

# Regulation of urine production with special reference to estrogen levels and to gender difference

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## ABSTRACT

This PhD dissertation is based on studies performed in the Institute of Clinical Medicine and Department of Urology, Aarhus University Hospital, Skejby section, Denmark.

Nocturia that is waking up during the night to void may occur at any age, even in children. The prevalence of nocturia in adults increases with age and seems to be similar in men and women. Enuresis nocturna is defined as an involuntary night time voiding, and it affects 7-10% of 7 year-old children and persist into adulthood to a considerable degree affecting 1-2% of adults. The prevalence of enuresis is higher in boys both in childhood and adolescents. In both conditions a lack in the nocturnal rise in arginine-vasopressin (AVP) may at least partly encounter for the pathology. During the past 20 years a lot of effort has therefore been put into research trying to elucidate the physiology and the pathophysiology behind the diurnal regulation of urine production. Previous reports have addressed the gender difference in AVP and urine production, but conflicting results exist. Additionally oxytocin has been shown to be antidiuretic, but the antidiuretic effect of oxytocin under normal physiological conditions still need to be clarified.

This dissertation is based on three studies. We report that the diurnal rhythm of AVP is unaffected by high endogenous as well as exogenous estrogen. High estrogen will decrease P-osmolality and P-sodium suggesting a resetting of the osmoreceptors for AVP-release. In spite of the resetting we found no influence on the final diuresis or urine osmolality. There was a trend towards sodium retention when endogenous estrogen was high. Exogenous estrogen given as combined oral contraceptives did not change the sodium excretion, but did raise the blood pressure significantly.

Furthermore we found a similar circadian rhythm between genders, and a tendency towards higher concentration of AVP in males.

It appears as if the renal sensitivity to AVP expressed as an increase in solute free water reabsorption is augmented in males. There was however no difference in the diuresis or the urine osmolality. We demonstrated a significantly increased excretion of PGE-2, which was not followed by increases in sodium excretion suggesting a gender specific renal handling of sodium in the male volunteers. Oxytocin did not contribute to the regulation of the diurnal urine production in either men or women.

In conclusion there is a gender difference in the diurnal urine regulation, but it is still not fully elucidated. There is a strong tendency towards involvement of sex hormones, but more studies addressing this issue are warranted.