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Cardiovascular Disease

Does the Lysyl Oxidase Gene *Lox* Play a Critical Role in Cardiovascular Disease?

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Inactivation of Lysyl Oxidase Gene *Lox* Leads to Aortic Aneurysms, Cardiovascular Dysfunction, and Perinatal Death in Mice

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The pathophysiology of the formation of an aortic aneurysm involves the degradation of elastin. The cross-linking of elastin and collagen is an important determinant of tensile strength, and this cross-linking is mediated by a family of five isoenzymes, called lysyl oxidases.

The study investigators from Finland created a mouse model in which one of the lysyl oxidase genes, called *Lox*, was knocked out. These mice died at birth, and a detailed examination showed fragmentation of elastin lamellae in the aorta, as well as aortic aneurysms and diaphragmatic hernias, in some of the mice. The aortic pulsatility index, as measured by Doppler ultrasonography, was significantly higher in *Lox*-null mice.

These observations suggest that the reduced cross-linking of elastin and collagens causes a reduction in the resilience and tensile strength of the arterial walls, which gives rise to abnormalities of aortic structure and cardiovascular function. It is of interest to note that the mottled blotchy mice that died of aortic rupture before 6 months of age also had a partial deficiency of lysyl oxidase activity resulting from an abnormal copper metabolism. Similarly, in lathyrism, there is an irreversible inhibition of lysyl oxidase, caused by β-aminopropionitrile in peas, in which there is evidence for aortic dissection and the formation of aortic aneurysms, besides other musculoskeletal abnormalities. Taken together, these observations suggest the possibility that *Lox* activity may play a critical role in human cardiovascular disease. ■

Myocardial Infarction

Anticoagulation Post-MI: Are Warfarin and ASA Superior to Aspirin Alone?

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It is well established that thrombosis plays a central role in the pathophysiology of acute myocardial infarction (AMI) and that treatment with thrombolytic agents, anticoagulants, and antiplatelet drugs significantly reduces mortality and morbidity.[1] It is also well known that a significant proportion of recovering MI patients will have reinfarction during the following 2–5 years.[2] Over the past 35 years, the optimal antithrombotic regimen to prevent reinfarction has remained unclear. Currently, there are two common treatments: 81–325 mg of aspirin daily or coumadin with an international normalized ratio (INR) of 2 to 3. Although both regimens have been shown to reduce mortality and morbidity in patients with AMI, it is most common in the United States to treat patients with acetylsalicylic acid (ASA), largely because of its ease of use and relative safety. In a meta-