Summary and Conclusion

A circadian clock, or circadian oscillator, is a biochemical mechanism that oscillates with a period of 24 hours and is coordinated with the day-night cycle.The circadian system is composed of many individual tissue-specific cellular clocks whose phases are synchronized by the master circadian pacemaker residing in the suprachiasmatic nucleus (SCN) in the anterior hypothalamus of the brain.

Circadian clocks are the central mechanisms which drive circadian rhythms. They consist of three major components:

1. A central oscillator with a period of about 24 hours that keeps time
2. A series of input pathways to this central oscillator to allow entrainment of the clock
3. A series of output pathways tied to distinct phases of the oscillator that regulate overt rhythms in biochemistry, physiology, and behavior throughout the organism.

It was demonstrated that there is an underlying generative molecular mechanism of the circadian clock that consists of a set of core clock genes and their protein products, which together participate in positive and negative autoregulatory feedback loops of transcription and translation.

The master pacemaker of the circadian clock is located in the suprachiasmatic nucleus (SCN), a pair of distinct groups of cells located in the hypothalamus of the brain.

Clock genes are expressed not only in the SCN, but also in extra-SCN brain regions as in most peripheral tissues.

Circadian signals from the suprachiasmatic clock are known to be distributed via neuronal outputs and diffusible/ humoral messages. Therefore, coupling between the SCN and the extra-SCN brain clocks can be achieved by nervous and/or neurohormonal routes

The most obvious manifestation of circadian rhythmicity of renal function is a well-marked difference in the volume of urine formation/ excretion between the day and the night.

Circadian rhythm of the blood pressure parallels oscillations of sodium excretion, showing maximal values during biological day and a 10–20% dip during the sleep phase.

Circadian oscillations in multiple regulators of ENaC activity indicate that circadian clocks may have a major influence on the transepithelial sodium reabsorption in the distal nephron and the collecting duct and, thus on blood pressure.

circadian oscillations in claudin-8 expression may provide a mechanism for circadian rhythmicity in the paracellular chloride permeability. A possible physiological meaning for the circadian rhythmicity of chloride reabsorption liesin the requirements for maintenance of the overall electroneutrality of NaCl transport across the cell under conditions when sodium reabsorption exhibits a clear circadian rhythm.

Circadian rhythms of urinary potassium excretion were reported many years ago with a peak in the middle of the day in humans. This rhythm is independent of activity, posture and dietary intake and persists for more than several days in individuals isolated from main external cues.

Cardiovascular events such as stroke and myocardial infarction are known to peak with the morning surge in BP and heart rate. BP increases in the early morning, followed by a plateau during the day, and then dips during sleep.

although the circadian BP rhythms between the patients and the healthy subjects were comparable, different patterns in the underlying hemodynamics were present.

Several reports link aldosterone signaling to the disruption of circadian BP patterns, suggesting a role for renal function in maintaining normal circadian changes in BP. Renal dysfunction, even in a mild form, as seen in healthy kidney donors, is capable of causing a non-dipping BP phenomenon without affecting its absolute levels.

Patients with CKD often have nondipping BP pattern. The causes of nondipping in these patients are not clear, but many factors have been proposed, eg, sodium sensitivity, autonomic activation, and endocrine dysfunction.

Chronotherapy, the scheduled administration of pharmaceutical agents with respect to an individual’s circadian rhythms, may increase the effectiveness and decrease the side effects of pharmacologic agents. The potential benefits of chronotherapy in the treatment of hypertension include

control of BP and normalization of the dipping pattern.

Indeed, the restoration of circadian variability in blood pressure appears to be an important factor in the control of cardiovascular disease.

Circadian rhythm sleep disorders are primarily caused by alterations in the circadian time-keeping system or by a misalignment between the endogenous circadian rhythm and the external factors that affect the timing or duration of sleep.

Sleep disturbances are much more prevalent in the dialysis population than in the general population. Patients on daytime hemodialysis and patients with chronic kidney disease (CKD) have reduced total sleep time and reduced sleep efficiency in comparison with healthy subjects.

hemodialysis may also affect the sleep–wake cycle by altering exposure to *zeitgeibers* that help set or entrain the circadian system. The melatonin rhythm was more likely to be abolished in patients on hemodialysis than in patients with chronic renal insufficiency who were not on hemodialysis, suggesting an influence of hemodialysis on the rhythm.

Decreased melatonin levels are associated with more severe sleep disturbances in hemodialysis patients.

Data on the existence of a circadian rhythm of EPO in healthy subjects are equivocal and scarce and incomplete in CKD. Theoretically, there are several arguments that support the existence of a circadian rhythm of EPO in CKD.