Genetic mutation found in peripheral artery disease

February 22 2008

The finding, appearing online in the journal *Circulation*, is the first to document a genetic mutation linked to PAD. Although the work was done in mice, researchers say it is likely to give them new insight into how PAD develops and progresses in humans.

Dr. Brian Annex, professor of medicine and director of vascular medicine at Duke, says the study stemmed directly from his clinical experience. “Over and over, I’d see two patients show up at the same time. They would be the same sex, same age, have identical risk factors and have similar blockages in their arteries. One of them would experience very slow progression of the disease, while the other would face limb loss or death within six months. I just knew there just had to be a genetic basis for it.”

Peripheral arterial disease occurs when major arteries in the legs become clogged with plaque, a fatty build-up that’s similar to the deposits in coronary arteries that can lead to a heart attack. Symptoms range from leg pain brought on by walking that goes away with rest – that’s the more benign form of the disease – to a more serious form, marked by continuous pain and sores and ulcers on the legs that often lead to amputation.

Annex says the mild form rarely progresses into the more severe form. “In reality, we may be looking at two types of diseases, although we’ve always thought of PAD as one.”

Annex had the perfect participants for the study right at his fingertips: two strains of mice with surgically-induced blocked blood flow that mimicked human response to PAD. One strain recovered well, showing restored blood flow and little tissue death; the other had greater tissue loss and poor recovery of normal blood flow.

In collaboration with Dr. Douglas Marchuk, a professor of molecular genetics and microbiology at Duke, researchers crossbred the two strains and eventually isolated a mouse that enabled them to identify a relatively small region on chromosome 7 that appears to protect the mice from the consequences of the surgically-induced, PAD-like injury.

“Essentially, we now have a field of about 20 genes that we think may be involved in shaping the way peripheral artery disease develops,” says Annex. “At this point, we are not certain which ones are playing an active role, however. Still, we feel strongly that our discovery opens a new wave of investigation that may one day yield novel prevention strategies or treatments.”

Source: Duke University Medical Center