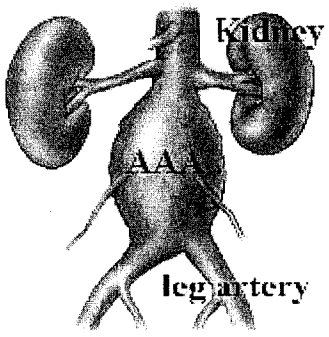
A recent paper shows that abdominal aortic aneurysm can be reversed.
Curcumin can potentially inhibit all the pathways leading to the disease.

CURCUMIN MAY REVERSE AORTIC ANEURYSM

Abdominal aortic aneurysm (AAA), a common and potentially life-threatening condition occurs in people above 65 years of age. Etiological factors include genetic susceptibility - 15 to 20 percent of patients have a family history. AAA is 2 to 5 times more common in men than in women, and more common in white than in black populations. They are usually asymptomatic and often go unnoticed for years, but they usually expand progressively and eventually rupture. AAAs are caused by pathological changes in the aortic wall that leads to segmental weakening, progressive dilation and spontaneous rupture[1]. The natural history is a gradual enlargement (from 1.75 cm at 25 years of age and 2.25 cm at 55 years[2]) of the aneurysm until it exceeds 5.5 cm, when risk of rupture increases exponentially. The risk of rupture is four times as high among women as among men[3].



AAAs develop as a result of atherosclerosis and chronic inflammation of the aortic wall, a decrease in aortic medial smooth muscle cells, and progressive destruction of structural connective tissue proteins, particularly elastin and collagen[4,5,6]. Resident vascular smooth muscle cells (VSMC) and infiltrating macrophages release matrix metallo-proteinase (MMPs), particularly MMP-9 and MMP-2.

5-Lipoxygenase (5-LO) is involved in the inflammatory process of AAA. This is a key enzyme in leukotriene sysnthesis and catalyzes the initial steps in the conversion of arachidonic acid to these biologically active lipid mediators, which exert proinflammatory effects in vivo[7,8]. Emerging data implicate 5-LO in cardiovascular diseases and in AAA induced by atherosclerosis. Animal studies involving transgenic mice indicate that there is a connection between 5-LO and aneurysm pathogenesis, through mechanisms that inviolve CC- and CXC-type chemokines[9]. Disruption of the gene encoding 5-LO reduces both the incidence and the extent of AAA development. In a setting of inflammation and mild liver injury, a situation that is likely to occur frequently in elderly population predisposed to aneurysm development, this effect is quite pronounced.

Increased expression of MMPs has been observed in human aneurysm tissue[10,11,12] which are believed to orchestrate the widespread matrix destruction. Proinflammatory cytokines secreted by macrophages enhance MMP production by human vascular smooth muscle cells and many of these cytokines are present in the AAA tissue. The MMPs involved in AAA are MMP-2 and MMP-9 and a concereted action of these

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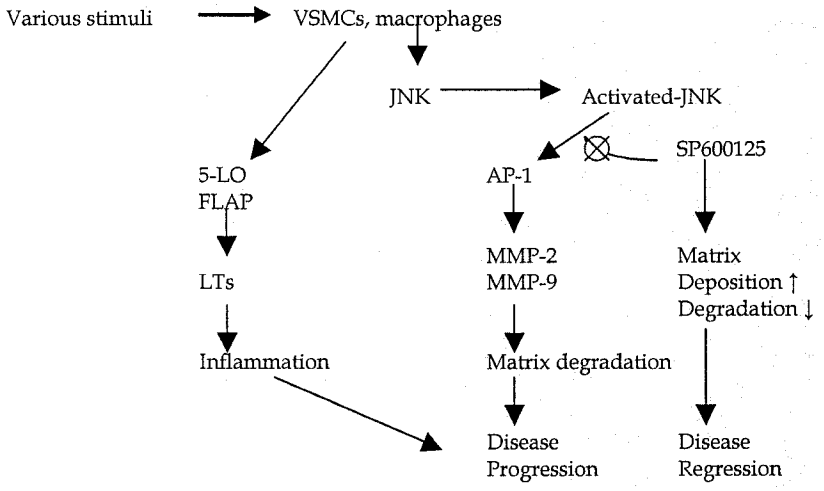
two are required for the aneurismal degeneration[13] in mice, and in animal models, genetic and pharmacologic inhibition of MMPs can suppress development of aneurysm[13,14,15] and early clinical studies using doxycycline as an inhibitor of MMPs show promise[16,17]. MMP-2 is believed to act as a collagenase initiating cleavage of the triple helix into one-quarter and three-quarter lengths[18]. The single α-chains could then be degraded by MMP-9.

Regression of AAA

A very recent publication by Yoshimura et al[19] show that AAA is indeed reversible by non-surgical methods by blocking c-Jun N-terminal kinase (JNK), in mice. The rationale was as follows. Various stimuli are linked to AAA, including mechanical stress, oxidative stress, angiotensin II (AngII), tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6 and interferon (IFN)-γ. Most, if not all, of these stimuli activate JNK (which is also known as stress-activated protein kinase) in vascular smooth muscle cells (VSMC), which synthesize extracellular matrix and secrete MMPs, and macrophages which secrete proinflammatory cytokines and MMPs. Because JNK is thought to be involved in a number of cellular stress responses[20], it may have an important role in AAA. No causal relationship between JNK and AAA has been reported so far, but Yoshimura et al decided to test this relationship, and screened the JNK-dependent genes in VSMCs. Yoshimura et al showed that levels of activated JNK were higher in human AAA tissues than in atherosclerotic lesions, and activation of JNK was relatively selective versus other stress-activated protein kinases. Further, in human AAA tissues, activated JNK co-localized with expression of MMP-9 in both VSMCs and macrophages. These findings provide intriguing evidence that activated JNK is not only increased in AAAs, but also localized to the cell and tissue types involved in the disease progression. Furthermore, they found that in vivo pharmacologic inhibition of JNK suppressed development of AAA in mouse models., with reduced inflammation of the aortic wall, reduced expression of MMP-9, and preserved architecture of the aortic wall.



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In VSMCs, the authors showed that activated JNK downregulated expression of several genes involved in matrix production, indicating that activated JNK may diminish the production of structural proteins (elastin and collagens). When mice with established AAAs were treated with the JNK inhibitor SP600125, there was a considerable decrease in aortic diameter, a measure of aneurysm. The aortic diameter in treated mice were smaller at the end of therapy than at start, suggesting that the aneurysm regressed during therapy.

This study convincingly shows that pharmacologic treatments can potentially induce regression of established AAAs. What is important to the present discussion is that curcumin is a known inhibitor of JNK, AP-1, MMPs, and 5-LO implicated in the different facets of the disease, and thus could be a safe therapeutic alternative. This argument needs to be tested in randomized clinical trials.

Postscript

At the time of writing this article, there were no published studies on the subject. However, a recent study in mice, corroborated these expectations. The authors conclude:

> *"These data demonstrate for the first time that oral administration of curcumin can suppress the development of experimental AAAs, along with structural preservation of median elastin fibers and reduced aortic wall expression of several cytokines, chemokines, and proteinases known to mediate aneurismal degeneration. The possibility that dietary ingestion of curcumin may have beneficial effect in degenerative aortic aneurysms warrants further consideration"* (Parodi FE, Mao D, Ennis TL, et al. Oral administration of diferuloylmethane (curcumin) suppresses proinflammatory cytokines and destructive connective tissue remodeling in experimental abdominal aortic aneurysms, *Ann Vasc Surg,* 2006, 20:360-68.).