



About the Obesity Epidemic

Obesity is a chronic disease, linked to many serious medical conditions such as type 2 diabetes, heart disease, high blood pressure, stroke, depression and some forms of cancer.

- Obesity is a public health crisis, with approximately one third of adults, or 75 million Americans, considered to be obese.
- Approximately 300,000 deaths per year in the U.S. are associated with obesity, according to the Department of Health and Human Services (HHS). It is the second leading cause of preventable death, just behind smoking.
- According to data presented at the Centers for Disease Control and Prevention's (CDC) inaugural Weight of the Nation conference, the annual medical burden of obesity in the U.S. has risen to almost 10 percent of all medical spending and amounted to \$147 billion per year in 2008.

Causes of Obesity

Obesity results from an imbalance, over an extended period of time, caused by the consumption of more calories than the body is able to burn. The cause of this imbalance is complex and is influenced by the convergence of various environmental, behavioral and genetic factors.

- People are naturally attracted to high-calorie, sugary or fatty foods and find them pleasurable and rewarding to consume. Our attraction to these foods is compounded by the modern environment where inexpensive and calorically dense foods are easily accessible. Often individuals eat these foods when they are not hungry or eat more than they need.
- People today live a more sedentary lifestyle than in the past, so they burn less energy, further compounding the challenge of maintaining an appropriate balance between calorie intake and expenditure.

Role of the Central Nervous System (CNS) in Obesity

At the crux of obesity is the role of the central nervous system (CNS) in regulating body weight. Over time, the brain of an obese person becomes insensitive to the "stop" signals from the body, resulting in consumption of food beyond the body's energy needs.

- The brain is the master regulator of the body, affecting every fundamental function including what we eat, when we eat, how much we eat and how many calories we burn.
- When a person starts to lose weight, the brain resists weight loss by increasing hunger and slowing down resting metabolism, making it more difficult to sustain weight loss. Thus, many interventions for weight loss may be successful in the short term, but results are typically difficult to maintain.

New Developments in Treating Obesity

The need for new interventions is paramount given the increasing prevalence of obesity, its health implications and burden to the healthcare system. Studies show that a >5% loss of body weight in obese patients can significantly reduce their risk of developing complications such as diabetes and cardiovascular disease.

- The complex pathways within the CNS and their interaction with other mechanisms involved in the regulation of body weight make obesity a difficult and complicated disease to treat. This helps explain why people with obesity have historically been challenged to achieve weight loss through diet and exercise alone.
- Medication can complement lifestyle modifications (e.g., healthy diet and exercise). However, there are few pharmacological options available for the treatment of obesity and their use has been limited.
- There is a growing understanding of how the CNS regulates appetite and metabolism as well as the mechanisms that limit weight loss over time. This understanding is the basis of new drug development strategies that may change how obesity is treated. Contrave® and Empatic™ reflect two different approaches to obesity treatment that leverage this understanding.

For additional information, visit www.orexigen.com

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