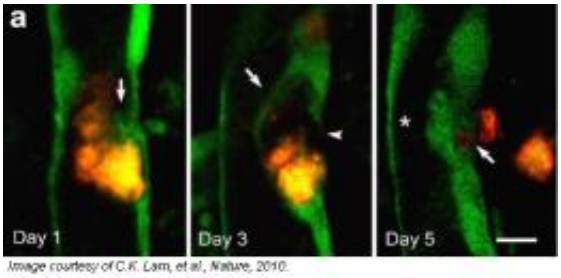
Tiny blood vessels in brain spit to survive

May 26 2010



Time-lapse images of a blood vessel in a mouse brain. On Day 1, the interior membrane of the blood vessel starts to extend around the orange cholesterol blockage (arrow). By Day 3, the membrane has surrounded the cholesterol and created a pathway to the outside of the blood vessel (arrowhead). On Day 5, the blockage has moved outside the blood vessel, which is now unimpeded. (asterisk). Image courtesy of C.K. Lam, et al., Nature, 2010.

Spitting can be a good thing when it comes to blood vessels.

Scientists at Northwestern University Feinberg School of Medicine have discovered capillaries have a unique method of expelling debris, such as blood clots, cholesterol or calcium plaque, that blocks the flow of essential nutrients to brain cells. The capillaries spit out the blockage by growing a membrane that envelopes the obstruction and then shoves it out of the blood vessel.

Scientists also found this critical process is 30 to 50 percent slower in an aging brain and likely results in the death of more capillaries.

"The slowdown may be a factor in age-related cognitive decline and may also explain why elderly patients who get strokes do not recover as well as younger patients," said Jaime Grutzendler, senior author and principal investigator of the study and assistant professor of neurology and of physiology at Feinberg. "Their recovery is much slower."

The study with mice, funded by the National Institute on Aging (NIA), will be published May 27 in the journal *Nature*.

Scientists have long understood how large blood vessels clear blockages: blood pressure pushes against the clot and may eventually break it down and flush it away, or clot busting enzymes rush to the scene to dissolve a blockage.

But very little was previously known about how capillaries clear blockages. The Northwestern study first demonstrated that enzymes and blood pressure aren't efficient at clearing capillary clots within the critical 24 to 48 hours. Those mechanisms only work half the time and only when blood clots are involved, not other types of debris, particularly cholesterol, which is difficult to dissolve.

"So what happens to the blood vessels that that aren't cleared out?" asked Grutzendler and colleagues. "Do they die, or does some other mechanism take over?"

To find out, they created micro-clots, tagged them with a red fluorescent substance and infused them into the carotid arteries of mice. Using a multiphoton microscope, the team examined the brains of live mice at various time intervals as clots traveled into the capillaries. Surprisingly, they discovered that the blood vessel cells next to the blockage grew a membrane that completely enveloped the debris. Then the original wall of the blood vessel opened up and spit the debris into the brain tissue, rendering it harmless. The envelope covering the clot became the new

vessel wall. This resulted in complete restoration of blood flow and salvaging of the tiny vessel and surrounding brain cells.

"These are intriguing findings," said NIA director Richard J. Hodes, M.D. "They open new avenues of basic research that may increase our understanding of microvascular maintenance in the brain and throughout the body."

Provided by Northwestern University