Why does dialysis fail?

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A protein implicated in the development of vascular diseases may also contribute to the failure of arteriovenous (AV) fistulas created for vascular access in dialysis patients, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN).

"Our findings raise the possibility that monocyte chemoattractant protein-1 (MCP-1) may contribute to the relatively poor outcomes regarding the function and longevity of human hemodialysis AV fistulas," comments Karl A. Nath, MB.ChB (Mayo Clinic, Rochester, MN).

AV fistulas are the preferred form of access to the circulatory system in dialysis patients. They are created by a surgical procedure to connect a vein to an artery, usually in the lower arm. The use of AV fistulas, compared to other types of dialysis access, leads to fewer complications such as infections, less hospitalization of dialysis patients, and overall, a better outcome for the dialysis patient.

However, AV fistulas are prone to certain problems. About half of AV fistulas never become functional for use in dialysis, while those that do become functional have a significant failure rate. "We thus need to understand why AV fistulas do not develop, or fail to function after a relatively short period of use," says Nath.

In a series of experiments in mice, the researchers found that MCP-1-an inflammation-promoting chemokine protein-was a "critical contributor"

to AV fistula failure. The failing fistulas showed increased levels of MCP-1, and of the gene that encodes it. In contrast, AV fistulas functioned much better in genetically altered mice that lacked MCP-1. In the absence of MCP-1, AV fistulas had less vein wall thickening, and the number of functional AV fistulas was substantially higher.

Take-away message: "The present study is the first…to directly demonstrate that
MCP-1 critically contributes to failure of an AV fistula," the researchers write. The results are timely, because drugs that act as MCP-1 blockers are currently under development. "Such agents, when clinically available, may be considered as a possible therapeutic approach to promote the maturation of AV fistulas, and/or extend their duration of function," says Nath.

The researchers emphasize that more research will be needed to confirm whether the results of these animal experiments are relevant to AV fistulas in humans.

More information: The article, entitled "MCP-1 Contributes to Arteriovenous Fistula Failure" is currently online at doi:10.1681/ASN.2010040373

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