

[*Nephron*, **84**, 218-223 (2000)]

[Lab. of Clinical Pharmaceutics]

**Protective Role of Extracellular Superoxide Dismutase in Hemodialysis Patients.**

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The superoxide anion and other oxygen radicals have been implicated in the progression of chronic renal failure, and are removed by extracellular superoxide dismutase (EC-SOD) in the extracellular space on the surface of the endothelium. A single-base substitution of the EC-SOD gene which reduces the binding capability to the endothelial cells resulting in an increased serum concentration, has been identified in healthy persons and hemodialysis patients. The proportion of patients with this mutation (R213) among hemodialysis patients was studied. The percentage of R213G positive patients declined 80 months after the start of hemodialysis in non-diabetes mellitus (DM) patients. In contrast, in DM patients, the rapid decrease was obvious as early as 40 months after the initiation of hemodialysis. By prospective study for 5 years, there were significant differences in the survival rate between patients with and without R213G in DM, but not in non-DM patients.

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[Lab. of Clinical Pharmaceutics]

**Plasma Levels of Extracellular Superoxide Dismutase in an Australian Population:  
Genetic Contribution to Normal Variation and Correlations  
with Plasma Nitric Oxide and Apolipoprotein A-I Levels.**

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Extracellular superoxide dismutase (EC-SOD) is a major superoxide scavenger and may be important to normal vascular function and cardiovascular health. We analyzed family data from 610 healthy Australians to detect and quantify the effects of genes on normal variation in plasma levels of EC-SOD and to test for pleiotropy with plasma nitric oxide (NO) and apolipoprotein A-I (apoA-I). Multivariate analyses of plasma levels of EC-SOD, NOx, and apoA-I detected significant genetic correlations, indicating pleiotropy between EC-SOD and apoA-I and between NOx and apoA-I but not between EC-SOD and NOx. In healthy individuals, over a third of the variance in EC-SOD plasma levels is due to the additive effects of genes. Some genes influence EC-SOD and apoA-I levels. The same is true of NOx and apoA-I but not of EC-SOD and NOx. These patterns of pleiotropy can guide subsequent attempts to identify the genes and physiological mechanisms underlying them.

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[Lab. of Clinical Pharmaceutics]

**Relationship between Homocysteine and Superoxide Dismutase in Homocystinuria:  
Possible Relevance to Cardiovascular Risk.**

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A modest homocysteine elevation is associated with an increased cardiovascular risk. Because homocysteine-induced oxidative damage may contribute to vascular changes and extracellular superoxide dismutase (EC-SOD) is an important antioxidant in vascular tissue, we assessed EC-SOD and homocysteine in patients with homocystinuria. There was a significant, positive relationship between EC-SOD and total homocysteine. In 2 newly diagnosed cystathionine  $\beta$ -synthase-deficient patients, treatment that lowered the markedly elevated pretreatment homocysteine level reduced the associated elevated EC-SOD in each by 50%. The positive relationship between circulating EC-SOD and homocysteine could represent a protective antioxidant response to homocysteine-induced oxidative damage and contribute to reducing cardiovascular risk in homocystinuric patients.

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[Lab. of Clinical Pharmaceutics]

**Analysis of Medicinal History (VI): Influence of Ready-made Hyper-alimentation Drip Infusion on the  
Total Body Potassium Volume in Terminal Stage Cancer Patients with Peritoneal Carcinomatosa.**

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We analyzed the medicinal history data of medicine controlled patients. It was found that terminal-stage cancer patients complicated with peritoneal carcinomatosa (pePT), who had been administered ready-made total parenteral nutrition (rmTPN) as a form of nutrition control, retained normal potassium levels in serum, although they exhibited signs of metabolic alkalosis. It was found that the amount of potassium in the body decreases in pePT even if the serum potassium level is normal, and the excessive potassium content in rmTPN promotes the loss of potassium from the body. Moreover, it was suggested that this phenomenon may be due to the alteration of  $\text{Na}^+, \text{K}^+$ -ATPase activity involving aldosterone. In addition, rmTPN seems to be inappropriate for nutritional control of pePT.