# Osmotically inactive sodium retention is correlated with low-grade metabolic acidosis

MARTINA HEER, PhD
DLR-Institute of Aerospace Medicine, 51147 Koeln, Germany
*email: martina.heer@dlr.de*

Water retention has been traditionally viewed as the only physiological mechanism available to keeping serum sodium levels constant following high salt. This seems to be mandatory in order to compensate for increased postprandial serum sodium concentration. However, we have recently shown in a human metabolic balance study that high salt intake led to sodium retention without concurrent fluid retention (Heer et al. AJP 2000) when –starting from an already high although average sodium intake level- sodium intake is further increased. This effect called osmotically inactive sodium retention was not only shown in humans but also in rat experiments (Titze et al. AJP 2004). Now, the question is, where and by which mechanism can sodium be stored in an osmotically inactive way. Titze et al. (AJP 2004) found in their animal experiments that osmotically inactive sodium retention is paralleled by an increased mRNA expression of glycosaminoglycans in skin. If this also holds true for humans the mechanism of osmotically inactive sodium retention could be as follows. The basic assumption is that osmotically inactive sodium must be bound somewhere so that the serum sodium concentration is no more increased. A high sodium intake would induce –under determined circumstances- an increased mRNA expression of glycosaminoglycans leading to a rise of glycosaminoglycan content in the interstitial space. Glycosaminglycans have sulphated sugar residues which could bind sodium by releasing hydrogen. If hydrogen was released, hydrogen concentration would increase in the interstitial space and possibly in blood. Concomitantly, blood bicarbonate levels as well as base excess concentration in blood would decrease. Now, this is exactly what happened in our metabolic balance study when we increased dietary sodium intake. We examined nine healthy male test subjects (age: 25.7 ± 3.1 year, body weight: 71.5 ± 4.0 kg, body mass index (BMI): 21.9 ± 3.1 $kg*m^{-2}$) for 28 days in our clinical research facility. The study consisted of six days of 50 mEq/d $Na^+$, six days of 200 mEq/d $Na^+$, ten days of 550 mEq/d $Na^+$ and again six days of 50 mEq/d $Na^+$. Fluid intake was kept constant at 40 ml/kg body weight/d. With a very high dietary sodium content mRNA expression of glyocosaminoglycans increased significantly ($p<0.05$) while blood pH, bicarbonate and base excess levels decreased significantly ($p<0.01$) indicating a low-grade metabolic acidosis. Lowering sodium intake reversed the increased blood pH, and the decreased bicarbonate and base excess levels to normal.

We concluded from these results that low-grade metabolic acidosis represents a pathophysiological mechanism involved in the development of diseases associated with high sodium intake.