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Akbar Nikkhah \* Mini Review

# Perspectives on Obesity Etiology: An Innovative Emphasis on Meal Timing

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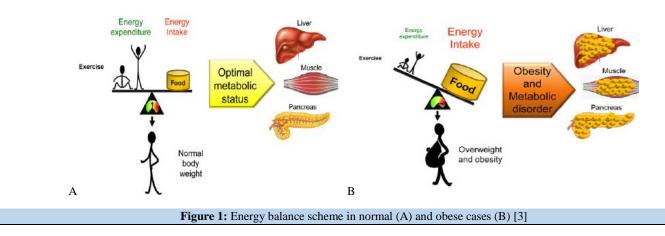
### Abstract

This perspective article aimed to explain mechanisms involved in the etiology of obesity and to provide a nutritional perspective to understand why the time, size and source of meals eaten during a circadian period should be carefully managed. The obesity outbreak has been investigated for many years with a variety of dietary protocols, but obesity remains a problem worldwide. The increasing trend of obesity and diabetes may suggest that current perspectives and insights into obesity are unable to considerably explain their causes and mechanisms. The most commonly accepted mechanism of obesity in both humans and animals is energy balance model (EBM; energy intake vs. energy expenditure). This model implies that the energy would be stored as fat when energy intake is above energy expenditure. However, as EBM is based on physics law, metabolic pathways of fat deposition seem to be disregarded. Nutrients reaching the bloodstream trigger hormonal responses, resulting in nutrients partitioning toward oxidation or deposition. For instance, insulin is secreted following increased blood glucose concentrations which drives positive energy balance and hence fat deposition. Such metabolic pathways represent a new concept known as carbohydrate insulin model (CIM). It is somehow believed that this model provides a better perception to explain obesity mechanisms. Given that glucose metabolism has circadian rhythmicity, it may be hypothesized that CIM and chrono-nutrition are interconnected. Preventing glycemic load via limiting the intake of carbohydrate-rich diets and attention to intake timing appear to benefit obesity and diabetes prevention programs. To conclude, energy source and meal timing should be contemplated together as key factors affecting energy partitioning and fat storage.

Keywords: obesity; diabetes; chrono-nutrition; meal timing

### **Introduction and Discussion**

The aim of this minireview article was to describe current mechanisms in the etiology of obesity and present a nutritional perspective to underline the importance of chrono-nutrition on glycemic load and obesity development. Obesity and diabetes are amongst the most common consequences of modern human eating habits and lifestyle. In recent years, consumption of energy-dense processed foods has increased dramatically. It is thought that these foods drive positive energy balance and likely overweight [1]. Energy balance, a prominent model of obesity, implies that when energy intake is greater than energy expenditure, surplus energy is deposited in fat form, thereby causing overweight and obesity. Energy balance model (EBM) is summarized schematically in Figure 1. Is the total energy intake or particular nutrient content of ultraprocessed foods that cause obesity? What are the possible roles of meal timing, size, and frequency on energy circulation and nutrient fate? It has been reported that food source and composition, and not merely energy content of foods, are involved in obesity occurrence [2]. The carbohydrate-insulin model (CIM) suggests that nutrients absorbed into the bloodstream (e.g., glucose overload) elicit hormonal responses that lead nutrient partitioning [2]. As an anabolic hormone, insulin is secreted in response to increased glucose supply from the digestive tract and plays a critical role in directing glucose towards muscle, liver, and adipose tissue.



Additionally, insulin suppresses glucagon secretion and stimulates lipogenesis simultaneously [4]. The postprandial insulin response would depend on how different foods raise the postprandial blood glucose or glycemic index (GI) [5]. It has been demonstrated that after having a high GI meal, serum insulin levels would increase sharply, developing a sequence of metabolic events resulting in excess food intake [6]. It seems that persistent exposure to such anabolic status increases cellular metabolite uptake (e.g., glucose and fatty acids) and lowers blood metabolites, making the brain to feel starvation signals, thereby cravings may occur [2]. As a result, metabolic fuels may be stored in fat depots, leading to positive energy balance [7].

Besides quantity and quality of foods eaten in a circadian period, meal timing and energy distribution are also critical in terms of glycemic overload and obesity. This might be closely interrelated with CIM. Glucose metabolism has circadian rhythmicity and any disruption in such rhythms (e.g., shifting from morning eating to evening eating) can result in adverse effects on metabolic health. The significance of eating time on the obesity outbreak and managing weight loss has been discussed previously [8]. Glucose tolerance decreases as day ends and night begins so, eating high GI foods overnight would probably result in higher glycemic load and abnormal insulin metabolism [9]. It has been suggested that the human body does not need elevated insulin levels during evening and night because of lower energy requirements for resting or sleeping [10]. As noted, insulin is responsible for known metabolic pathways such as glucose and fatty acids uptake, and lipolysis-lipogenesis [10]. The elevated insulin may be attributed to obesity [10]. Overweight or obesity in 7 years old children was associated with eating high energy lunch and mid-afternoon meals when they were at 4 years of age [11]. Such a response is supported by CIM. Moreover, skip-breakfast could a main risk factor for obesity in children. Lowering glycemic index by moderate increase of protein intake has attenuated gestational weight gain in pregnant women with obesity, further indicating beneficial effects of low glycemic index diets [12]. As recommended, and according to natural circadian rhythms, optimized glucose metabolism is a must for reduced pregnancy issues thus. As such, large evening meal should be avoided in pregnant women [13].

In addition to timing, frequency, and source of meals, daily exercise is also synchronized with circadian rhythms and has an important role in glycemic control [14]. The optimal timing of eating and exercise as well as lower intake of high glycemic index diets are amongst the most important tips that the public should consider carefully. More research is needed to completely identify metabolic pathways involved in obesity development. The interaction of other macronutrients with circadian rhythms should be studied.

### Conclusion

Traditionally, obesity is defined as a consequence of imbalance between energy intake and energy expenditure. However, according to a more recent carbohydrate-insulin model, consuming energy-dense highly processed foods is associated with higher glucose load which activates metabolic and hormonal pathways involved in nutrient partitioning towards fat deposition. Obesity and diabetes are among the most common consequences of disruption in glucose and insulin metabolism, being interconnected with natural circadian rhythms. Eating low glycemic index diets at a proper time provides a nutritional framework to have a healthy metabolism.

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