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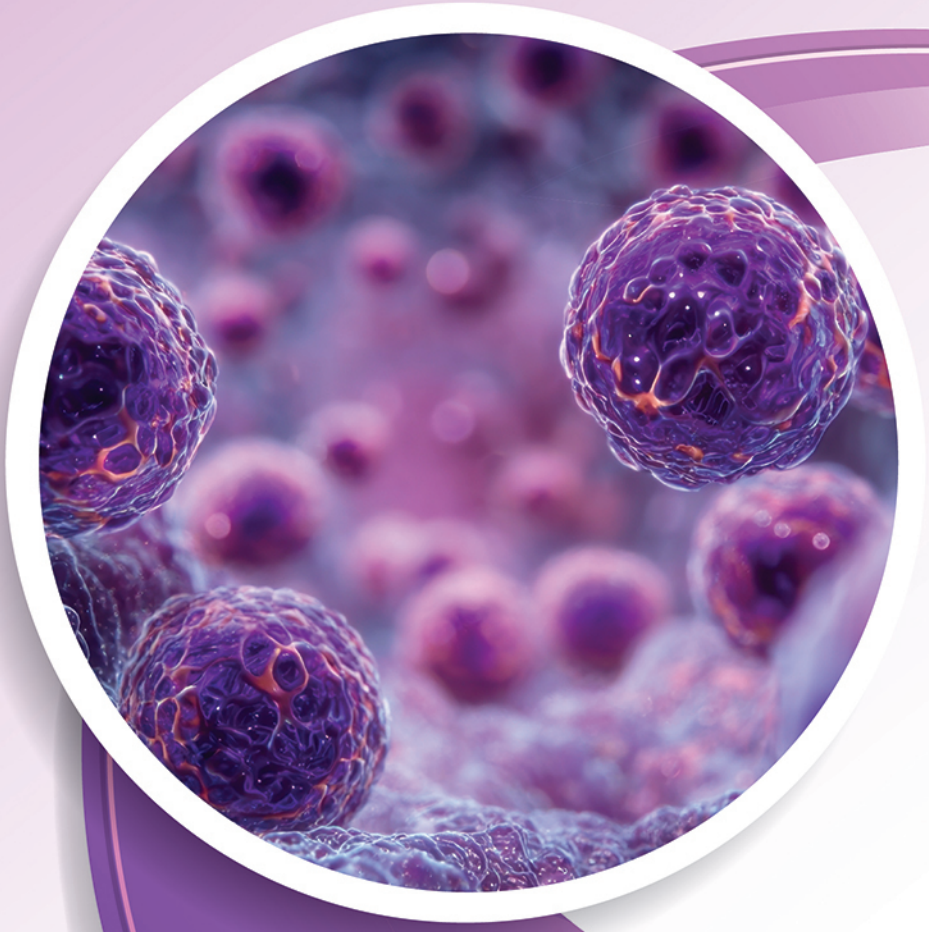
Prediabetes Unveiled

A Comprehensive Guide to Risk, Biology and Intervention



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CHAPTER

14 The Science of Timing—Chronobiology: Meal Patterns and Sleep

Smitha Bhat, Narsingh Verma

ABSTRACT

Chronobiology explores how our body's internal clock shapes daily patterns of sleep, eating, and metabolism. The main timekeeper—the suprachiasmatic nucleus (SCN) in the brain—coordinates rhythms across organs, responding to cues such as daylight, mealtimes, and social activity. When these rhythms are in sync with the natural day–night cycle, the body works more efficiently, using energy where and when it is needed. Modern lifestyles, however, often disrupt this harmony through shift work, irregular late-night eating, excess screen exposure, or a natural tendency toward evening activity. Such disruptions can impair how the body handles glucose and fats, raise inflammation, and, over time, increase the risk of diabetes, obesity, and heart disease. Sleep plays a central role, acting like a master switch for the body's repair and hormonal balance, while the timing of meals—known as chrononutrition—proves equally important. Evidence shows that eating earlier in the day, keeping a consistent meal schedule, and limiting eating hours can improve weight control, blood sugar levels, and overall metabolic health. By applying these principles, health professionals can offer simple, practical guidance rooted in the body's natural rhythm.

INTRODUCTION

The study of the impact on health of the circadian rhythm and its disruptions is called chronomedicine.

The sleep/wakefulness, feeding/fasting, and behavioral states of an organism vary over the course of a day, and this rhythm is known as the circadian rhythm. Various physiological parameters—the body temperature, the rate of digestion, metabolism and nutrient absorption, secretion of hormones, and various cellular processes—are controlled by the circadian rhythm. Circadian variation occurs in the levels of glucose and insulin, in glucose tolerance, lipid levels, energy expenditure, and appetite. All systems of the body—the cardiovascular system, the central nervous system, and the gastrointestinal tract are impacted by the circadian cycle. In mammals, this cycle lasts for 24 hours, and is controlled by the suprachiasmatic nucleus (SCN) which is located in the anterior hypothalamus **(Fig. 1)**. The rhythmicity of the SCN is because of periodicity in the molecular circadian clock. Proteins are transcribed from genes, and these proteins, in a negative feedback loop, inhibit further transcription of these genes. In mammals, this cycle of transcription-inhibition-transcription

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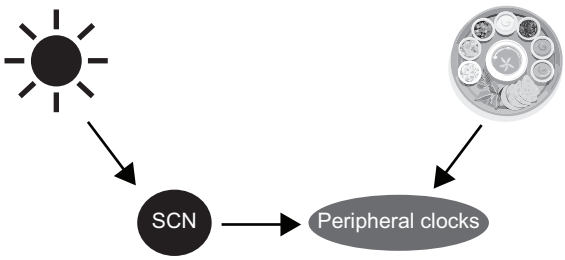

Fig. 1: Entrainments of the central and peripheral clocks.

lasts for 24 hours. It is important to note that periodicity is present in all tissues and organs of the body, not just the SCN. The SCN is entrained by light. The rhythm of the peripheral circadian system is set by the SCN, but it can be affected by various factors such as feeding, exercise, and social interaction. The endogenous, environmental, and behavioral factors which act upon the central and peripheral circadian systems are referred to as "zeitgebers" (light givers).

From an evolutionary perspective, the point of the circadian rhythm is to optimize metabolic efficiency. Thus, during daylight hours, when the energy required by the organism is higher, glucose metabolism is more efficient because of increased insulin secretion and sensitivity. Conversely, in the absence of daylight, the body goes into conservation/consolidation mode and insulin resistance is increased. This diurnal variation in insulin sensitivity is governed by the rhythmic secretion of insulin and cortisol.

The implication of this is that aligning feeding/fasting and sleep/waking with the natural rhythm of the day is conducive to health. When feeding/fasting and sleep/waking are not synchronized with external environmental light cues, it results in asynchrony between the central and peripheral circadian systems, leading to circadian disruption.

CIRCADIAN DISRUPTION

Circadian disruption can occur when a mistimed exposure to zeitgebers causes either an asynchrony between the SCN and the peripheral clocks, or a disconnect between the body's rhythm and external environmental cues. Chronobiologically, active elements which can affect the central and/or peripheral circadian rhythms are termed chronodisruptors. Disruption of the circadian rhythm results in cardiometabolic disease—diabetes, obesity, and dyslipidemia.

Causes of Circadian Disruption

- Shift work
- Jet lag
- Evening chronotype
- Irregular lifestyles—consumption of food at night, exposure to artificial light, and screens at nighttime.

CHRONOTYPES

Chronotype is the phenotypic manifestation of an individual's preference for morning or evening as the period of maximal activity. It is determined by biological, psychological, and genetic components. In its turn, the chronotype influences cognitive function, hormonal rhythms, sleep/wake and feeding/fasting preferences. Based on these preferences, individuals may be classified into owls, larks, or indeterminate. The chronotype does not remain static but may change with age. It can be assessed by various techniques, including the composite scale of morningness.

Similar to shift workers, patients with evening chronotypes suffer from a misalignment between rhythms dictated by external factors and the endogenous rhythms of the body.

Evening chronotypes are more prone to type 2 diabetes mellitus (T2DM) and cardiovascular

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disease; this is ascribed to the dysregulated secretion of melatonin, leptin, and adiponectin as well as altered expression of the clock gene.

Other factors may contribute to the increased prevalence of dysglycemia and metabolic disease in the evening chronotype.

- Evening chronotypes have less sleep on the whole. This is because of the fact that though the time at which they fall asleep is dictated by themselves, their waking time is dictated by society.
- Decreased sleep quality
- Depression is more common.
- Sleep variability is higher as measured by mid sleep time because they can follow their own clock on weekends.
- Poor diet
- Higher exposure to light as they sleep later.

Many of these factors are associated with increased inflammation as indicated by higher C-reactive protein (CRP) levels, but the evidence is not completely convincing.

Recent literature proposes that adjusting the work schedule, the after-work schedule, and food timings for evening chronotypes may promote cardiometabolic health.

SLEEP AND ITS ROLE IN METABOLIC CONTROL

Metabolism and the circadian clock talk to each other in the languages of sleep and food. In fact, sleep is referred to as the metabolic master switch, and the sleep wake cycle reflects the rhythmicity of the master clock, the SCN. Energy allocation differs between sleep and wakefulness. During sleep, energy is allocated to regenerative, adaptive, and anabolic processes namely immune functions, synaptic plasticity, and glycogen storage.

Sleep cycles in mammals are regulated by two components: The homeostatic desire to sleep, which increases with continued wakefulness, and the circadian clock, which aligns the times of falling asleep and waking up with the solar day.

If the quantity of sleep is adequate (between 7 and 9 hours) and the quality is good, the sleep is considered to be restorative. On the other hand, sleep disruption (both extremely short and abnormally long sleep durations) affects the secretion of leptin, ghrelin, and melatonin.

Metabolic consequences of poor sleep hygiene include:

- Increased gluconeogenesis
- Decreased insulin secretion
- Increased insulin resistance
- Increased markers of systemic inflammation

The importance of sleep is underscored by the fact that present the American Diabetes Association (ADA) recommendations state that sleep is one of the prime components of diabetes management.

CHRONONUTRITION

Food intake times were initially dictated by the availability of sunlight, resulting in a homeostatic feeding pattern. However, in the present day, hedonic and social eating are key factors which influence the feeding/fasting cycle.

Chrononutrition deals with the timing and distribution of energy intake throughout the day and the impact this has on health. It hinges on the premise that it is not only what is eaten, but when it is eaten that influences weight and metabolism. This is based on the principle that metabolism is optimal when the central clock is synchronized with the peripheral clock—that is, when the SCN (entrained by light) is in synchrony with the peripheral clock (entrained by food and fasting).

Apart from the quality and quantity of food, the following factors influence weight balance and metabolic profile.

- Eating window—restricting the eating window to 12 hours or less is beneficial—the effect is believed to be due to the duration of the eating window altering gene expression.
- Within a meal, the sequence of macronutrient consumption alters the glycemic response to food intake.

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The effect of meal timing on metabolism is supported by evidence:

- Highest energy intake at dinner and breakfast and were respectively associated with a greater and lesser risk of obesity **(Fig. 2)**.
- Individuals who consumed a larger quantum of their daily intake at breakfast were less likely to become obese, even if their total calorie intake was more than those who consumed a larger portion of their calories at dinner.
- Individuals with an evening chronotype were more likely to become obese and less likely to lose weight than those with a morning chronotype.
- Skipping breakfast is associated with increased insulin resistance.
- Meals after 8 PM in patients with T2DM is associated with higher glycated hemoglobin (HbA1c) levels.
- It is interesting to note that some evidence shows that unlike in healthy individuals, those with T2DM have increased insulin resistance and higher postmeal glycemic excursions in the morning rather than evening.
- An earlier first meal and a nighttime fast longer than 13 hours decreases the incidence of diabetes.

The mechanisms proposed for the influence of early meal timing on nutrition are numerous:

- Those who eat a high calorie breakfast were less likely to eat later in the day.
- Higher levels of low-density lipoprotein (LDL) because of less fat oxidation.
- Lower diet induced thermogenesis (DIT) in the evening.
- Lower degree of satiety after consumption of food in the evening.
- Sustained increased in ghrelin and rapid decrease in leptin after evening meals.
- Hormones involved in metabolism such as insulin, glucagon, adiponectin, corticosterone, leptin, show a diurnal variation and function

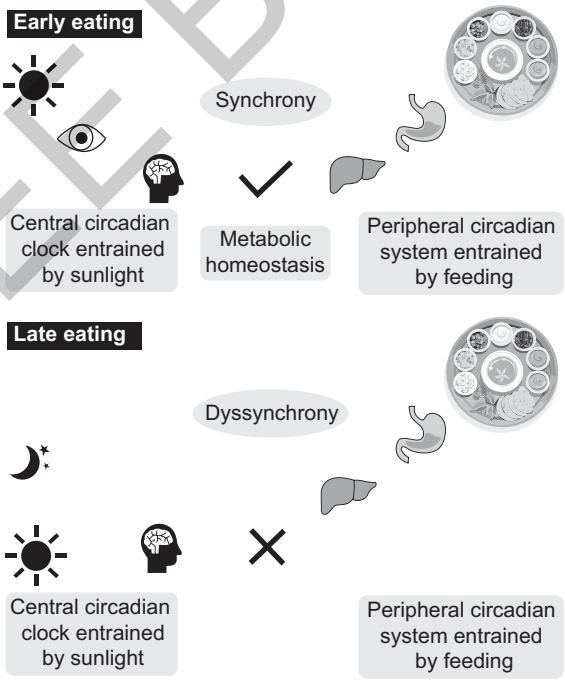

Fig. 2: Eating later in the day causes a misalignment between the suprachiasmatic nucleus (SCN) and the peripheral clocks.

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optimally when feeding occurs in the active phase (in chronobiology, the active phase coincides with the solar day).
- The gut microbiota which plays a role in various metabolic processes also shows a cyclical activity in synchronization with the circadian rhythm.

CHRONOMEDICINE IN PREDIABETES

Poor sleep quality, though not waking time, is a predictor of prediabetes. In patients with prediabetes, a later chronotype is associated with higher HbA1c, independent of factors like social jet lag and sleep disturbance. Patients with prediabetes with shorter sleep duration had higher HbA1c and a higher conversion rate to diabetes. Studies are ongoing about the decreased conversion of prediabetes to diabetes with bright light therapy.

It is interesting to note that prediabetes is also associated with abnormal circadian variability (ACV) of blood pressure in the form of high mean blood pressure, high pulse pressure, and circadian hyperamplitude-tension which means an excessive variability of blood pressure range. This ACV is what contributes to the increased cardiovascular risk of prediabetes.

Poor sleep predisposes to prediabetes. The Korea National Health and Nutrition Examination Survey found that individuals with sleep duration <7 hours per day had a higher risk of prediabetes. In patients with prediabetes, digital cognitive behavioral therapy for insomnia (DCBTI) ameliorated dysglycemia. The China health and retirement study showed that sleep <7 hours increased the risk of prediabetes. Conversely, patients with prediabetes also were likely to have a shorter sleep duration. The link between sleep and prediabetes was postulated to be systemic inflammation as indicated by higher CRP levels.

NIGHT EATING SYNDROME

In the "night eating syndrome" most of the calorie and carbohydrate content is consumed at dinner or in after dinner snacks is unhealthy, and results in an increase in HOMA–IR (Homeostatic Model Assessment for Insulin Resistance) and increased fasting plasma glucose.

SOCIAL JET LAG

Social jet lag is a particular type of chronodisruption that occurs due to a mismatch between social rhythms and the circadian clock (because of differing sleep/wake times on weekdays and weekends). It results in chronic sleep disruption which in turn predisposes to T2DM and obesity.

INTERMITTENT FASTING

Intermittent fasting (IF) is a broad term that describes any eating pattern that cycles between periods of eating and voluntary fasting. It includes:
- *Time-restricted eating (TRE)* is a specific type of IF where eating is restricted to a certain window of time each day.
- *Alternate-day fasting:* Eating normally one day and fasting the next.
- *5:2 diet:* Eating normally for 5 days a week and restricting calories for 2 days.
- *16/8 method:* Fasting for 16 hours and eating within an 8-hours window.

Evidence that TRE benefits individuals with obesity, prediabetes, and diabetes is rigorous and plentiful. Original research and systematic reviews show:
- TRE improves body mass index (BMI), but has no significant effect on waist circumference.
- Both body weight and fat mass decreased significantly in TRE, but only when the fasting window exceeded 12 hours.
- HOMA–IR decreased, especially in long-term intervention, more so in overweight participants.
- TRE did not improve the lipid profile significantly. There was a slight decrease in total cholesterol and LDL.
- TRE resulted in a reduction of systolic (up to ~5–11 mm Hg) and diastolic (up to ~7–10 mm Hg) blood pressure (BP).

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- Improvement in self-reported sleep, energy level, subjective feeling of hunger at bedtime, quality of life, and well-being
- Early time-restricted feeding (TRF) improves some aspects of cardiometabolic health even without weight loss.
- Higher risk of metabolic syndrome (MetS) in evening chronotype.
- Early TRF improved fasting plasma glucose, reduced total body mass and adiposity, ameliorated inflammation, and increased gut microbial diversity.

The beneficial effects of TRE may be due to:

- Inadvertent calorie restriction
- Enhancement of circadian clock oscillations
- Restoration of diurnal eating and fasting rhythms
- Improved metabolic flexibility
- A more efficient integrated stress response (ISR: In the presence of stressors, the integrated stress response inhibits general protein transcription as a whole but increases quality control).
- Improvement in gut function and gut microbiota.

THERAPEUTIC IMPLICATIONS AND PATIENT MANAGEMENT TIPS

Since calorie restriction is difficult to sustain, the principles of chronobiology and chrononutrition may be used to give patients advice which is easier to follow. Patients may be advised that earlier food intake may be a nutritional tool for dietary and metabolic control.

- Sequence of eating food—it is better to consume fiber (in vegetables) followed by protein or fat and consume carbohydrate after this. This limits postprandial glycemia.
- Eating earlier in the day decreases risk of obesity—those who consumed <33% of their daily calorie intake in the evening were less likely to develop obesity.
- Increase in carbohydrate and protein and decrease in fat at the morning meal—allocating a larger portion of the daily carbohydrate consumption to breakfast, especially in patient with diabetes, reduces postprandial sugars.
- Increase in protein consumption at night.
- Restricting intake to 2–3 meals with at least a 14-hours fasting period improves glycemia and promote weight loss in patients with T2DM.
- If it is not possible to abstain from late night eating, portion size and meal composition may be adjusted.
- Consistent meal timing.
- It is crucial to educate patients with prediabetes and diabetes about the metabolic impact of night eating syndrome and breakfast skipping, and the importance of sleep.
- Green tea (when consumed in the evening) and coffee (when consumed in the afternoon) decrease the risk of diabetes.
- Eating low gastrointestinal (GI) foods in the morning improves glycemic response to a greater effect than at night.
- *Implementation of TRE:*
  - Concurrent with active phase to coordinate with circadian rhythms in metabolism and sleep.
  - Avoid eating when melatonin is high (1 hour after waking and 3 hours before sleep onset).
  - To be effective, the eating window should be consistent daily—on workdays and holidays.
  - Early eating window is better.

Chronomedicine is a low cost, effective method for the clinician to improve outcomes in metabolic disease. Thus, it behooves clinicians to be familiar with the principles of chronobiology and wield them wisely for maximal patient benefit.

CONCLUSION

Our body functions best when its internal rhythms work in harmony with the environment. Aligning sleep and meal patterns with daylight hours helps maintain healthy metabolism, supports energy

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balance, and reduces the risk of chronic diseases. When these rhythms are disturbed—whether by irregular hours, late-night meals, or poor sleep—the effects can ripple through hormone regulation, appetite control, and blood sugar management. Clinicians can use chronobiology as a practical tool, encouraging earlier meals, consistent eating windows, smart sequencing of foods, and quality sleep. These approaches don't require extreme diets or costly interventions, but they do call for mindful adjustments in daily routines. By respecting the body's natural timing, individuals can improve metabolic efficiency and promote long-term health.

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- *Comprehensive overview:* Presents an in-depth exploration of prediabetes, integrating basic science, clinical detection, and practical intervention strategies.
- *Expert contributions:* Features chapters authored by leading clinicians and researchers offering diverse perspectives on epidemiology, insulin resistance, beta-cell function, adipose biology, and genetics.
- *Contemporary topics:* Covers emerging areas such as chrononutrition, digital health, and precision medicine, reflecting current trends in metabolic research.
- *Evidence-based insights:* Provides practical recommendations derived from landmark clinical trials and public health initiatives for prevention and early intervention.
- *Global and public health relevance:* Addresses the expanding global burden of prediabetes and calls for action from clinicians, policymakers, and program developers.
- *Enduring reference:* Serves as a valuable guide for clinicians, educators, researchers, and health leaders committed to advancing metabolic health and combating diabetes worldwide.

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