The frequency of cardiovascular disease-related events is far more prevalent at specific times of day and loss of circadian rhythms increases the risk of chronic cardiovascular disease. Time-of-day-dependent rhythms in renal function are secondary to neuro-humoral changes associated with sleep-wake and feeding-fasting cycles. Bmal1 and other so-called “clock genes” are transcription factors that are expressed in a synchronous manner to carry out various physiological processes in a time of day cycle. Recent studies suggest that the molecular clock in the kidney can control responsiveness to factors that regulate sodium and water transport. We have compelling new preliminary data showing that renal medullary clock gene expression is phase-shifted or suppressed during a high salt diet with Bmal1 being phase-shifted in an endothelin-dependent manner. These effects were not evident in the renal cortex thus providing the first report of dyssynchrony of clock genes within a single organ. In cultured collecting duct cells, we observed that endothelin inhibits Bmal1 expression and knockdown of Bmal1 increases nitric oxide production and transepithelial transport. Furthermore, we recently observed that loss of endothelin B receptor function attenuates natriuresis in response to an acute salt load and that the extent of this attenuation depends upon the time of day the salt load is administered. Accordingly, our overall hypothesis is that diurnal regulation of sodium excretion relies on endothelin receptor-dependent regulation of Bmal1. These studies highlight the necessity to consider time of day when assessing renal handling of salt and the potential complications associated with high salt intake.