Dear Sir,

I would like to add a few comments to what I wrote about the cellular biology of glomerulosclerosis [1], since knowledge in this area is advancing rapidly. At the EDTA in Paris, Gonzalez-Rubio et al. [2] (abs. p 93) nicely demonstrated that the glomerulosclerosis that develops in ageing rats is accompanied by an increased malonyldialdehyde content of the glomeruli and a reduction in anti-oxidant glutathione. Thus an oxidative stress operates in ageing animals. Clearly, there are differences between rat strains in their liability to glomerulosclerosis.

In the context of smoking in humans, the relationship between atherosclerosis and glomerulosclerosis as emphasised by Diamond and Karnovsky [3] has been taken a stage further by observations that oxidised LDL in such persons is related to smooth muscle cell hyperplasia and a high collagen content of the aorta and other arteries [4]. It is known that oxidised LDL enhances platelet aggregation and the formation of thrombox-anes [5] and thus it might also lead to the excessive release of growth factors. Also, oxidised lipids can prime PMNs and macro-phages for the production of more oxygen radicals [6]. Since oxidised LDL binds to me-sangial cells, in fact to proteoglycans, its actions will be similar to those on macrophages in the aorta [7].

From studies on fibrosis of the liver, it has been established that acetaldehyde derived from ethanol causes oxidative damage on Ito cell surfaces and that is followed by transcription of type I collagen and of fibronectin [8]. Indeed, lipid peroxidation in general will stimulate collagen synthesis by cells [9, 10]. Collagen synthesis by fibroblasts is stimulated by superoxide anions, and one might expect mesangial cells to react similarly. Lipid peroxidation is recognised to alter transcription of some genes. A clue might be derived from the observation that there is redox regulation of c-fos and jun DNA binding as a consequence of reversible oxidation of cysteine residues [11].

Not only does probucol lower LDL and prevent its oxidation, it is also an effective inhibitor of oxidative reactions within cells [12]. It is known to protect endothelial cells against oxidative stress [13]. Furthermore, it is interesting that Hirano and Morchoshi [14]

References


were able to prevent the development of focal glomerulosclerosis in aminonucleoside nephrosis by the use of probucol. One can anticipate that probucol will prevent local lipid peroxidation and production of collagen by mesangial cells [15].


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