

## ADVANCES IN SCREENING, TREATMENT AND RESEARCH

Ask Patrick Moriarty, MD, division director of Clinical Pharmacology, what he loves about his work, and his face lights up. At the University of Kansas Medical Center (KUMC), the clinical pharmacology division has developed a multidisciplinary program that brings together an array of professionals—pharmacists, clinical nurses, dieticians, nurse practitioners, ultrasound technician and research study coordinators—in a quest to manage patients’ LDL cholesterol and contribute to the body of research on atherosclerosis.

As a leading authority on atherosclerosis, the abnormal accumulation of LDL cholesterol, Moriarty divides his time between his office, laboratory and clinics; and this diverse set of work is what keeps him energized and motivated to advance knowledge in the area of atherosclerosis? He has completed over 75 clinical research studies as principal investigator or co-investigator.

On grand rounds, he shows residents, medical students and fellow physicians slide images of arteries clogged by cholesterol. He holds their rapt attention, as the slides are the result of carotid ultrasonography, an imaging technique that reveals structural details of the carotid artery, enabling early diagnosis of cardiovascular disease in asymptomatic patients. The KUMC is one of few medical centers that perform carotid ultrasound screening, which can help physicians discern the difference between naturally occurring cholesterol and abnormal buildup of cholesterol.

On one slide, he points to the tell-tale “foam cell,” inflammatory cells with cholesterol that have accumulated in the artery. “You would never know it’s there by any kind of test,” Moriarty says. “A stress test wouldn’t show that.”

Eventually, he says, enzymes form, weakening the carotid wall and leading to a rupture. “That’s what kills people,” he says.

He shows another slide, this one of an asymptomatic patient with a family history of early heart disease.

“This 42-year-old male has a carotid wall thickness of an 80-year-old guy; his vascular age is twice that of his chronological age,” Moriarty says. “The good news is you can reverse that, you can go backwards on wall thickness.”

Many such patients who present with elevated plasma concentrations of LDL (above 190) at a young age have a genetic disorder, familial hypercholesterolemia (FH). It is one of the most common genetic disorders, affecting one in 500 people. Patients who inherit the gene for FH from both parents—homozygous FH—do not respond to statins or dietary changes.

Moriarty and his staff see many of these patients at their lipid control clinic. The clinic is the largest in North America to perform apheresis, a procedure that filters LDL cholesterol from the blood in a process that is similar to dialysis. After a two-hour treatment, apheresis can reduce LDL cholesterol levels by up to 80 percent.

The Clinical Pharmacology division also participates in clinical trials. Each year they conduct about 10 studies, half of which are initiated by KUMC researchers.

Highlights of current and upcoming studies include these:

- Gene therapy study with University of Pennsylvania. Researchers are working on a gene-modifying therapy for patients with homozygous FH. These patients present clinical signs of high cholesterol at a very young age, and do not respond to medication. Current treatment options are liver transplant or LDL-apheresis. This study will recruit patients from around the world, who will come to Kansas City in order to receive treatment. Patients will undergo a one-time infusion and be followed through several visits within a 12-month follow up period.
- EECP study. The clinical pharmacology division is collaborating with the Alzheimer’s Disease Center from the Department of Neurology on a pilot study of patients with mild

cognitive impairment. Patients will undergo enhanced external counterpulsation, a noninvasive technique used in patients with congestive heart failure to improve blood perfusion to the heart.

Researchers want to know if this treatment will similarly improve blood flow to the brain and either slow progression of cognitive impairment, or retard it altogether.

- PCSK9 protein. An exciting new class of drug inhibits this protein and lowers LDL cholesterol. Current studies underway target several populations including patients with heterozygous FH, statin intolerance, and high cardiac risk patients.
- Coenzyme Q10. KUMC researchers are conducting a study to detect changes in CoQ10 levels in patients taking statin therapy. Statins can deplete CoQ10 levels, which may be related to increased incidents of side effects. The study compares three FDA-approved statins and their effect on endogenous CoQ10 levels.



Patrick Moriarty, MD

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