For the past many decades, humans have experienced significant changes in diet and lifestyles. Environmental and lifestyle factors play a major role in human disease. Nephrotoxicity is the common side effect of environmental insults. Physiological and biochemical features of the kidney make it more sensitive to environmental chemicals. Large blood flow, presence of metabolizing enzymes and transporters are the important factors for the sensitivity of the kidney. Although biomarkers for nephrotoxicity are available, improved biomarkers could contribute greatly to the monitoring of renal injury after exposure to environmental toxicants. Biochemical and pathological studies of the kidney will reveal toxicity of chemicals at certain extent. Culturing of good quality renal proximal tubule cells derived from known segments of the nephron provides an important model to evaluate toxicity. Transport studies will reveal the quality of the proximal tubules while in toxicity. Exposure to nephrotoxicants induces ET-1 production that leads to a rapid decrease in transport activity. Excessive ET-1 formation may cause renal injury and many renal diseases are associated with elevated ET-1 levels. A specific group of enzymes of the cytochrome-P-450 family in the kidney can be induced by environmental chemicals and this can be evaluated through micro array technology. Thus, kidney is the major organ to evaluate toxic and transport properties and also the mechanism of toxicity of environmental chemicals.