

## EXACERBATED IMMUNE STRESS RESPONSE IN EARLY MAGNESIUM DEFICIENCY IN THE RAT

A. Mazur, C. Malpuech-Brugère, W. Nowacki, E. Rock,  
and Y. Rayssiguier

Centre de Recherches en Nutrition Humaine  
Unité Maladies Métaboliques et Micronutriments  
INRA, Theix, 63122 St Genès Champanelle  
France

Magnesium (Mg) plays an essential role in a wide range of fundamental cellular functions and many clinical signs and disease states are attributed to the altered Mg homeostasis. In a variety of animal models, Mg deficiency was shown to affect the immune system. In the rat Mg deficiency leads within a few days to the characteristic inflammatory syndrome. Since it appears that this deficiency affects the maintenance of host regulatory mechanisms in inflammation we have evaluated the immune stress response in Mg-deficient rats. As previously reported we have observed inflammatory symptoms associated to this deficiency, with the maximum after about one week on the deficient diet. These symptoms were concomitant with increased leukocyte count, plasma IL6, acute phase proteins and the presence of a large number of activated peritoneal macrophages. After one week on the Mg-deficient diet LPS challenge resulted in 70% mortality within 3 h induced, while there was no lethal effect of LPS in control rats. The vulnerability of Mg-deficient rats to LPS was associated with higher TNF alpha plasma values. Mg-deficient animals that received Mg supplementation before endotoxin challenge had significantly higher survival. At day 2 of Mg deficiency there was also a significant increase in plasma TNF after LPS challenge in deficient rats as compared to controls. Other results showing the increased sensitivity to the immune stress of Mg-deficient animals were also obtained by using PAF and live bacteria. Peritoneal cells (mainly macrophages) from deficient rats showed enhanced superoxide anion production and calcium mobilizing potency following in vitro stimulation, as well as after 2 and 8 days of deficiency. These studies indicate that an abnormal calcium handling induced by low extracellular Mg in vivo may be at the origin of exacerbated inflammatory response. These results also suggest that activated or primed state of immune cells is an early event occurring in Mg deficiency. Whether inflammatory response is also sensitive to Mg status in man merits further examination.