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Stress-induced disorders of reproductive functions

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The review provides a pathophysiological analysis of what is currently known about the impact of acute and chronic stress on the functional state of the male and female reproductive systems. The relevance of research on the negative effects of stress on the reproductive system has increased significantly in recent years due to the COVID-19 pandemic and even more so after Russia's aggression against Ukraine. Stress disrupts gamete maturation, libido, sexual behavior, mating, fertilization, pregnancy and delivery. In the structure of the etiology of these disorders, psycho-social stress prevails. The characteristics of stress-induced disorders of the reproductive system have features depending on the lifestyle of future parents, as well as on the period of life, starting from the embryonic to the end of the reproductive age. The hypothalamic-pituitary-adrenocortical and hypothalamic-pituitary-gonadal systems, as well as oxidative-nitrosative stress, play a leading role in the pathogenesis of stress-induced disorders of the reproductive system. Modern data on the pathogenesis of stress-induced reproductive disorders should be the basis of preventive and therapeutic strategies.

Key words: stress; reproduction; ovaries; testes; hypothalamus; pituitary gland; adrenal glands.

INTRODUCTION

Although the problem of the influence of stress on the reproductive function of humans and animals has always been the focus of attention of many researchers [1-7], it not only does not lose its relevance, but on the contrary, is gaining momentum, especially in the conditions of numerous social challenges and military conflicts today. Russian aggression against the Ukrainian state has created many stressful situations, first of all, in war zones and occupied territories. Missile, aviation and artillery attacks do not stop. The psycho-emotional and physical load turned out to be too great. The rapid growth of almost all types of pathology in Ukraine is largely due to stressogenic and environmental factors. The latter, such as air, water and soil pollution by combustion products, explosives, lubricants and fuels, heavy metals, etc., are also the cause of the development of stressful conditions. Special attention is paid to post-traumatic stress disorder (PTSD).

Stress is a stereotypical systemic reaction to any agents of the external or internal environment that disrupt homeostasis. If the stressor is too strong and long-lasting, the adaptive nature of stress turns into maladaptation with negative consequences for human health [8]. In the scientific literature, such a state is sometimes called distress.

The etiology of distress is extremely diverse. Mechanical and chemical trauma, burn, electric current, overheating, hypothermia, frostbite, excessive physical exertion, hypoxia, starvation, ultraviolet and ionizing radiation, acceleration, excessive noise, vibration, excessive lighting, poisoning, infection, etc. are considered as stressogenic factors.

One of the consequences of stress is the limitation of the reproductive potential of the organism [9-13], the biological feasibility of

which is obvious. In men and male animals, acute stress causes a decrease in the secretion of gonadotropic hormones and testosterone, and chronic stress causes a decrease in the fertilizing capacity of seminal fluid and quantitative and qualitative changes in spermatozoa, a decrease in libido, and erectile dysfunction. The female body reacts to distress with the disruption of cyclic processes in the hypothalamic-pituitary-ovarian system (HPOS), complete or partial blockage of ovulation, menstrual cycle disorders (for example, the so-called wartime amenorrhea), dyshormonal tumors, and failure to carry a pregnancy to term. The endocrine system of reproduction plays a key role in these changes.

The endocrine system of reproduction is understood as a set of organs and cells that produce hormones and provide all reproductive functions – maturation of gametes, libido, sexual behavior, mating, fertilization, pregnancy and childbirth. Its cores are the HPOS and the hypothalamic-pituitary-testicular system (HPTS) with the general name "hypothalamic-pituitary-gonadal system" (HPGS). In this review, the problem of the effects of stress on the endocrine system of reproduction and associated disorders of the reproductive system and sexual behavior in different age periods is discussed in a pathophysiological aspect.

Neuroendocrine and metabolic mechanisms of stress

The classic concept of stress as a systemic reaction of the body, in which the main role is played by the response of the hypothalamic-pituitary-adrenocortical system (HPAS) to stressful stimuli, should be clearly distinguished from certain types of accompanying changes at the level of organelles (endoplasmic reticular stress, mitochondrial stress), cells (cellular stress) and tissues (tissue stress), biochemical processes (oxidative stress, nitrosative stress, metabolic stress), etc. Such diversity "blurs" the classical concept of stress, the basis of which is the general adaptation syndrome (stress syndrome), however, these options are widely used in scientific literature.

The state of stress is characterized by phasic physiological, neurohormonal and metabolic changes, which are caused by the activation of the sympatho-adrenal system with the subsequent immediate activation of the HPAS [5-7, 14, 15]. In response to a stressor, the reticular formation of the brainstem activates the cortical and subcortical structures of the central nervous system. Catecholamines of the hypothalamus (primarily, noradrenergic terminals of the tuber cinereum) cause the excitation of neurosecretory parvocellular neurons of the paraventricular nuclei of the hypothalamus, from where deposited corticotropin-releasing hormone (CRH) and arginine-vasopressin are released into the blood vessels of the pituitary portal system. Under their stimulating influence, the secretion of a number of peptides derived from the common precursor, – proopiomelanocorticotropin, increases. The main products of proopiomelanocorticotropin cleavage are adrenocorticotropic hormone (ACTH), β-endorphin and alpha-melanocyte-stimulating hormone. It is ACTH that stimulates the synthesis and secretion of glucocorticoids (cortisol, corticosterone) of the adrenal cortex, while β-endorphin and dynorphin limit the physiological effects of excessive stimulation of corticosteroid secretion. Synthesis and secretion of CRH, which stimulates the secretion of ACTH, are regulated by norepinephrine, serotonin, angiotensin II, opioids and other neuropeptides, as well as neurosteroids. Stress-activating and stress-limiting systems interact in the central nervous system. The latter, in addition to endogenous opioids, melatonin, serotonin, and neuropeptide Y, includes γ-aminobutyric acid, the main inhibitory neurotransmitter in the central nervous system.

An important mechanism for regulating the secretion of corticosteroids is the negative feedback between the cortex of the adrenal glands and the subcortical structures of the brain – the hypothalamus and the hippocampus. Thanks to the inhibitory effect of corticosteroids on the secretion of CRH and ACTH, a stable level of

hormones is maintained within the HPAS. The inhibitory effect is realized through glucocorticoid and mineralocorticoid receptors of the hippocampus and hypothalamus. The mineralocorticoid receptors of the hippocampus, which have a high affinity for circulating glucocorticoids, are of primary importance in maintaining hormonal balance. Glucocorticoid receptors of the hypothalamus and hippocampus have low-affinity, they are sensitive only to high, stressful concentrations of corticosteroids. Under conditions of stress, the sensitivity threshold of the hypothalamus and hippocampus to glucocorticoids increases, which automatically leads to inhibition of the secretion of CRH, ACTH and corticosteroids. As well, the role of the amygdala as a modulator of the HPAS activity has been proven.

The stress response covers all physiological systems of the body. Heartbeat and breathing speed up, arterial and venous pressure increases, blood vessels of the skin and internal organs narrow, instead, muscle arteries dilate; blood clotting ability increases, its morphological composition changes in the direction of eosinopenia and lymphopenia, Glucocorticoids inhibit reactions of the immune system. Metabolic manifestations of stress are hyperglycemia, gluconeogenesis and glycogenolysis, lipolysis (hyperlipidemia), increased oxygen consumption, protein catabolism, increased lipid and protein peroxidation, and activation of the kinin-kallikrein system.

Under conditions of stress in cells, increased energy production by the electron transport systems of mitochondria and microsomes is observed, with an increase in oxygen consumption. Endoplasmic reticular stress is characterized by the accumulation of abnormally conformed or denatured proteins in the endoplasmic reticulum, a violation of calcium homeostasis in the cell. The final outputs of cellular stress can be apoptosis, autophagy or necrosis.

An important pathogenetic mechanism of stress-induced damage to cells and tissues is oxidative stress and nitrosative stress. According to professor V.A. Baraboy's concept, reactive oxygen species and other peroxidation products can play the role of primary stress mediators, i.e., they initiate the activation of the sympatho-adrenal system and HPAS [7]. In fact, in all cases of stress-induced damage of the reproductive system, oxidative stress is not only present, but also plays an important pathogenetic role [16, 17].

Relationship between HPAS and HPGS

HPAS and HPGS are in reciprocal relations, that is, they are interdependent regulatory systems. Accordingly, the body's reaction to a stressful stimulus depends on sex and sex-dependent hormonal profile [9].

Under conditions of stress, the secretion of ACTH and glucocorticoids increases, which leads to a decrease in the activity of HPGS. The main mechanism of this phenomenon is the action of β-endorphin of hypothalamic origin. This opioid directly inhibits the activity of gonadotropin-releasing hormone (GnRH)-producing hypothalamic neurons, reducing tonic LH secretion and blocking pulsatile rhythm and pre-ovulatory surge of LH from the pituitary [18]. According to electron microscopy, CRH and arginine-vasopressin neurons have synaptic contacts with GnRH neurons of the hypothalamus. In recent years, it has been found that stress excites two types of kisspeptin neurons that have afferent connections with GnRH neurons, stimulating their activity [19]. Of course, this mechanism also "works" in the male body, inhibiting testosterone secretion and spermatogenesis. There is evidence that stress-induced CRH, β-endorphin, glucocorticoids, and other physiologically active substances of HPAS inhibit HPGS at all its structural and functional levels [1, 20, 21]. As reported by Tilbrook et al. [9], in general 18 mediators of the impact of stress on the reproductive system are known. Kisspeptin and some other substances have been missing from this list.

It should be noted that an increase in the level of glucocorticoids during stress is not al-

ways associated with a decrease in the secretion of LH and FSH, especially during acute stress. This relationship is more often observed in a long-term state of stress [12]. In animal studies, it depends to some extent on the species of laboratory animals [22].

Gonadal hormones have a noticeable effect on the HPAS both in a state of physiological rest and in stressful situations. A more pronounced reaction of the HPAS to stress in women and female animals, compared to males, is caused by the effect of estradiol. The direct stimulating effect of estradiol on the adrenal cortex, in particular, its sensitivity to ACTH, has been shown [23]. The presence of estradiol receptors in the paraventricular nuclei of the hypothalamus indicates the possibility of a direct effect of estrogens on CRH neurons. Androgens and estrogens modulate the secretion of arginine-vasopressin, a stimulator of ACTH secretion in the pituitary, in the supraoptic nuclei of the hypothalamus, as well as in the paraventricular nuclei. These effects are realized with the participation of androgen and estrogen receptors, which are present in the specified brain structures. In experiments on adult female rats, which were implanted subcutaneously with testosterone capsules at the age of puberty, we observed inhibition of the response of the HPAS to an acute stress and central noradrenergic stimulation [24].

Another mechanism of the effect of sex steroids on HPA function is the participation of their metabolites. These include catecholestrogens, 5-alpha-reduced metabolites of testosterone and progesterone and others.

Preconception and gestational stress

To the best of current knowledge, stress exerts an extremely negative effect on the course of pregnancy and the state of the fetus, and can lead to premature birth and other complications in mother and child. Objective proof of this is the establishment of an association of stress-induced elevated cortisol levels with the risk of spontaneous abortions at the term of three weeks of pregnancy which is firmly established [25]. Psycho-social stress (in the first place) and other types of stress create a high risk of early pregnancy loss due to the insufficiency of the luteal body and, therefore, the deficiency of progesterone, which is the key hormone necessary for preservation of pregnancy [10, 26, 27].

Maternal emotional stress from beginning up to 30 days of pregnancy increases the blood estradiol levels in young human males [28]. Based on the results obtained from the program “The Raine Study” [29], 20-year-old men, whose mothers experienced various stressful events during pregnancy, have decreased reproductive potential. The most negative impact was caused by the stress in the first trimester of pregnancy. Later, the authors reported that a similar medical examination of girls at ages of 14-16 years showed early menarche as a result of episodes of maternal gestational stress [30] and an association of stress in late gestation with increased uterine size and numbers of large ovarian antral follicles [31].

According to the research by L.Yu. Sergienko [32] on the offspring of rats whose mothers were subjected to social emotional stress during the first week of pregnancy by placing a pregnant female in a cage with non-pregnant rats, the negative consequences were as following: delayed sexual maturation, weakening of the hormonal activity of the testes and ovaries, a decrease in fertility. Piquer et al. [33] traced the state of the reproductive system of females of 4 generations after their mothers were subjected to cold stress (at 0°C for 3 h daily throughout pregnancy). Except for the third generation, cystic changes were found in the ovaries. Fertility potential was significantly reduced, as well as the number of pups born. Fertile potential was restored in the fourth generation, but the number of the progeny was still reduced.

Systematic pathophysiological analysis of neuroendocrine and other effects of stress on the reproductive system is presented in a number of monographs and reviews [5, 7, 15, 34, 35]. Most of these studies were carried out on laboratory animals, mainly rats. The most

interesting are the functional disorders in the offspring that occur against the background of the absence of anatomical anomalies, after stressing the animals in the critical period of sexual differentiation of the brain (SDB) (15-21 days of pregnancy) [15]. This is the so-called prenatal stress syndrome, manifested in the male offspring of humans and animals by complete or partial demasculinization of the brain, homo- or bisexual behavior, features of female sexual behavior, weakening of the response of pituitary gonadotropocytes to GnRH, acceleration of the age-related involution of spermatogenesis and a number of other changes. Changes in the hormonal profile of adult male rats, whose mothers were subjected to immobilization stress during the same time period, consist of a decrease in the levels of LH, FSH and testosterone with a simultaneous increase in the level of estradiol in the blood [36].

We experimentally substantiated the neurochemical concept of androgen-dependent SDB [37], according to which the determinants of brain programming in the male fetus are hypothalamic norepinephrine and 4-hydroxyestradiol-17-beta. The latter is formed in the hypothalamus by the conversion of fetal testicular testosterone into estradiol followed by its hydroxylation.

Chemical endocrine disruptors are also considered as stress factors. We obtained experimental evidence of the negative impact of dibutyl phthalate, bisphenol A and ibuprofen, fed to rats during the last week of pregnancy that corresponds to critical time window of SDB, on the reproductive system and sexual behavior of male offspring [38-40].

The results of population studies on humans correlate with the conclusions of experimental studies. Dorner et al. [41] were the first to prove that the occurrence of homosexual and/or bisexual orientation is significantly increased in the male progeny of mothers who experienced severe psychological stress during the Second World War or as a result of domestic violence. This was later confirmed in a large population study by other researchers [42].

It is known that the main producer of estradiol in the female body is the ovaries. Hypoxia, to which rats were exposed from the 6th to the 20th day of pregnancy (the usual gestation period lasts 21-22 days), causes a decrease in the reserve of ovarian primordial follicles and premature aging of the ovaries in female offspring, creating conditions for hypofertility. Interestingly, the length of ovarian telomeres and the DNA-induced repair capacity of the protein-kinase complex significantly decreased in adult females [43]. Immobilization of the rats from 17 to 20 days of pregnancy led to delay of maturation of the female offspring, a decrease in the blood estradiol level and the expression of the kissteptin gene in the hypothalamus. The lordosis reactions, which characterize the female type of sexual behavior, were suppressed in prenatally stressed females [44]. According to our observations, daily one-hour immobilization stress from the 15th to the 21st day of pregnancy also leads to a delay in puberty, a decrease in fertility potential in female rat offspring.

Disorders of sexual behavior in prenatally stressed females are the result of stress-induced secretion of adrenal androgens, which disrupt SDB through its masculinization. As for the disorders (demasculinization) of the sexual behavior of male offspring, they depend to some extent on the partial refractoriness of the nerve centers, including the cerebral cortex, to the activating effect of testosterone in adulthood. This happens against the background of maintaining a normal level of testosterone in the blood.

An important finding is that not only gestational stress affects the reproductive health of the offspring, but also chronic psychological stress of the father and mother before conception. Maternal stress associated with the death of a close relative in the year before conception or during pregnancy increases the risk of infertility in female offspring [45] Immobilization of male mice from postnatal age of three weeks for 90 days caused epigenetic changes in spermatozoa, which were inherited by the male offspring of the next two examined generations. They had a sig-

nificant decrease in the concentration of spermatozoa and their mobility, as well as the number of offspring. Sequential analysis revealed changes in the methylation of some DNA regions in the gametes. In addition, dysregulation of transport, ribosomal and micro-RNAs was detected [46]. These data indicate the importance of the psychological health of parents for the reproductive health of the offspring.

Consequences of stress in adolescence

The adolescent period of life is characterized by the beginning of puberty, when the neuroendocrine system, pituitary gland, gonads, adipose tissue, which produces, in particular, leptin, are activated. The levels of gonadotropins and sex hormones in the blood increase sharply, and their daily rhythms are established. Spermatogenesis is stimulated, ovulatory cycles and menstruation appear in girls. Violation of the hormonal balance caused by various types of stress has a negative impact on puberty and reproductive function. This is facilitated by the fact that at the beginning of puberty, the response of the HPAS to stressful stimuli in humans and animals of both sexes, especially in women and female animals, is significantly higher compared to that in adulthood [47-49].

The main attention of PTSD researchers in adolescents was focused on the manifestations of depression and anxiety, the state of cognitive functions, learning abilities, symptoms of aggressive and impulsive behavior. Regarding the state of the reproductive system, there is a well-founded point of view, according to which stress in pre- and pubertal age delays puberty in boys, but accelerates it in girls, as evidenced by the early onset of menarche. However, stress in adolescent girls is often the cause of primary hypothalamic amenorrhea. This pathology occurs as a result of stress-induced suppression of the secretion of GnRH, LH, FSH, and disorders of pulsatile secretion of gonadotropins [50] and is a common cause of infertility [51]. It is accompanied by polycystic ovaries in almost 60% of patients [52].

The pathogenesis of reproductive disorders was studied mainly in laboratory animals. Housing of pubescent male rats one at a time in a cage (emotional stress) for 25-50 days led to a weakening of sexual motivation at the age of 3 months [53]. Immobilization of male rats for 6 h during 15 days starting from pre-pubertal (forty-days) age caused increased sexual activity on the background of a twice-prolonged latent period of the first mount in young (45-day-old) rats. Stress for 60 days led to hypofertility due to the deterioration of the fertilizing ability of spermatozoa and increased pregnancy losses in fertilized females [54]. Chronic stress by immobilization of pubertal male rats increased blood testosterone levels but decreased LH concentrations and delayed testicular maturation [55]. On the other hand, similar other reports refer to a significant decrease in the level of testosterone in the blood serum, as well as a decrease in the level of LH and FSH and an increase in prolactin and estradiol. Histological examination revealed damage to the structure of the testicles [56]. It has been proven that the delay in puberty in males is due to corticosterone as an effector hormone of HPAS [57]. A similar result was obtained in female rats when CRH was administered from the age of 28 days for two weeks [58], although this is inconsistent with clinical observations of the timing of puberty in girls (see above).

The neuroendocrine system regulates the sexual behavior of humans and animals. Undoubtedly, an important role in the pathogenesis of reproductive changes induced in early puberty belongs to the imbalance of neurotransmitters in the brain, in particular, dopamine [59]. Social isolation of female mice from 25 to 60 days of age reduced quantitative indicators of receptive behavior (lordosis responses in the presence of an active male), and subsequent return to social groups did not restore sexual behavior [60].

Stress in the reproductive age

A great body of clinical evidence show that the reproductive function of women is more

vulnerable compared to men. Stress-induced endocrine disorders are three times more common in women than in men. On the one hand, this is explained by the greater emotional excitability of women and the increased response of the HPAS to stress agents, on the other hand, by the more complex structural and functional organization of the reproductive system, the cyclical nature of its activity. Among the many factors that cause stress in women, psycho-emotional ones are in the first place. Stress is the cause of infertility in about 30% of cases. Manifestations of PTSD regarding the reproductive system of women are extremely diverse. Disorders of the hypothalamic-pituitary regulation of the hormonal and generative functions of the ovaries and oxidative stress play a leading role in this. In particular, the increased level of cortisol in the blood inhibits the secretion of GnRH and gonadotropins, disrupts the pulsatile rhythm of their secretion. Thyroid dysfunction and stress-induced hyperprolactinemia play a significant role [61], because prolactin not only inhibits GnRH secretion in the hypothalamus, but also disrupts steroidogenesis in the ovaries, reduces progesterone production, and causes premature luteolysis. Against the background of these disorders, there is a reduced production of LH and FSH, hypoprogesteronemia, and low levels of estradiol.

The most common type of PTSD related to the reproductive health of military women who were in the combat operations in Donbas is menstrual dysfunction described as menstrual cycle disorders and uterine bleeding. They arise against the background of increased progesterone levels in the first phase of the menstrual cycle [62]. The authors rightly assume that the source of the stress-induced high level of progesterone is the cortex of the adrenal glands.

Stress in women of reproductive age causes ovulation blockade, luteal phase insufficiency, functional hypothalamic oligo- or amenorrhea, irregular menstruation, premenstrual dysphoric disorders, hypofertility, infertility (about 30% of stress cases), embryo implantation disorders, early pregnancy loss, premature birth, provokes endometriosis, early menopause etc.[4, 13, 63-68]. In almost 60% of patients, a violation of the neuroendocrine regulation of the ovarian cycle is accompanied by polycystic ovaries [52]. Stress impairs egg quality [69]. There is evidence that stress-induced disorders of embryo implantation are caused by impaired function of adrenoceptors of decidual cells. According to the data on the content of alpha-amylase in morning saliva as an objective indicator of the strength of stress, it was concluded that the success of in vitro fertilization is inversely correlated with this indicator in potential father and mother [70]. This result is caused by the deterioration of sperm motility and the number and quality of embryos for transfer to the uterus.

One of the manifestations of PTSD in women is a decrease in libido and sexual activity [71, 72], difficulties in achieving orgasm [73].

Experiments on animals with simulation of stress revealed some mechanisms of reproductive disorders. Overheating of female rats for 90 days for 2 h per day led to lengthening of estrous cycles and a series of changes in the hormonal profile, similar to those during stress in women. Violation of gene expression of estradiol, progesterone, LH, FSH, prolactin receptors in the uterus and ovaries was also detected [74]. Cold stress in rats reduces the number of mature ovarian follicles through irreversible DNA damage of cumulus cells [75]. In mice, social psychological stress reduces the levels of LH, FSH, anti-müllerian hormone and ovarian reserve, which is associated with an increase in the concentrations of angiotensinogen and angiotensin II in the ovaries and blood serum [76].

It is generally accepted that in men, chronic stress causes impaired fertility potential, suppression of sex drive, deterioration of sperm quality and oligospermia, premature andropause and other reproductive disorders [4, 13, 77, 78]. The sharp increase in PTSD cases in men is primarily related to participation in hostilities or being in the hostilities zone and in the occupied territories of Ukraine. As reported by the

Danish authors [79], the quality of semen in the examined men depended on the strength of the stress (according to self-assessment): the stress of the greatest strength led to a decrease in the concentration of spermatozoa by 38% and their total number by 34%, as well as a 15% smaller sperm volume than in men with moderate stress. An important pathogenetic mechanism of damage to the germinal cells of the testis and spermatozoa is the incorrect assembly (processing) of regulatory proteins, which are manifestations of the so-called cellular, endoplasmic reticular and mitochondrial stress [80].

Stress in men, especially psycho-emotional stress as the most common in human society, is a common cause of the disappearance or weakening of sexual desire, erectile dysfunction [3]. A short-term reaction to acute stress is the release of testosterone, which should increase a man's resistance to external aggression or other danger, but regular emotional exhaustion leads to a gradual decrease in the level of testosterone in the blood. PTSD in military veterans and active military personnel is associated with deterioration in all components of sexual behavior, including decreased libido, premature ejaculation, erectile dysfunction, etc. [81]. However, there are other reports that there is a risk, especially in men, of hypersexuality as a symptom of PTSD [82].

Studies in male rats have shown that acute stress activates mitochondria formation and biogenesis, including transcription factors and associated kinases in Leydig cells, enabling adaptive steroidogenesis [83]. Data on the kinetics of testosterone content in the blood plasma of rats under conditions of acute stress are quite contradictory. A decrease in hormone levels after 3- or 6-hour immobilization has been reported, despite the maintenance of normal LH levels [84]. The authors explain this by the direct inhibitory effect of the increased level of corticosterone on steroidogenesis in Leydig cells, which is carried out through the glucocorticoid receptor NR3C1.

CONCLUSIONS

1. The relevance of research on the negative effects of stress on the reproductive system of humans and animals has increased significantly in recent years due to the covid-19 pandemic and even more so after the aggression launched by Russia against Ukraine.

2. Acute and especially long-term (chronic) stress disrupts the maturation of gametes, libido, sexual behavior, mating, fertilization, pregnancy and childbirth. In the structure of the etiology of these disorders, psycho-social stress prevails.

3. The characteristics of stress-induced disorders of the reproductive system have features depending on the lifestyle of future parents, as well as on the period of life, starting from the embryonic to the end of the reproductive age.

4. The leading role in the pathogenesis of stress-induced disorders of the reproductive system is played by GHAS and GGHS, as well as oxidative-nitrosative stress.

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О.Г. Резніков

СТРЕСІНДУКОВАНІ РОЗЛАДИ РЕПРОДУКТИВНИХ ФУНКЦІЙ

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В огляді наведено патофізіологічний аналіз того, що нині відомо стосовно впливу гострого та хронічного стресу на функціональний стан чоловічої та жіночої репродуктивних систем. Актуальність досліджень негативних наслідків стресу щодо репродуктивної

системи значно зросла останніми роками через пандемію Covid-19 і ще більше – після розпочатої Росією агресії проти України. Стрес порушує дозрівання гамет, лібідо, статеву поведінку, спарювання, запліднення, вагітність і пологи. У структурі етіології цих розладів переважає психо-соціальний стрес. Характеристика стресзумовлених розладів репродуктивної системи має особливості залежно від стилю життя майбутніх батьків, а також від періоду життя, починаючи від ембріонального і до закінчення репродуктивного віку. Провідну роль у патогенезі стресзумовлених розладів репродуктивної системи відіграють гіпоталамо-гіпофізарно-адренокортикальна і гіпоталамо-гіпофізарно-гонадна системи, а також оксидативно-нітрозативний стрес. Сучасні дані про патогенез стресзумовлених розладів репродукції мають бути основою профілактичних і лікувальних стратегій.

Ключові слова: стрес; репродукція; гіпоталамус; стрес; яєчники; сім'яники; гіпоталамус; гіпофіз; надниркові залози.

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