

Medical sciences

UDC 616-056.257

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MAINTAINING LOST WEIGHT AND LONG-TERM OBESITY MANAGEMENT: AN OVERVIEW OF THE MECHANISMS OF BREAKDOWN

Summary. *Obesity is now recognized as a chronic and recurrent disease, and maintaining a reduced body weight for a long period remains one of the major challenges in modern medicine. Many patients who have successfully lost weight experience weight regain within the first few years. This article aims to systematize current scientific knowledge about the biological, psychological, and environmental factors that contribute to weight loss and regain. The text examines in detail the concept of metabolic adaptation and neuroendocrine changes, such as decreased levels of leptin and GLP-1, and increased levels of ghrelin, which can lead to a biological predisposition towards weight regain. Additionally, it discusses the impact of chronic stress, cognitive-behavioral factors, and a "depleted" environment on weight management. It has been concluded that the lack of weight loss is not due to lack of motivation, but rather a natural response of the body's homeostatic systems. This emphasizes the need for a shift in treatment approaches, from short-term diet plans to long-term obesity management strategies. The review discusses the potential of comprehensive approaches, including cognitive behavioral therapy, modern pharmaceutical drugs, and bariatric surgery. These strategies are aimed at addressing metabolic issues and promoting sustainable weight loss. This review*

is intended for endocrinologists, nutritionists, bariatric surgeons, psychotherapists, and researchers working in the field of metabolic disorders.

Key words: *obesity, weight maintenance, weight loss, metabolic adaptation, hormonal regulation of appetite, relapse, reward system, behavioral factors, chronic disease, weight management.*

Relevance of the study. The relevance of this study stems from a fundamental shift in the way obesity is understood in the modern medical community. It is now recognized as a chronic, recurrent disease that requires lifelong management. While there are many strategies for weight loss, maintaining the results achieved remains a critical challenge in clinical practice.

According to statistics, the vast majority of patients who successfully lose weight through dietary changes or lifestyle modifications regain the weight within three to five years. The traditional approach, which attributed relapse solely to the patient's lack of motivation or willpower, has been shown to be ineffective.

Modern scientific research convincingly demonstrates that weight fluctuations are the result of a complex interaction of many factors: biological, neuroendocrine, psychological and external. One of the key factors is the phenomenon of metabolic adaptation, which is characterized by a decrease in energy consumption at rest. This process is accompanied by compensatory hormonal changes, such as a drop in the level of leptin and peptide YY against the background of an increase in ghrelin concentration. As a result, a persistent biological mechanism is formed that causes hunger [2].

In addition, changes in the mesolimbic reward system associated with neuroplasticity may increase cravings for high-calorie foods. And the constant exposure to a "desogenic" environment creates additional obstacles to weight maintenance. Understanding these multilevel disruption mechanisms is necessary to create effective and evidence-based strategies for long-term obesity

management. This will help to introduce modern pharmacological drugs and prevent serious metabolic complications.

The purpose of the study. The aim of this study is to carry out a comprehensive and systematic analysis of modern scientific knowledge about the biological, neuroendocrine, behavioral, and environmental factors that contribute to the long-term weight regain after successful weight loss.

To achieve this goal, we propose to examine the pathophysiology of metabolic adaptation and hormonal changes in the body during the post-weight loss period, assess the influence of chronic stress and cognitive-behavioral factors on relapse, and investigate the role of neurobiological alterations in the brain's reward system.

An additional aspect of the goal is to critically evaluate existing approaches to the long-term management of obese patients. This includes cognitive behavioral therapy, bariatric surgery, and new classes of pharmacotherapeutic agents. The aim is to identify their effectiveness in overcoming biological barriers to weight maintenance, and to form evidence-based recommendations for optimizing clinical practice.

Materials and research methods. The research materials and methods were based on the principles of evidence-based medicine and involved an in-depth narrative review with elements of scientific literature systematization. Information was searched in leading international and national databases, including PubMed, Scopus, Web of Science, Cochrane Library, and eLibrary. A combination of keywords and medical subject headings, such as "obesity", "weight maintenance", "weight loss", "relapse", "metabolic adaptation", and "neuroendocrine regulation of appetite", and their English-language equivalents, were used.

Criteria for inclusion were full-text, peer-reviewed, original studies, systematic reviews, meta-analyses, and current clinical guidelines published over

the past 15 years. These criteria reflected the most up-to-date data, including those related to the use of GLP-1 receptor agonists.

The results of the study. The modern understanding of the causes of weight loss and return is based on the concept of obesity as a chronic disease in which the body perceives weight loss as a threat to life. In response, powerful compensation mechanisms are activated both at the physiological and behavioral levels. The key biological process that leads to relapse is metabolic adaptation, or adaptive thermogenesis. When weight decreases, the body tends to restore energy balance. To do this, it significantly reduces resting energy consumption (RMR), which exceeds the expected result from the loss of fat and fat-free mass.

Simultaneously with the adaptation to changes in metabolism, there is a serious restructuring in the work of the neuroendocrine system. As the amount of adipose tissue decreases, the level of leptin, the key hormone of satiety, drops rapidly. In the study "The Biggest Loser" it was found that in the active phase of weight loss, the level of leptin decreases by more than 90% and even years later remains significantly lower than the initial level. At the same time, the concentration of ghrelin, the hunger hormone, increases, and the level of anorexigenic peptides such as peptide YY (PYY) and glucagon-like peptide-1 (GLP-1) decreases. This leads to a constant feeling of physiologically justified hunger [4].

The neurobiological mechanisms of breakdown are closely related to changes in the mesolimbic dopaminergic reward system of the brain. Prolonged calorie restriction and subsequent energy deficiency lead to a decrease in the density of dopamine D2 receptors in the striatum. This, in turn, reduces a person's sensitivity to natural rewards and at the same time enhances the attractiveness of high-calorie and ultra-processed foods (Table 1).

Table 1

Negative aspects of prolonged calorie restriction [5; 7]

No.	The negative aspect	How does this manifest itself and why does it occur
1	Adaptive thermogenesis (slowing of metabolism)	The body perceives deficiency as hunger and reduces the basic energy consumption. Shivering and drowsiness appear, and when returning to a normal diet, weight gains instantly (the "yo-yo" effect).
2	Loss of muscle mass (catabolism)	Without enough energy, the body begins to break down muscle tissue to produce amino acids and glucose. The body loses its tone and becomes flabby (the "skinny fat" effect).
3	Hormonal failures	The levels of leptin, testosterone, estrogen, and thyroid hormones (T3) are falling. In women, this leads to amenorrhea (the disappearance of menstruation), in men – to a decrease in libido and problems with potency.
4	Micronutrient deficiency	A small amount of food = a critical lack of vitamins and minerals. Anemia develops (iron deficiency), the immune system deteriorates, hair falls out and nails peel off.
5	Decreased bone density	Due to a lack of calcium, vitamin D, and sex hormones, bone tissue loses minerals. The risk of osteopenia, osteoporosis, and stress fractures increases dramatically.
6	Psychological disorders	The constant stress of hunger causes irritability, anxiety, and depression. A "dietary mindset" is formed, obsessive thoughts about food and a high risk of developing RPP (anorexia, bulimia, compulsive overeating).
7	Cognitive impairment	The brain consumes up to 20% of the body's total energy. With severe deficits, memory deteriorates; concentration decreases, "brain fog" and apathy appear.
8	Gastrointestinal problems	Intestinal motility slows down due to a small amount of food and a lack of fiber or healthy fats. There are chronic constipation, bloating and microflora disorders.
9	Deterioration of skin quality	The skin loses its turgor, becomes dry and dull. Due to the lack of proteins (collagen) and healthy fats, wrinkles appear early, peeling and acne are possible.
10	Drop in physical performance	Glycogen stores in muscles and liver are depleted. Training is difficult, endurance decreases, and recovery from stress takes many times longer.

In modern research using functional magnetic resonance imaging (fMRI), it has been found that people who have successfully lost weight have significantly more activity in the nucleus accumbens and orbitofrontal cortex when they see images of high-calorie foods than people who have never suffered from overweight. This may explain why in a "desogenic" environment, where ultra-processed foods rich in sugar and saturated fats are available everywhere, cognitive control over eating behavior can quickly weaken [1].

Statistics confirm that the environment plays a key role in weight maintenance: according to systematic reviews, about 80% of patients who achieved weight loss solely through lifestyle changes (diet and physical activity) face a complete return of the lost kilograms within the first three to five years (Fig. 1).



Fig. 1. The influence of environmental factors on weight loss [3]

Constant stress, which is characteristic of modern life, exacerbates this process by activating the hypothalamus-pituitary-adrenal system. Chronically elevated cortisol levels not only contribute to the accumulation of visceral fat, but are also directly linked to episodes of emotional overeating. Research in the field

of behavioral psychology shows that up to 40-50% of cases of diet breakdown occur not because of physiological hunger, but in response to negative emotional triggers or due to cognitive fatigue from constant self-control, known as "dietary exhaustion" [8].

Despite the generally disappointing data, the study of successful weight maintenance examples opens the door to valuable knowledge about factors that can overcome the biological resistance of the body. The largest source of such information is the US National Weight Control Registry (NWCR). Since 1994, he has been collecting data on more than 10,000 adults who have successfully lost at least 13.6 kg (30 lb) and have been able to maintain this result for more than one year. According to NWCR statistics, the average weight maintenance among this group is about 30 kg for more than five years [6].

An analysis of their behavior revealed several common patterns. 78% of the participants have breakfast every day. 75% are weighed at least once a week. 62% consume less than 24% of their calories from fat. Most importantly, 90% of people maintain weight by exercising for about 60 minutes a day, usually in the form of brisk walking. However, even among this highly motivated group, there is a gradual increase in weight by one to two kilograms per year, which indicates an ongoing struggle with biological factors.

The era of modern pharmacological drugs, particularly GLP-1 and GIP receptor agonists, has revolutionized our understanding of the role of biological mechanisms in disruption. Data from clinical trials, such as the STEP program for semaglutide, show that these drugs can compensate for hormonal deficiencies, leading to a 15-20% reduction in body weight.

However, the most significant study in terms of understanding the mechanisms of weight regain was the STEP 4 trial, in which patients who had achieved success with treatment were switched from the drug to a placebo. The statistics showed that within one year after the drug was stopped, patients regained approximately two-thirds (67%) of the weight they had lost, and their

cardiovascular and metabolic parameters returned to their baseline levels. This clearly demonstrates that without continuous pharmacological, surgical, or behavioral support, long-term weight loss maintenance in most obese patients is unlikely. This confirms the status of obesity as a chronic condition that requires lifelong treatment [10].

It is important to note that the main problem in weight maintenance and long-term management of obesity is a serious gap between the evolutionarily formed biological mechanisms that help us survive and the conditions of modern life. This gap is exacerbated by outdated approaches in medicine and society.

One of the main physiological problems is the phenomenon of a "set point" of weight and pronounced metabolic adaptation. The body perceives weight loss not as an improvement in health, but as a threat of starvation. In response, powerful compensatory mechanisms are activated, which include a decrease in basic energy expenditure and hormonal changes such as a drop in leptin levels and an increase in ghrelin concentrations. These processes lead to a constant, intractable feeling of hunger [9]. Such biological protection makes long-term weight maintenance without constant external intervention a physiologically complex and unstable process. Most patients are doomed to an inevitable relapse.

Equally, acute problems arise in the psychological and behavioral aspects of weight loss. Patients who achieve weight loss often face the phenomena of "dietary fatigue" and cognitive exhaustion. The need for lifelong nutritional control requires enormous willpower resources.

The constant restriction and suppression of natural food desires lead to chronic stress. This often triggers episodes of emotional overeating and disruption, through the mechanism of the "abstinence-violation effect". An accidental mistake is perceived as a total collapse, leading to a return to old, destructive habits. In addition, the lack of stable self-regulatory skills persists. Many patients focus only on short-term weight loss goals, ignoring the need for a deeper transformation of eating habits and attitudes towards their bodies.

The most significant obstacle to long-term success is the pervasive dominance of the "unhealthy" environment. Modern humans find themselves in a world of aggressive marketing, 24/7 availability, and low-cost ultra-processed foods, which are specifically designed with ideal ratios of sugar, fat, and salt to hyperstimulate the reward centers in our brains.

It is almost impossible to resist factors such as increased hunger after losing weight without special cognitive strategies. This is especially difficult for people with low socio-economic status who live in "food deserts" and do not have access to high-quality products or safe spaces for physical activity.

In addition, there are serious problems in the healthcare system. Obesity is often perceived as an acute condition or the result of an unhealthy lifestyle, rather than as a chronic recurrent disease. Because of this, there are no well-defined protocols for long-term follow-up and support of patients after the active phase of weight loss. Doctors often limit themselves to general recommendations on nutrition and physical activity, without offering specific strategies to prevent relapses.

The situation is aggravated by stigmatization and discrimination based on weight, including by medical professionals. People often accuse the patient of being "weak-willed" without considering the pathophysiological nature of the disease. This may cause the patient to feel guilty and unwilling to seek help. In addition, the high cost and limited availability of effective long-term treatment methods, such as modern GLP-1 receptor agonists or bariatric surgery, remains a serious problem. There is also a lack of psychotherapeutic support that could help most patients overcome the biological mechanisms of breakdown and maintain the achieved result throughout their lives.

Conclusions. To summarize, maintaining weight loss and managing obesity long-term is one of the most challenging tasks in modern medicine. It requires a fundamental revision of clinical approaches. The review of the mechanisms behind weight gain convincingly shows that relapse is not the result

of behavioral issues or lack of willpower, but rather a natural and predictable consequence of powerful biological, neuroendocrine, and environmental factors that have evolved to preserve the body's energy reserves.

Metabolic adaptation, compensatory hormonal changes, and neuroplastic alterations in the reward system create a stable physiological resistance to weight loss, firmly establishing obesity as a chronic, recurrent disease. This means that the focus of medical care needs to shift from short-term dietary interventions solely aimed at achieving specific weight goals, to a lifelong patient management approach that optimizes metabolic health continuously.

Successful long-term management of obesity requires a shift away from stigmatization and an introduction of comprehensive, personalized strategies. These strategies should integrate lifestyle modifications, cognitive behavioral therapy, and, if necessary, long-term pharmacotherapy using modern medications or bariatric surgery to address biological barriers.

Recognition of the pathophysiological nature of relapses and overcoming weight discrimination are crucial steps. Transitioning to continuous medical support protocols can help minimize the risks associated with weight loss and ensure sustainable improvement in quality of life for patients.

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