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# OBESITY AND REPRODUCTIVE FUNCTION OF WOMEN OF FERTILE AGE

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✓ ***Resume***

***The article considers the impact of obesity on fertility, since metabolic disorders lead to the emergence of various forms of menstrual function disorders both from the moment of menarche formation and in active reproductive age (irregular cycles, infertility, hypomenstrual syndrome, amenorrhea). The data on this issue are quite contradictory, however, the undeniable impact on the state of the reproductive system is caused by the pathology of the hypothalamic-pituitary system that occurs in any form of obesity and leads to ovarian insufficiency.***

***Keywords: obesity, reproductive function, infertility.***

# ОЖИРЕНИЕ И РЕПРОДУКТИВНАЯ ФУНКЦИЯ ЖЕНЩИН ФЕРТИЛЬНОГО ВОЗРАСТА

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✓ ***Резюме***

***В статье рассмотрена влияниеожирениена фертильность, поскольку нарушение обменных процессов приводит к возникновению различных форм нарушений менструальной функции как с момента становления менархе, так и в активном репродуктивном возрасте (нерегулярные циклы, бесплодие, гипоменструальный синдром, аменорея). Данные, касающиеся этого вопроса, достаточно разноречивы, тем не менее бесспорное воздействие на состояние репродуктивной системы оказывает возникающая при любой форме ожирения и приводящая к овариальной недостаточности патология гипоталамо-гипофизарной системы.***

***Ключевые слова:ожирение, репродуктивнаяфункция, бесплодие.***

# РЕПРОДУКТИВ ЁШДАГИ АЁЛЛАР РЕПРОДУКТИВ ФУНКЦИЯСИ ВА СЕМИЗЛИК

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✓ ***Резюме***

***Мақолада семизликнинг фертилликга таъсири ўрганилган, чунки метаболик касалликларменархе шаклланишидан бошлаб вафаол репродуктив ёшдаги (тартибсизликлар, бепуштлик, гипоменструел синдром, аменорея) ҳайз функцияси бузилишининг турли шаклларининг пайдо бўлишига олиб келади. Ушбу муаммобўйича бир-бирига зид маълумотлар кўп, аммо семизликнинг ҳар қандай шаклида юзагакеладиган репродуктив тизимнинг ҳолатига таъсир ва тухумдон етишмовчилигига олиб келадиган гипоталамик-гипофиз тизимининг патологиясидан келиб чиқади.***

***Калит сўзлар: семизлик, репродуктив функция, бепуштлик.***

## Relevance

Obesity is one of the most common diseases in economically developed countries, where a quarter of the population has a body mass more than 15% higher than normal. According to the forecasts of who experts, if the current growth rate of the disease rate is maintained, by 2025, there will be more than 300 million people diagnosed with obesity in the world [1, 6.5].

Although obesity is defined simply as excess body fat, it is a complex condition that clinicians currently regard as a chronic disease associated with cardiovascular and a range of other pathological conditions. Factors for the development of obesity have a wide range and can act both jointly and separately. The most common of them are genetic predisposition, behavioral features (overeating, inactivity), endocrine disorders, and the environment. Like all normal diseases, obesity contributes to the development of other diseases, which essentially makes it impossible to distinguish the pathogenesis of a number of diseases from each other. The risk of developing obesity-related diseases is largely determined by the characteristics of adipose tissue deposition in the body. The most unfavorable is the abdominal type of obesity, which is usually combined with a complex of hormonal and metabolic risk factors. It is believed that the abdominal type of obesity is more often accompanied by insulin resistance and hyperinsulinemia, dyslipidemiaand arterial hypertension, hyperandrogenism and hirsutism, forming the basis of the metabolic syndrome.

The pathogenesis of obesity is not completely clear, which makes it difficult to develop optimal methods of treatment and prevention. It is believed that the basis of obesity is an energy imbalance, which consists in a mismatch between the number of calories coming from food and the energy expenditure of the body. In turn, the imbalance is the result of an inadequate interaction of genetic (found genes responsible for the accumulation and distribution of fat in the body) and external environmental (social, food, psychological, physical activity) factors.

In the United States, 33% of people are overweight, especially women-34%, among African Americans, obese and overweight - 49%, among latinomericans-47%. In

Australia, 37% of the population is either overweight or directly obese (Anon, 1994), with more of them the older they get, 34% of astral women have a body mass index (BMI - body weight in kg divided by height squared) greater than 25 kg/m$^2$. Of these, 12% have a BMI>30 kg / m$^2$ [3-5]. Among more than 5,000 female patients at the University of Adelaide's reproductive health Clinic surveyed between 1991 and 2007, 39.8% had a BMI>25 kg / m$^2$ and 17.4% had a BMI > 30 kg / m$^2$.

The impact of obesity on fertility is widely discussed in the scientific literature, since the violation of metabolic processes leads to the emergence of various forms of menstrual function disorders both from the moment of the formation of menarche, and in active reproductive age (irregular cycles, hypomenstrual syndrome, amenorrhea). The data on this issue are quite contradictory, however, the undeniable impact on the state of the reproductive system is caused by the pathology of the hypothalamic-pituitary system that occurs in any form of obesity and leads to ovarian insufficiency.

In order for a woman to have a normal menstrual cycle, and therefore the ability to procreate, a threshold, minimum amount of fat must accumulate in her body, since adipose tissue is involved in the regulation of reproductive function. When analyzing a woman's reproductive function, the premorbid background is judged by the age of the menarche. In recent years, menarche occurs at an earlier age, with an average age of 12.6 years. According to various authors, the timely onset of menarche in women with various forms of obesity and reproductive disorders is observed only in 31% of cases. Consequently, the reproductive system in childhood and youth in the process of functional differentiation is highly sensitive to the influence of damaging external and internal influences. It becomes the most vulnerable in comparison with other functional systems of the body. As a result, by the onset of the period of reproductive maturity, it is damaged in a significant number of young women [6-8].

In obese adolescents, either late or early menarche is formed. Earlier menarche is due to acceleration, since there is a certain relationship between the average body weight at the time of menarche and average age. The average ratio of fat-free body weight to fat for the population as a whole may allow us to predict a "critical" value for the onset of menarche [2, 6, 7].

As a rule, obesity in women increases the risk of diseases such as diabetes, cardiovascular diseases, cancer and infertility. Women have more significant fat reserves than men, but the type of distribution of adipose tissue is peripheral ("pear"), rather than abdominal ("Apple"). Overweight and obese women are the most frequent patients in gynaecological and reproductive clinics.

Obesity and infertility associated with polycystic ovary syndrome (PCOS) are described in detail in the basic research of Mitchell and Rogers (1953) and Haitz et al. (1979). According to the authors, obesity is 4 times more likely to accompany menstrual disorders: 45% of women with amenorrhea are obese, and only 9-13% of overweight women did not have menstrual disorders. Among 26,638 women, a survey was conducted (Hartz et al., 1979), which showed that anovulation was associated with obesity, while obese women experienced 3.1 times more anxiety about menstruation than those whose body weight was within the normative values. Adolescent obesity have shown a connection with violations of the duration of the menstrual cycles and hirsutism. About 5,800 women born in 1958 and examined at the age of 7, 11, 16, 23, 33, 43 years (Lake et al., 1997), and who were obese, complained of serious problems of reproductive function. At the same time, 23-year-old women with overweight (BMI 23.9-28.6 kg/m$^2$) 1.32 times, and obese (BMI≥29.9 kg/m$^2$) 1.75 times more likely to have problems with menstrual disorders. At the same time, if overweight or obesity were present during menarche (9, 10 and 11 years), then menstrual function disorders were more pronounced. Research on the health status of nurses in 1994 showed that in 2527 married infertile nurses, the risk of ovulation disappearing increased depending on the level of BMI. If the BMI was below 24 kg / m$^2$ or above 32 kg / m$^2$ (Rich-Edwaids et al., 1994; Grodstem et al., 1994), the frequency of anovulatory infertility increased in 1880 and 4023 patients, respectively [2-7]).

Interesting research data from Lake et al. (2007), who found an interesting relationship: body weight in childhood does not affect upcoming physical maturity and reproductive function, but an increase in BMI at age 23 increases the percentage of anovulatory disorders. In 23-year-old overweight and obese women, the possibility of getting pregnant was reduced, and infertility was detected in 33.6% of cases, compared to women with normal body weight (18.6%). Zaadstia et al. (1993) found that women with the first stage of obesity (33.1 kg/m$^2$) have a significantly reduced chance of conceiving a child during in vitro fertilization. In 204 women from North America, studied by Gicen et al. (1988), when the actual body weight exceeded the ideal by only 20%, fertility rates decreased by 35%. However, this pattern was not observed in women who had previous pregnancies and childbirth [8].

According to most researchers, menstrual disorders are secondary and are a consequence of obesity. The formation of menstrual function has a significant impact on the reproductive system, although data on the features of reproductive function in obesity are quite contradictory. Thus, in obesity, longer reproductive life is associated with earlier menarche and pleiotropic effects of beta-3-AR gene mutation on a number of physiological systems, including body mass index, reproductive status, which may be an evolutionary reason for support in the population. Others consider the early age of menarche not only a reproductive factor, but also an independent predictor of the increase in body mass index and other complications of obesity. The most unfavorable for the subsequent violation of reproductive function is later menarche, postponing cycles and a long period of formation of the menstrual rhythm. During the implementation of reproductive function, the prognosis for spontaneous termination of pregnancy in postpartum obesity is unfavorable. With alimentary obesity, menstrual disorders are 6.1 times more common and primary infertility is almost 2 times more common.There is adirect relationship between the increase in body weight and the severity of ovarian disorders accompanied by anovulation, the inferiority of the luteal phase and the decreasing frequency of pregnancies in alimentary obesity [2, 6, 7, 9].

A necessary method of treatment for obese women is to reduce body weight, while changing the hormonal profile of obese women, increasing the frequency of pregnancies by an average of 29%, restoring menstrual function in 80%.

Based on the accumulated experience, scientists are developing programs for the treatment of obesity with

the inclusion of diets, physical activity, medication for obesity and correction of menstrual disorders. The first stage of treatment is a reduction diet aimed at reducing body weight. The caloric content of the daily diet is calculated according to certain schemes. But in the treatment of obesity of various origins only with the help of a diet the desired result is rarely achieved.

Until now, drug - based treatments for obesity are limited. Behavioral therapy, which consists mainly in motivating the patient to reduce caloric intake and increase physical activity, is often accompanied by poor compliance with medical recommendations. In most cases, after weight loss, it increases again. The use of medication facilitates compliance with dietary recommendations and contributes to faster and more intensive weight loss, as well as helps to maintain the results achieved and prevent the development of relapse.

According to the mechanism of action, drugs for the treatment of obesity can be divided into three groups: reducing food consumption (anorexics): teronak, minifig, meridia, prozac, Solian, trimeks; increasing energy consumption (thermogenic sympathomimetics): ephedrine, caffeine, sibutramine; reducing the absorption of nutrients: xenical.

To date, in our country for the first time registered and recommended for use of a drug of domestic production - reducsin. Reducsin is a sibutramine, the main clinical effects of which are the result of activation of serotonin and adrenergic pathways at the level of the Central nervous system. As a result of this double action Reduxine has an impact on both sides of energy balance - intake and energy expenditure.

## Conclusions

First of all, reducsin allows you to feel satiated faster, which leads to a decrease in the amount of food, on average by 20%, and also prolongs the feeling of satiety, as a result, you do not want to eat for longer. This is extremely important because the need for food decreases, adaptation to a healthy diet is facilitated without compromising the quality of life, and adherence to treatment is achieved. On the other hand, Reduxine increases the energy expenditure for thermogenesis - in other words, people spend more energy on warming that is also of great importance. When you reduce the amount of food you eat, the body also reduces "expenses", which can reduce the rate of weight loss. Additional energy expenditure supports the speed of the main exchange (the key item of energy consumption), intensifying the process of weight loss. As a result, patients receiving Reduxine, it is easier and faster to lose those extra pounds [1].

Studies have shown a dose-dependent effect of the drug on body weight. Thus, reducsin is available in the form of tablets in a dosage of 10 and 15 mg, which are recommended to take once, in the morning, regardless of food intake. As a rule, treatment should begin with a minimum dose of 10 mg / day, under the control of blood PRESSURE and heart rate. Only after 1 month, the dose of the drug can be increased depending on the dynamics of body weight. It is particularly important that marked reduction of body mass on the background of Reduxine is mainly due to the adipose tissue, particularly visceral localization. A predictor of the effectiveness of long-term treatment is the loss of body weight more than 2-3 kg for 3 months of treatment. Weight loss on the background of Reduxin may be accompanied by an improvement in the blood lipid spectrum, glycemic indicators, and a decrease in uric acid levels. Large-scale international programs have proven the safety of continuous administration of the drug for 2 years [1].

Treatment of obesity is a difficult task for all categories of patients, but there are some patients who are particularly difficult to reduce body weight due to additional concomitant diseases, in particular type 2 diabetes mellitus (DM). It is especially important for these patients to normalize their body weight, since this makes it easier to manage type 2 diabetes, slows down its progression, and prevents the development of serious vascular complications. Thus, there is every reason to say that the first Russian drug for the treatment of obesity - reducsin can effectively help in correcting the body weight of women of reproductive age with obesity, including the most resistant to treatment.

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