Endothelial dysfunction and kidney

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The endothelium is the monolayer of endothelial cells lining the lumen of all blood vessels.The endothelium is an active dynamic organ that fulfills many crucial roles.First, it is a physical barrier, ultra-structurally defining the components of the vessel wall and the contents of the vessel lumen.Second, this barrier affords movement of some small solutes (O2, glucose, etc.), in preference to large molecules (e.g., albumin), therefore, involved in tissue autoregulation.Third, the endothelium affords an antithrombotic environment and mediates vasoactivity.Finally, the endothelium mediates adherence of platelets and white blood cells to the vessel wall during injury and inflammation, respectively.Endothelial function may be tested by two approaches:The first, is functional in nature and is based on the forearm haemodynamic response to acetylcholine (a pharmacological stimulus impinging upon the enzyme NO synthase) or to ischaemia [flow mediated vasodilatation (FMD) a physiological stimulus to the same enzyme].Endothelium-dependent vasodilation can be assessed in the coronary circulation in humans and is used for assessment of endothelial function.The second, approach rests on the measurement of the plasma concentration of specific biomarkers, i.e. a series of compounds, synthesized within the endothelium and that are released into the systemic circulation when endothelial integrity is hampered by noxious factors: LOX-1, CD40 ligand, CRP, and ADMA, Long pentraxin 3 (PTX3) ET-1 Microalbuminuria. The intercellular (ICAM) and vascular (VCAM) adhesion molecules, endothelial selectin (E-Selectin) and vonWillebrand Factor (vWF) are currently held as the most reliable biomarkers ofendothelial dysfunction/damage.The two approaches look at different aspects of endothelial function and therefore haemodynamic and biomarker-based tests provide complementary rather than overlapping information on endothelial integrity.Haemodynamic studies appear of particular value in clinical research, because altered endothelium dependent vasoregulatory control predicts cardiovascular complications in a variety of clinical settings.The definition of endothelial cell dysfunction, its pathophysiology and therapy remain poorly defined.Based on the diversity of endothelial functions, it is logical to expect that the definition of the syndrome of endothelial cell dysfunction (ECD) should be broad enough to encompass disturbances in the barrier function of the vascular endothelium; its impaired antithrombogenic properties; perturbed angiogenic competence; inappropriate regulation of vascular smooth muscle tonicity, proliferative capacity and migratory properties; perturbed synthetic functions and deterrent of neutrophils and monocytes from diapedesis.The pathophysiology of

endothelial dysfunction is complex and involves multiple mechanisms. However, some of these seem to be common to most conditions.• Reduced Nitric oxide (NO).• Elevated Asymmetric Dimethylarginine .• Oxidative excess.• Ang II.• OXLDL.• Endothelin system.• Alterations in the local balance of angiogenicand endothelial survival factors.• Hyperhomocysteinemia.• Diabetes mellitus.• The adipose tissue.• Hyperuricemia.• Inflamation.The most common causes of CKD are atherogenic diseases (hypertension, dyslipidemia, and type 2 diabetes mellitus), diseases in which the underlying histologic alteration is commonly represented by nephroangiosclerosis.The most typical finding in nephroangiosclerosis is represented by intimal hyperplasia of medium and small renal arteries. Such an alteration is the expression of systemic endothelial damage being extended to the whole arterial system, from small vessels to the aorta.Therefore endothelial damage seems to be the basic anatomic alteration that eventually leads to disastrous vascular events in the kidney.The pathophysiology of endothelial dysfunction and the kidney involves multiple mechanisms:1-Hypertension.Arterial hypertension is the most common cause of mild to moderate renal insufficiency in the general population and one of the major causes of ESRD. Renal dysfunction per se may be an underlying abnormality conducive to hypertension because hypertension “goes with the kidney” in cross-transplantation experiments, and a congenital reduction in the number of nephrons likely represents an important cause of glomerular endothelial dysfunction and hypertension in humans.2-Diabetes mellitus.Hyperglycemia leads to advanced glycation end products (AGE), which were shown to quench NO and impair endothelial function. AGE induce ROS and promote vascular inflammation, with enhanced expression of interleukin-6, VCAM-1, and MCP-1. This turns into a vicious circle in diabetic nephropathy, because in renal failure, clearance of AGE is delayed, which further promotes vascular and renal injury.3-Reduced Nitric oxide (NO).NO contributes to the control of renal hemodynamics and the process of urine formation, by interfering at multiple and physiologically critical steps of nephron function. NO dilates both the afferent and the efferent arteriole, may augment the glomerular filtration rate (GFR) and influence renal sodium handling along various tubule segments from the thick ascending limb to the distal tubule and the collecting duct.Thus inhibition of NO synthesis has profound effects at systemic and renal levels.4-ADMA.An endogenous competitive inhibitor of eNOS. Reduced NO bioavailability may contribute to renal disease progression. Cross-sectional studies documented that high ADMA is associated both with oxidative stress and endothelial dysfunction (i.e., compromised flow mediated vasodilation). Relatively higher ADMA levels (i.e., ADMA > median vs. ADMA