A discussion of dissection

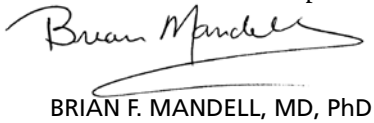
Few medical emergencies are as dramatic as an acutely rupturing aortic aneurysm. I recall a Thanksgiving in the emergency room about 25 years ago. We were evaluating a man who had suffered a syncopal episode at his holiday dinner table. It was an odd presentation in the ER: hypotension and bradycardia, no inferior myocardial infarction, and no obvious reason to be persistently "vagal." Initial blood cell counts were normal. He described ill-defined back and then abdominal pain. As the chief surgical resident and I repeated the examination, the patient's belly became distended, his breath sounds decreased on the left, and within minutes, the surgical team raced him to the operating room.

Dr. Alan C. Braverman, in this issue of the *Journal* (page 685), discusses thoracic aortic dissection. To most of us who do not routinely treat aortic disease, it may not seem that much has changed since that Thanksgiving in Philadelphia. Atherosclerosis is still a common risk, surgery is the treatment for ascending dissection, beta-blockers are useful for chronic descending dissections, and the mortality rate is enormously high when dissections bleed.

As internists, we consider the possibility of genetic disorders in patients with a family history of dissection or aneurysm, but we don't really expect to find many, and most of us don't often track advances in the understanding of these disorders at the molecular level. At the time I was working in that emergency room, Marfan syndrome was viewed as a connective tissue disorder, with a structurally weak aortic wall and variable other morphologic features. When the molecular defect was defined as fibrillin-1 deficiency, I didn't think much more than that the weak link of the aorta's fibrous belt was identified.

But it turns out that fibrillin is not just an aortic girdle; fibrillin lowers the concentration of the cytokine transforming growth factor (TGF)-beta in the aorta (and other organs) by promoting its sequestration in the extracellular matrix. Absence of fibrillin enhances TGF-beta activity, and excess TGF-beta can produce Marfan syndrome in young mice. In maybe the most striking consequence of this line of research, Dietz and colleagues[1] have demonstrated that the specific antagonism of the angiotensin II type 1 receptor by the drug losartan (Cozaar) also blocks the effects of TGF-beta and consequently blocks the development of murine Marfan syndrome. And in a preliminary study, it slowed aneurysm progression in a small group of children with Marfan syndrome.

This does not imply that the same pathophysiology is at play in all aortic aneurysms. But at a time of new guidelines for screening for abdominal aneurysm, these observations offer a novel paradigm for developing drug therapies as an alternative to the mad rush for the vascular operating suite.



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1. **Brooke BS, Habashi JP, Judge DP, Patel N, Loeys B, Dietz HC 3rd**. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. N Engl J Med 2008; 358:2787–2795.

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