Investigators at The Scripps Research Institute Discover Clues About the Causes of Aortic Aneurysms

La Jolla, CA. July 3, 1995 — Scientists at The Scripps Research Institute (TSRI) in La Jolla, and Sheba Medical University Center in Tel Aviv, Israel, have discovered a possible underlying mechanism for the formation, progressive enlargement and eventual rupture of aortic aneurysm, a permanent swelling of the aorta that, when burst, leads to hemorrhage and death in 25,000 Americans each year. Increased knowledge about the cause of this condition may direct scientists to blocking the cascade of biological events that results in aneurysm formation, according to the study’s lead authors, David J. Loskutoff, Ph.D., Chairman of the Department of Vascular Biology at TSRI, and Jacob Schneiderman, M.D., from Sheba.

Complicated atherosclerosis—commonly known as hardening of the arteries—involving the abdominal aorta, the largest blood vessel in the body, is frequently associated with the formation of aneurysms. Expansion of the aneurysm itself appears to result from the gradual destruction of major components of the vessel wall and loss of structural integrity.

A ruptured aneurysm frequently results in the collapse of the entire circulatory system, a condition that is often fatal. Even when it does not burst, aortic aneurysm causes turbulence in the flow of blood that can cause the formation of blood clots, with all the associated dangers.

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To uncover possible mechanisms that may initiate this destructive process, scientists at TSRI and Sheba compared samples of abdominal aortic aneurysm with normal aortic wall for the presence of enzymes capable of digesting structural proteins in the vessel wall.

The work appeared in the July issue of The Journal of Clinical Investigation, in an article entitled, "Expression of fibrinolytic genes in atherosclerotic aortic aneurysm wall: A possible mechanism for aneurysm expansion."

In limited studies with eight patients, the researchers for the first time detected newly formed capillary blood vessels and increased levels of plasminogen activators—enzymes that convert the inactive circulating precursor, plasminogen, into the active enzyme, plasmin—within discrete areas of inflammation in the aortic aneurysm wall. Plasmin is known to chew up certain components of the vessel wall and may also activate other destructive enzymes. The newly formed capillary blood vessels may further weaken the aneurysm wall.

Loskutoff explained, "These findings suggest a cause and effect relationship between the local synthesis of plasminogen activators by inflammatory cells, and the generation of plasmin and other enzymes capable of degrading the vessel wall. Further, the observations enable us to better understand the reasons for progressive destruction of the vessel, with local physical weakening and inevitable aneurysm expansion."

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