



## Circadian Synchrony of Insulin and Intake Patterns: Towards A Rational Anti-Obesity Theory

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### Editorial

This editorial seeks to develop and a global anti-obesity theory based on circadian patterns of insulin-mediated appetite regulation. Insulin is globally known as the storage hormone because it stimulates glucose entry into the peripheral fat and muscle cells [1,2]. Ruminants serve as suitable sophisticated models to therapeutically study human endocrinology and metabolism. Much less glucose crosses into the portal vein in ruminants compared to non-ruminants. In consequence, insulin would not have as significant impacts on hepatic glucose metabolism in ruminants as it would in non-ruminants [1,7].

Nervous system, gut peptides, other pancreatic secretions, and nutrient absorption are the main routes of stimulating pancreatic insulin release [3]. The nervous system affects insulin release regulation via sympathetic and parasympathetic neurons. The vision, odor, and flavor of foods induce insulin secretion by activating parasympathetic neurons in humans [7,8]. The long-time research has led to the proposal that neural impulses and gastrointestinal hormones are involved in postprandial insulin response to food presentation. Secretin and pancreozymin (cholecystokinin) stimulate insulin release in sheep. Blood insulin in sheep rises sooner than does blood glucose, suggesting that glucose may not be a major cause of the initial rise in postprandial insulin release. Nevertheless, the ultimate increase in blood glucose may contribute to maintaining the high postprandial insulin concentrations. In goats fed ad libitum for a 3-h period daily, a postprandial rise in blood insulin occurs that is probably caused by volatile fatty acids (VFA) stimulation of the pancreatic  $\beta$ -cells [4].

A post-meal rise in blood insulin is observed whereas no such a peak is noticed in blood VFA. It is speculated that the nervous signals (rather than VFA) either directly or through gut hormones may result in post-meal insulin responses. A similar post-feeding rise in blood insulin has been shown in lambs fed chopped dry grass in two equal meals at 0900 and 1600 h [5]. Blood insulin in lactating cows fed once daily during day exhibits distinct circadian rhythms, peaking in the afternoon and falling to a nadir overnight or during the dark phase. A comparable zenith time in blood insulin occurs in the afternoon and early evening [12].

The circadian patterns of peripheral blood insulin are closely linked to the circadian patterns of feed intake. Cows fed forage and concentrate separately exhibits sharp rises in blood insulin upon concentrate deliveries in morning and afternoon and declines in blood insulin shortly thereafter, remaining lower overnight. Similarly, food intake shows two major peaks after concentrate deliveries. Food intake is considerably lower between from midnight through dawn, which is similar to humans that are diurnal animals. The fact that insulin works more effectively in morning and early afternoon than in evening and overnight in humans lends support to the circadian rhythmicity of

peripheral insulin and food intake [7,9,10]. These observations and contemplations suggest that circadian rhythms of peripheral blood insulin relate to circadian rhythms of pre- and post-ingestive readily digestible carbohydrates supply. Since human insulin action and peripheral cellular glucose entry are impaired as day leaves for night [6,10,11], prominent nocturnal rhythms of food intake will severely affect insulin efficiency, most likely increasing insulin resistance and obesity.

To integrate, by shifting the timing of major food meals from evening and night towards day and morning, more synchronous patterns of food intake and insulin dynamics will occur. This synchrony will largely avoid glucose, amino acids, and fatty acids overloads overnight when human peripheral cells have limited capacity of nutrient assimilation. As a result, obesity, glucose intolerance, insulin resistance, and metabolic syndrome are less likely to develop. Future research must enlighten the various chronoendocrinogenomic properties of this global theory.

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