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Introductory Chapter: Regulation of Ovarian-Menstrual Cycle as a Systemic Problem of Physiology of Humans

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Additional information is available at the end of the chapter

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1. Introduction

One of the main manifestations of the vital activity of the female body is the menstrual cycle, which begins during puberty and has a rhythmic (monthly) character.

Endocrine relationships in the hypothalamic-pituitary-ovarian system are formed throughout the period of puberty. This process is regulated by certain neuroendocrine processes, which have different activities depending on age. The determinants of this regulation are the hypothalamus, pituitary gland, gonads, thyroid gland, and adrenal cortex; therefore, a certain interest is the study of the peculiarities of the formation of the hypothalamic-pituitary-ovarian hormonal system.

Back in the late nineteenth century, leading scholars D. O. Ott, S. S. Zikharev, and A. V. Reperov found that menstrual cycle is not a local process, but a wavelike reaction of the organism associated with changes in the system of the hypothalamus-pituitary-ovaries-uterus, which appears from the outside of uterine bleeding. These changes in vital processes in the body of women were called “menstrual wave” [1, 2].

So, the normal menstrual cycle is a finely coordinated cyclic process of stimulating and inhibiting effects that lead to the release of one mature egg. Various factors involved in the regulation of this process, including hormones, paracrine, and autocrine factors, are identified so far [3].

The regulation of the menstrual function passes through a complex neurohumoral path [4–6]. According to modern concepts [7–9], cyclic changes in the body of a woman are related to the implementation menstrual function and occur with the obligatory participation of five levels (or levels) of regulation. Each of them is regulated by the structures located above according to the mechanism of feedback.

The levels (links) of regulating the menstrual (reproductive) function:

1. the cerebral cortex is a cerebral structure;
2. hypothalamus-subcortical centers;
3. pituitary gland-brain application;
4. ovaries-gonads; and
5. uterus-organ-target.

Nowadays, leading scientists insist that the multilateral morphological features are closely related to the functional manifestations of sexual dimorphism [10, 11], which, in its turn, causes the sexual specificity of the processes of adaptation of the organism to external influences and, in particular, to physical activity. For women, the role of estrogen and progestogens is predominant, and for men, androgens. The degree of saturation of the body by sex hormones determines their biological effect [12–16].

Estrogens are an important link in the chain of adaptive-trophic reactions in the body [17, 18]; they have an anabolic effect but are slightly weaker than androgens, determine the degree and nature of the distribution of fatty tissue by female type, increase the growth of pelvic bones, create a female type of body proportions [19, 20], contribute to the closure of epiphyseal bone growth zones, and hinder the development of osteoporosis (resorption of bone tissue). Estrogens suppress erythropoiesis (red blood cells), reduce thrombocytopenia, promote growth of shock and minute volume of the heart, increase cardiac output, increase the volume of circulating blood, and have a positive effect on myocardial tropism and vascular tone [21, 22].

Progesterone, like estrogens, increases systolic and temporal volumes of blood and the frequency of heart contractions. Progesterone has a sodium diuretic effect and reduces the peripheral resistance of the blood vessels, which contributes to lowering blood pressure [23, 24].

Estrogens cause narrowing of the lumen of bronchioles by increasing the release of histamine and serotonin, increasing pulmonary resistance. Its direct effect increases the excitability of the respiratory center; improves the patency of bronchioles by increasing their lumen; decreases the overall pulmonary resistance; as a consequence, increases alveolar ventilation; and decreases the tone of the respiratory muscles [18, 25].

The change in the balance of steroid hormones, in particular the deficiency of progesterone and the excess of estrogens involved in the regulation of water-salt metabolism, increases reabsorption (reabsorption) of sodium in the kidneys while increasing osmotic pressure. As a result, in order to maintain homeostasis, the water is delayed in the body to compensate for the homeostasis, and, as a consequence, the body weight increases in the premenstrual and menstrual phases of the cycle. Scientists have established the influence of sex hormones on the emotional state of women [22, 26]. All of the above suggests that reproductive and exogenital functional systems are closely interrelated, and the reproductive system, in turn, has a different effect on the organs and tissues of other functional systems, which correlates the adaptation, resistance, and reactivity of the female body. In recent years, the distribution

and extension theory has intensified, according to which the influence of sex steroids to one degree or another extends to the functional state of all organs and systems [10, 27, 28].

The functional state of the cardiovascular system in women has a number of features due to hormonal changes that accompany the menstrual cycle [29]. In recent years, the study of the role of estrogens and progestogens in the regulation of the function of the cardiovascular system [30].

The increased resistance of women in comparison with men to cardiovascular diseases is associated with the dynamics of cardiodynamics parameters in stressed women [23], which is determined by the sexual characteristics of the nervous and humoral regulation of the cardiovascular system. During stress, more catecholamines are released in the female body [31, 32], and their influence on the heart rhythm becomes more pronounced, but pressor responses are less prolonged than in men, which suggests that the control of the sympathetic adrenal system is more effective in the female body [33]. The factors limiting its activity include the presence of estrogens, which enhance the tone of the parasympathetic nervous system and reduce sympathetic effects on the cardiovascular system. The influence of estrogens on the vegetative level of regulation, along with their peripheral effects on the heart and blood vessels, is the basis of cardioprotective properties of estrogens. Information on the influence of androgens on the cardiovascular system and the mechanisms of its regulation are few and contradictory. Testosterone contributes to the development of hypertension and has an atherogenic effect [34]. At the same time, testosterone improves coronary blood flow in coronary arteries [35] and positively affects the mechanical function of the heart by activating the expression of heavy α chains of myosin [36]. Sexual features in cardiovascular stress reactivity are largely due to differences in the autonomic regulation of the cardiovascular system in the female and male body. Investigation of the mechanisms that determine the differences in the activity of the autonomic nervous system departments convinces in the need to study the role of sex hormones. The scarcity and contradictory nature of research data on the role of autonomic regulation of the cardiovascular system in the female and male organisms, as well as the influence of sex hormones on the autonomic balance, justify the carrying out of complex studies of the revealed phenomenon [37, 38].

Significant are the effective attempts to decipher the mechanism of the influence of sex hormones on the central nervous system that are highlighted in the works of well-known scientists [33]. The beginning of puberty is marked by a significant increase in the threshold of the sexual centers of the central nervous system (gonadostat) to steroids in the feedback system, which was first noticed by Hohlweg and Dohin (1932) and then Donovan and van der Werff Ten Bosch (1965) [38]. Further animal studies and human observation fully confirmed this assumption. The enhancement of the inhibitory effect of sex steroids on the hypothalamus has been linked with a change in the puberty of the spectrum of sex hormones—the shift in the ratio of estrogen to testosterone in favor of the latter, which is allegedly less effective in suppressing the production of gonadotropins. However, this is unlikely.

The scientific assumptions about the importance of changing the metabolism of testosterone and other androgens during puberty have been supported. So, in an experiment in many species of animals, it was discovered and demonstrated that the metabolic activity of the liver and kidneys, aimed at inactivating androgens, increases with age. Small amounts of

sex hormones produced by gonads of immature animals give a more pronounced inhibitory effect due to the fact that in adult animals the inactivation of hormones is more pronounced [38]. However, this hypothesis was subjected to devastating criticism, as the androgenic effect on other target organs during puberty does not decrease but increases.

An important role in the onset of puberty may be played by not only inhibiting but also stimulating effects of sex hormones, in particular estrogens. We have convincing evidence of the leading role of estrogens in the formation of systems of the hypothalamic neurons responsible for regulating the gonadotropic function of the pituitary gland. This process begins during the period of sexual differentiation of the hypothalamus, but its final stage falls on the puberty period. It has been experimentally shown that the administration of small doses of sex hormones can cause premature puberty. Although the role of estrogens is particularly significant in the formation of pubertal in girls, however, in boys, estrogens are also an effective stimulator for secretion of gonadotropin and gonadotropins, since central nervous structures do not lose their ability to respond to the stimulating effect of estrogens during sexual differentiation [33].

During the menstrual cycle, there are significant changes in the hypothalamic-pituitary system and in the body as a whole. Cyclical changes in the structures of the hypothalamus and in the anterior lobe of the pituitary gland regulate all processes that ensure the reproductive function of the woman.

Fluctuations in mental processes and functional state during the menstrual cycle have been proven by many researchers, and the association of these oscillations with the nature of secretion of sex hormones is evident. These changes were detected in the attitude of emotional and motivational behavior [39], the electrical activity of the cerebral cortex [23, 40], the autonomic tone [41], the activity of the cerebral hemispheres [42], and the physical and mental performance [80].

However, the clear dependence of the change in the psycho-functional state, depending on the phases of the menstrual cycle, cannot be identified, and the results of the research are mainly controversial (especially concerning the premenstrual and menstrual phases). Thus, the follicular phase is considered by most researchers as a period of high mental and physical working capacity. As for the phase of ovulation, as a period of poor performance, researchers have quite controversial thoughts. At the same time, some scholars tend to believe that the menstrual cycle does not affect the psycho-functional state of the woman [43], and there are those who record a significant deterioration or improvement [26] of mental and physical performance in the premenstrual and menstrual periods.

Investigating the indicators of the functional state of the soccer players in various phases of the ovarian menstrual cycle, Buzzin VR (2009) [44] concluded that the dependence of the level of physical performance in the first phase of CMC depends mainly on the state of central hemodynamics, in stages II and V (from repolarization of the ventricles), in the IV phase (the state of the atrium), and in the III phase (from the general state of the organism). Body mass swims on the studied indicators of the body of soccer players throughout the entire biological cycle. Given that it is an integral indicator of the general state of the organism, the data obtained can be evidenced by the fact that the pursuit of football contributes to the coherence in the activity of the studied systems of the body of athletes. Perhaps, this is due to

the individual nature of the body's response to the fluctuations of sex hormones during the menstrual cycle, depending on many variables of psychophysiological factors, mediating the influence of hormones on the central nervous system and higher nervous activity.

The factors that may affect the condition of women in the premenstrual phase include age, type of constitution, level of health, and typological peculiarities of higher nervous activity. Confirmation of the influence of the identified factors can be, in particular, significant differences in the level of sex hormones between people with different typological peculiarities: type of constitution [12], functional asymmetry [23], temperament [45], as well as differences between adolescent and adolescent girls [41].

The study of Naumova [71] illustrates the different effects of the phases of the ovarian-menstrual cycle on the psychomotor quality and properties of the nervous system of women. The author measured these indices during the premenstrual phase (1–3 days before menission), the menstrual phase (1–2 days), and the postmenstrual phase (1–2 days) during the 3-month period. The obtained data were compared with each other and with the background (from the beginning of menstruation on the 10th–12th day). The premenstrual phase is characterized by deterioration of psychomotor performance. Compared with the background (the period between menstruations), muscle strength and maximum frequency of movements decreased much more often than they increased. Endurance in relation to static forces varied slightly during this period and in the direction of increase [47, 48].

The menstrual phase is characterized by an increase in the muscle strength of the majority of the girls studied (but only to the background level) and the maximum frequency of movements (excess of the background level), but the endurance is somewhat reduced. At the same time, the second component of endurance attracts attention—maintaining the effort against the background of increasing fatigue [46–49]. The postmenstrual phase was accompanied by a variety of changes in the studied parameters. The maximum frequency of movements increases even more, and muscle strength and endurance are greatly reduced.

In the premenstrual phase, the mobility of the nervous processes has increased. These changes indicate an increase in the emotional and motor reactivity of women in the premenstrual phase, which corresponds to the findings of the researchers in the literature on increasing the irritability of women before menstruation [50, 51]. It is explained by the fact that thyroid gland swelling is observed in the premenstrual phase of CMC and there are symptoms of thyrotoxicosis, that is, increased production of thyroid hormones [52]. In the postmenstrual phase, the return of the neurodynamics to the background level is observed. Excitement increases, and mobility of nervous processes decreases somewhat.

The strength of the nervous system in various phases of the OMC did not undergo significant and logical changes. Consequently, as can be seen from the data presented, in different phases of the CMC, the psychomotor functions change unevenly and differently, so that the deterioration of performance on one indicator may be accompanied by an improvement in the ability to work after another [53–55]. Thus, the indicators of “external” and “internal” balances in certain phases of CMC vary in a different direction [56]. The effect of phases of the CMC on functional parameters, well-being, and mood should be taken into account in studies related to the female contingent [23, 57, 58].

The revealed neurovegetative and endocrine regularities of regulation of the ovarian-menstrual cycle are realized through individual-typological peculiarities of the hormonal status and morphology of the female body.

1.1 Individual features of central hemodynamics and cardiac rhythm variability in women of reproductive age

The variability of the heart rate (HRV) is a fundamental physiological property of the human body and reflects the state of regulating mechanisms, in particular the autonomic tone of the autonomic nervous system; its study contributes to the development of quality diagnosis, prognostication, and prevention of various diseases [43].

In recent years, the number of studies on the variability in the duration of the interval RR [31, 32, 34, 59, 60], blood pressure [60, 61], shock volume of blood [35, 60], respiratory arrhythmia [31, 32, 40], and communication wave changes in various hemodynamic parameters. This is due to the wide introduction of information technologies to medicine and physiology, as well as to the confirmed or highly diagnostic value of parameters of regulatory rhythms of hemodynamics.

On the adaptive-trophic role of the sympathetic department of the VNS, including in the reproduction, one of the first pointed academicians Orbeli [27]. However, until now, the study of the state of the VAS, including heart rate activity, in women during the normal menstrual cycle and in the physiological and complicated pregnancy, remains insufficient. A number of review papers [43, 62] provide data on age and gender changes in some HRV indices. However, they relate mainly to short (2–5 min) records of RR intervals and performed on contingents of persons with different pathologies. At the same time, the characteristics of the wave structure of oscillation of hemodynamic indices in healthy women in different physiological conditions and loads in the ontogenesis process are insufficiently analyzed. Studies by Ketel et al. [12], conducted in randomized tubes for 149 men and 137 middle-aged women, revealed that HRV levels were inversely related to age and heart rate in both sexes. The level of LF in men is significantly higher in women than in women and is negatively related to the level of triglycerides, insulin. The power of the R-R interval for women is higher than that of men.

The widespread introduction of the ECG Holter monitoring method into the clinical practice allowed the evaluation of HRV values in the course of the day and at certain intervals and also used this method for studying the state of autonomic regulation of the cardiac rhythm [64]. Extreme values of total power of the spectrum and power in the range of very low and low frequencies in Holter monitoring of women compared to men were also recorded in Fluckiger et al. [65]. At the same time, the power in the ranges of low and high frequencies was negatively correlated with age. The total power of the spectrum decreased relatively between 20–29 years and 60–69 years by 30%.

The same gender and age characteristics of the wave structure of the cardiac rhythm were also confirmed in measurements of 302 men and 312 women conducted by Bai et al. [36], with 653 persons performed by Aubert et al. [66], and on 276 persons conducted by Barrett et al. [67]. The gender differences of HRV are measured at the sixth decade of a person's life cycle. Changes in the heart rhythm and its spectral components during orthopedic trial at this age did not have sexual differences.

There are significant differences in the reactivity of fluctuations in the duration of the R-R interval and the peripheral pressure of men and women on physical, mental, and cold loads. So in studies OV Peshakova [68] shows that women under these conditions have a greater centralization of mechanisms of regulation of the cardiovascular system, and for men—an increase in the activity of the sympathetic link of the autonomic nervous system.

Many researchers [39, 69] point out that cardiovascular analysis is more appropriate to detect minor fluctuations of the VNS activity during the menstrual cycle than the use of traditional indicators such as heart rate and arterial pressure. However, the results of studies of changes in cardiac rhythm in different phases of the menstrual cycle are still controversial. It should be noted that significant changes in HRF in women of reproductive age, whether alone or in psycho-emotional stresses, may be due to the ovarian cycle [70]. SDNN in young women was highest during the follicular phase of the menstrual cycle [26]. According to Kravchenko and co-authors [71] in women during the luteal phase compared with the follicular showed an increase in the activity of the sympathetic department of the autonomic autonomy of the autonomy according to the HRV indices. However, a group of researchers Grossman et al. [70] insists on the absence of differences in the parameters of the wave structure of blood pressure and heart rate when performing orthopedic and stimulating carotid sinus in women in different phases of the ovarian cycle.

Japanese scientists [39] demonstrate a significant increase in sympathetic and decreased parasympathetic activity in the luteal phase compared to follicular, as evidenced by an increase in LF/HF and LF values, as well as a decrease in HF in the luteal phase. The facts of the increase in the level of LF/HF in the early and middle luteal phase are presented in Hirshoren et al. [72], with the late lutein phase showing a tendency to decrease the level of LF/HF. At the same time, some researchers, Princi et al. [69] and Sato et al. [39], refute this assumption, indicating that there is no significant change. Although some researchers point to an increase in the level of HF in the follicular phase compared with the luteal and menstrual phase, measurements were made only one [15] or twice a week [73] during the cycle. Since hormonal and physiological changes during the menstrual cycle are complex, they cannot be characterized by two measurements, indicating the need for long-term research.

In studies [45], with ten completely healthy women, it was found that spontaneous baroreceptor sensitivity increases during the luteal phase compared to the follicular phase. It was stated that there were certain differences in the logRSA fluctuations during the menstrual cycle, which were related to the average NSC indices.

According to Fleischman [28], there are significant changes in both the wave structure of the cardiac rhythm and its reactivity to the burden on women in the first 20 weeks of pregnancy. So, normally in this period, the power of OT components increases, and often the synchronization of respiratory and baroreflexor waves is observed. In pathological development of pregnancy, there is an inversion of such regulatory relations.

The variability of the cardiac rhythm during the physiological course of pregnancy is reduced, which indicates an increase in the activity of the sympathetic department of the autonomic nervous system [12, 13]. In women with gestosis, HRV is more pronounced. Revealed by scientists the facts of changes in HRV with other hypertensive states in pregnant women, as well as in normal and complicated childbirth, are few and controversial. The emphasis is on the prospect of further study of sympathetic activity in relation to the change in HRV in

pregnant and childbearing women, as well as on the need for widespread introduction of cardiointervalography in obstetrics.

Many scientists [13, 64, 74] note that in the second and third trimesters of pregnancy, the activity of the VNS is higher (by characteristics of the wave structure of the cardiac rhythm) than in nonpregnant women. The analysis of these works shows that the decrease in HRV during pregnancy is manifested in the reduction of the values of the mathematical expectation, the mod, the mean square deviation, the variational magnitude, the variation coefficient, the power of the OT waves, the normalized power of the OT waves, and the pHN50, as well as in the increase of the amplitude of the mod, index voltage, autonomic equilibrium index, LF wavelengths, normalized LF wavelengths, VLF wavelengths, and LF/HF ratios.

At the same time, it should be noted that until now scientists have not agreed on the change in HRV at the beginning of pregnancy. Thus, Vae et al. [36] investigated that in the first trimester the HRV increases and in the second and third trimesters it decreases. According to other scholars [45, 63], HRV progressively decreases, starting with the first trimester. According to Klinkenberg et al. [75], HRV in the first trimester remains unchanged. The question remains as to the nature of the changes in BCR before delivery: according to some data [64], it increases and it contributes to the normal course of labor, and for the other [1, 13]—does not change.

The reasons for increasing the excitability of VNS during pregnancy are still not studied. Some scientists believe that increased activity occurs under the influence of chronic stress, which is considered pregnancy; others regard it as a compensation in response to systemic vasodilatation, which occurs under the influence of NO, whose production will increase significantly in pregnancy. According to Klinkenberg et al. [75], the increase in VNS activity during pregnancy is the result of a true increase in the activity of higher sympathetic centers under the influence of changes in the production of various hormones during pregnancy, as well as the result of an increase in the effectiveness of b-adrenergic effects on the heart (or a decrease in the effectiveness of M-cholinergic effects). The latter is due to an increase in the content of endogenous b-adrenergic agonists (b-AP) and endogenous b-AP sensitizers or endogenous M-cholinoreceptor blockers (M-HRP) in the blood. Previously, it was shown that in pregnancy, indeed, the content in the blood b-AP increases, while the content of M-HRP does not change. Most likely, in general, the increase in sympathetic activity is a manifestation of adaptation to pregnancy and is aimed at the formation of mechanisms that ensure the growth and development of the fetus, including inhibition of contractile activity of the uterus, increased pumping function of the heart, and gas transport function of the blood.

Studying the health of women during menopause is of great interest, both for practitioners and for theoretical scholars. This is a separate branch of health care that is socially important in all countries of the world, because in connection with the prolongation of life expectancy, the number of women over 50 years old has increased threefold [76, 77], and more than one-third of her life, a woman holds in postmenopausal care [78].

To date, some research on HSR has been devoted to the study of this phenomenon in women engaged in physical exercise and sports. Thus, the specific features of the female body and its response to intensive, often extreme, training and competitive loads, characteristic of certain sports, are rather negligible. It is believed that this circumstance does not allow to accurately formulate the extent of the impact of occupations on various sports and the desire for the

highest sports results in the condition of the female body [60, 79]. However, in the HSR studies on women-tongue-men in comparison with the group of men of masters of sports and masters of the international class, it was found that men had more frequencies of HRV, in particular TP, VLF, LF, LF/HF but less HF and HF percentage (%). Thus, we see that the women of single fighters in comparison with men are noticeable strengthening of the sympathetic link of the VNS.

In the study of the variability of the heart rate in the mode of the training day in the gymnasts, it was established that the relationship between the cardiovascular system and the degree of centralization in the management of cardiac rhythm not only is preserved but also varies. At the same time, the dynamics of integral indicators of the functional state of the circulatory system in gymnasiums is rather informative for the assessment of "urgent" training effect [31, 32].

It should be noted that many researchers point out that the athlete's affiliation with a particular sports specialization determines his "vegetative portrait," which is related to the nature of the exercise, which can be offset by gender differences in HRD [78].

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