solid clinical training experience while also promoting bench to bedside, translational research. In this issue, you will hear from two of our fellows, one junior faculty and two of our more seasoned researchers, describing their late-breaking and exciting research projects. Dr. Kapuku is a Co-Director of the recently formed Cardiovascular Discovery Institute which will further developments in translational research across multiple disciplines and coordinate this research throughout the MCG community.

It is of note that Dr. Patton’s research is supported through the Kimmerling Foundation which provides funds to support the education and research of promising trainees. I would kindly ask you to keep the MCG Cardiovascular Center in mind for any contributions to our education and research missions. Thank you!

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Chest Pain Center
The MCGHealth Chest Pain Center recently became the first and only in the CSRA to be accredited by the Society of Chest Pain Centers.

The Chest Pain Center allows physicians to speed treatment to patients during the critical early stages of a heart attack, when intervention is most effective, and to better monitor patients when it is unclear whether they are having a coronary event. Careful observation helps ensure that a patient is neither sent home prematurely nor admitted to the hospital unless a significant medical problem is confirmed.

New Training Program in EP
We are pleased to announce our first EP Fellow, Dr. Prabul Guha. Dr. Guha completed his Cardiology Fellowship at SUNY Upstate Medical University in Syracuse, NY. He will be receiving advanced training from MCG’s expert electrophysiology faculty.
Peripartum Cardiomyopathy is heart failure presenting in a woman toward the end of pregnancy or within the several months following childbirth. Fortunately, it is a relatively uncommon diagnosis, occurring in between 1 in 300 and 1 in 3000 births in the United States. However, the consequences of peripartum cardiomyopathy can be devastating, particularly given that the patients are typically previously healthy young women with new babies. Approximately 50% of patients will recover within 6 months and the other 50% continue to have varying degrees of disability ranging from mild symptoms of shortness of breath all the way to the need for heart transplant or even death. Many etiologies have previously been investigated, but currently there is not a clear explanation for what causes the condition or what treatment strategies are optimal.

My research has recently focused on fully characterizing the traits of the population of patients at MCG with peripartum cardiomyopathy. We have found a relatively high incidence in our population of 1 in 500 deliveries. Additionally, by characterizing this population we have identified risk factors that predispose a woman to development of the condition. The risk factors that we have identified to this point include African-American race, a history of hypertension, being unmarried at the time of delivery, not breast-feeding, and blood types B and O. The hope is that identifying risk factors will lead to a better understanding of the causes. This is vital to identifying optimal preventative and treatment strategies of this potentially devastating disease that affects young women.

Heart Failure Associated with Low Levels of Corin

In order to combat the physiological changes caused by congestive heart failure, the body produces atrial natriuretic peptide (ANP). Pro-ANP, the precursor to ANP, must be cleaved before turning into its more beneficial form. The protein that is needed to actually perform the cleavage is known as corin. Although current tests cannot distinguish between cleaved and uncleaved forms of ANP, previous studies have shown that total ANP levels are highest in individuals with heart failure. This is surprising, given that ANP normally works against the progression of cardiovascular disease. This suggests that defects in the cleavage of pro-ANP by corin may play a role in the development of heart failure. We proposed that the markedly elevated total ANP levels may predominantly consist of the biologically inactive pro-ANP. To examine this hypothesis, we developed new tests that, for the first time, measured corin and active forms of ANP.

Using this novel ELISA technique in our current study, we were able to show that patients with heart failure had lower plasma levels of corin (the pro-ANP converting enzyme) compared to the control group. We also showed that the cleavage of pro-ANP to its active form, ANP, is impaired in heart failure patients. This potentially diminishes the ability of ANP to reverse the progression of heart failure.

This research has important implications for the management of congestive heart failure. It may be possible for clinicians to carry out targeted ANP therapy with patients that have low levels of active ANP. Our goal is to translate these discoveries from the lab to the bedside.

Co-Investigators: Inna Gladysheva PhD, Guy L. Reed MD
Atherosclerosis

The development of plaque in the wall of an artery, or atherosclerosis, can result in cardiovascular events such as heart attack and stroke. This disease is the leading cause of death in the United States. Atherosclerosis is an inflammatory process involving many different types of blood cells. One of these cells, the platelet, is well known for its ability to assist in clot formation. Current evidence suggests that platelets also play a role in plaque development by promoting vascular inflammation. Granules within the platelet cell contain molecules that promote inflammation, which may attract additional inflammatory cells to the wall of an artery.

Researchers at MCG are assessing the effects of platelet granule secretion on atherosclerosis formation. Studies have focused on Apolipoprotein E (atherosclerosis prone) mouse models that also have difficulty secreting platelet granules. Interestingly, mice with reduced platelet granule secretion demonstrate profound decreases in atherosclerotic plaque size. Less granule secretion reduces the infiltration of inflammatory cells into the vessel wall, and enhances plaque stability. When compared to control mice, these data suggest that platelet granule secretion might prove to be an effective therapeutic target for the prevention of atherosclerosis.

Additional experiments in the cardiovascular biology laboratory have focused on determining the role of platelet granule secretion on the vascular response to injury. Preliminary results suggest that platelet granule secretion plays an equally important role during this acute process. Future experimental efforts will be aimed at a better understanding of the platelet granule secretory process, so that maximal therapeutic benefit can be obtained while minimizing potential side effects.

Co-Investigators: Rachel McNamee, Sarah King PhD, Hitesh Mehta MD, Guy Reed MD
Mental Stress has a Negative Effect on the Heart, Even in Young People

Abnormalities occurring when the heart is relaxing and filling with blood are now recognized to play an important role in the occurrence of congestive heart failure even when the heart seems to be pumping properly. This study was conducted to evaluate the effect of mental stress on heart relaxation and filling properties in teenagers of different ethnic backgrounds. We found that during stress, blood flow to the heart and cardiac muscle relaxation were reduced. This decrease in heart function was associated with blood pressure elevation and faster heart rate. Atrial natriuretic peptide (ANP), a hormone secreted by the heart to control blood volume and pressure, was found in lower levels in patients with relatively high blood pressure. These individuals were mainly African-Americans. All in all, the study suggests that mental stress is detrimental to heart function even in teenagers (especially, African-American) in apparently good health. These provocative results were presented at the American Society of Hypertension Scientific Session (New Orleans, May 2008).

Emergence of Novel Genetic Effects on Left Ventricular Structure in Adolescence: Longitudinal Evidence from the Georgia Cardiovascular Twin Study

The strong relationship between increased cardiac mass and increased cardiovascular morbidity and mortality is well established. Mild-to-moderate genetic contributions and possible ethnic differences in the heritability of heart size have been reported. However, earlier studies have predominantly been performed in European-Americans precluding from testing whether there are ethnic differences in heritability of cardiac mass. The Georgia Cardiovascular Twin Study includes the largest number of African-American pairs. This may offer a more conclusive answer as to the importance of the genetic influence on cardiac mass in African-Americans in whom an increased cardiac mass is highly prevalent.

The research revealed moderate tracking and moderate-to-high heritability of heart structure and geometry after taking into account body size, age, gender, and ethnicity. A great deal of cardiac mass variability was linked to age-related changes in genetic expression. There was a significant amount of new genes expressed between 14 and 18 years of age in all but African-American females. Further work is required to provide the clinical implications of this observation.
Improving the Accuracy of Nuclear Cardiac Imaging

Myocardial perfusion imaging is crucial for the safe management of patients with coronary blockages. These tests are important in determining when patients with known coronary blockages can be safely managed with medication rather than invasive treatments such as cardiac catheterization and stents. These myocardial perfusion scans are affected by areas of soft tissue which reduce the accuracy of the image. These include large breasts which can simulate perfusion defects (blockages).

The myocardial perfusion study produces two sets of images. One image is taken at stress, when a snap shot is obtained during exercise or simulated exercise (induced by medication). The second image looks at whether or not all the areas of the myocardium are still living and functioning, known as viability. Two scans of the heart are compared, with a time lapse of at least one and a half hours in between the images. During this period of time the patient is encouraged to eat, which can cause a shift in the position of the heart from one image to the next. This re-registration artifact can affect the accuracy of the readings.

With this problem in mind, we in the Nuclear Cardiology Laboratory have identified a new pattern, known as encircling reperfusion. This occurs where the edges of a defect show increased uptake of radiotracer. We have determined that this pattern allows for improved sensitivity for detecting true blockages. This noninvasive test utilizes the myocardial perfusion scan without any significant increase in the number of false positives. Overall, our confidence in the diagnosis improved when we saw this pattern of encirclement on the scans. These findings are published in the March 2008 issue of *Nuclear Medicine Communications*.

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