Letter to the Editor

The pathogenesis of arterial aneurysms and associated lesions

William E. Stehbens

Department of Pathology, Wellington School of Medicine, PO Box 7343, Wellington South, New Zealand

Received 2 August 1996; accepted 21 January 1997

Keywords: Arterial aneurysm; Atherosclerosis; Polycystic kidney; Cardiac myxoma; Diverticulosis

Citing three histories involving berry, oncotic and atherosclerotic aneurysms Weber [1] recently introduced Herron’s proposal [2] that proteolytic digestion was responsible for the aneurysms and associated renal cysts, diverticula, mitral valve prolapse and hernia. Aneurysms develop when intravascular pressure is greater than the wall can withstand, and as blood pressure never approaches levels necessary to rupture healthy arteries or veins, aneurysms indicate mural weakness. Aneurysms are not specific diseases but pathological dilatations complicating many diseases each with individualistic pathogenesis [3]. A common pathogenesis cannot be assumed.

The outmoded congenital theory of cerebral aneurysms was based on assumption and fallacious evidence [4]. The initial mural atrophy and florid aneurysms are acquired and reproducible experimentally by hemodynamics [5,6]. This is facilitated by hypertension and lathyrism which are predisposing factors, not prerequisites [6]. Similarly hypertension and connective tissue disorders predispose to premature vascular fragility and human berry aneurysms which are acquired [3]. They complicate aortic coarctation and adult renal polycystic disease, both occurring with hypertension, although in the former the water hammer pulse of aortic valve insufficiency is contributory as in afferent arteries of arteriovenous shunts [3]. No scientific evidence suggests that the preceding mural atrophy or berry aneurysms are attributable to protease activity.

Adult polycystic renal disease is purportedly an epithelial rather than a connective tissue disorder. Cyst dilatation results from excess epithelial production of cyst fluid without adequate drainage. Increasing intracyst pressure causes dilatation possibly aggravated by hemorrhage. Dilatation ceases when epithelial cells cease producing cyst fluid against intracystic pressure. Assuming enzymatic degradation of interstitial and perirenal connective tissue, tubular dilatation would require reduced or negative interstitial pressure which has no pathological basis.

Mitrval valve prolapse, diverticulosis and inguinal hernia are more probably due to repetitive extensile stresses leading to premature loss of tensile strength of connective tissues consequent upon engineering fatigue perhaps aggravated by a predisposing, metabolic connective tissue disorder or forme fruste (e.g., mitral valve prolapse in Marfan’s syndrome—a disorder of fibrillin). Similar repetitive stresses account for aneurysms [3] and ballooning of trumpet players’ cheeks. There is no more reason for assuming a pathogenetic role for proteases in these phenomena or in oncotic aneurysms associated with cardiac myxoma than in aneurysms due to bacteria, fungi, trauma or choriocarcinoma. Finding such enzymes in atherosclerotic aortic aneurysms [7,8] can be confounded by leucocytes and platelets in mural thrombus secondary to mural disruption. Cause and effect cannot be assumed nor does correlating macrophage numbers with coronary intimal tears [9] indicate causality. Deep mural tears with dissection occur in human aortae and experimental arteriovenous fistulae when macrophage accumulation is absent.

Atherosclerotic aneurysms develop in therapeutic venous bypass grafts, arteriovenous shunts [3] and aortae following leg amputation [10]. Evidence favoring biomechanical degradation of connective tissues in atherosclerosis is strong [11,12]. Aneurysm beyond aortic coarctation or aortic valvular stenosis is a non-specific response to hemodynamic vibrational stress in humans and experimental aneurysms; a similar phenomenon is plausible in atherosclerosis. Poststenotic dilatation develops in rubber tubing when bioengineering fatigue is hydrodynamically induced and is not enzymatically mediated [3]. The causal role of hemodynamic biomechanical stress is becoming increasingly obvious. The presence of proteolytic enzymes,
inhibitors and other cytokines does not warrant assumed causation of pathological lesions. Speculative tissue self-destruction by proteolytic enzymes resulting in various pathological weaknesses, distensions and tissue disruption is contrary to the very essence of biological survival and misleads the unwary.

References