

# CONCEPT OF COMPLICATIONS OF REPRODUCTIVE AGING IN WOMEN FOR ANTI-AGING THERAPY

## LITERATURE REVIEW

*There is nothing in life you need be afraid of, there is only what you need understand.*

*Maria Skłodowska-Curie, 1933*

*Old age is when you still love life, but not loved by it.*

*Tatyana Kleiman, 1983*



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## INTRODUCTION

The illusion of women's protection lies in the fact that cardiovascular diseases (CVD) in women develop a decade later than in men, this can mislead the clinician and create the illusion of patient protection simply on the basis of gender [1]. Often, doctors of other specialties, not gynecologists, forget that after menopause, estrogen protection quickly disappears, and the presence of uncorrected risk factors sharply increases the likelihood of cardiovascular complications in this age period [2].

The fact that over the past decades the diseases of the circulatory system of women have become "younger" enough does not add optimism [3]. The "fight for every heartbeat" in the United States reduced mortality from cardiovascular disasters in people over the age of 65, but the rate has not changed in the age category less than 55 years. According to experts, this can be explained by the "lack of an effective preventive strategy" [4].

According to the European Society of Cardiology, despite the later onset of cardiovascular diseases in women, their total deaths are higher than that of men (55 vs. 43%). The rate of coronary heart diseases (CHD) in women slightly increases already in the perimenopausal period, but exponentially increases in postmenopausal women, which may reflect the cumulative effect of earlier changes in cardiovascular risk factors [2]. That is why the main task of the doctor is to identify women at risk as early as possible in order to begin timely prevention, aimed primarily at slowing down cardiometabolic changes and subclinical manifestations of atherosclerosis.

Reproductive aging occurs little by little. Biological changes associated with the extinction of ovarian function in women occur even before the manifestation of significant disorders of the menstrual cycles.

According to the criteria of STRAW+10 (Stages of Reproductive Aging Workshop) the late reproductive period is divided into 2 stages. The first is char-

acterized by regular menstruation and the absence of significant fluctuations in the concentration of follicle-stimulating hormone (FSH) in the early follicular phase, and the second is characterized by insignificant changes in the menstrual cycles (most often shortening) against the background of a progressive increase in the level of FSH [5, 6].

In practice, the stratification of the menopausal transition is difficult due to the wide variety of clinical endocrine characteristics of individual menstrual cycles. In this regard, the term "perimenopause" is a widespread term – a transitional period and the first year of postmenopause [5]. It is perimenopause that for several years has been accompanied by vasomotor disturbances, mood changes, decreased sleep quality, and sexual dysfunction. Vasomotor instability reflects an increased sensitivity of the cardiovascular system to estrogen deficiency [7]. There was found a relationship between this kind of symptom complex and endothelial dysfunction [8], increased aortic calcification [9], increased thickness of the carotid artery intima-media complex [9] and the level of markers of coagulation and inflammation disorders [10].

As S.V. Yureneva et al. [1] figuratively expressed it is possible to achieve menopause in physical well-being, minimize negative effects, improve the quality of life and increase longevity, the main thing is to timely start "throwing brushwood" of rational combinations of combined oral contraceptives and menopausal hormone therapy (MHT), not letting fade away the "flickering fire" of estrogen effects.

## RELEVANCE OF THE TOPIC

Biological aging is a continuous process that occurs throughout life, which causes changes in the structure and functions of all organs, leading to a decrease in the reserve capacity of most systems. There are many theories of aging, one of them is endocrine, proving that it is the decrease in the level of sex hormones that is the trigger for the development of aging [11].

Improving the quality of life of women in peri- and post-menopausal period, preventing CVD and their complications, metabolic disorders and osteoporosis are urgent problems of modern medicine in all countries of the world, regardless of the level of economic development. Today, there are many medications and non-medications for the correction of menopausal complications, which greatly complicates the choice of the optimal one, route of administration, dosing. However, hormone phobias, as well as an established opinion about the risk of developing endometrial and mammary glands cancer against MHT taking, significantly limit the administration of estrogen and progestogen drugs, which, in contrast to biologically active additives, with the effectiveness of being equivalent to placebo, can significantly increase the quality of life and longevity of women during menopause. As V.P. Smetnik often noted in her speeches “sex hormones are not only appearance, it is an opportunity to be active and enjoy life. Women who use MHT differ from those of their age by a happy eye shine, joy of life, an aura of happiness” [12].

The global nature of this problem, according to UN forecasts, indicates that in 2025 the proportion of the elderly will be 26.3%, and by 2050 – 38%, the proportion of senile people will be 16% in 2025 against 19.7% in 2050. The appearance of old age has a “female face”: in 2000 the proportion of women over 60 years old was 24.6%, over 80 years old – 3.2% of the total population, and men over 60 years old – 15.9%, over 80 years old – 1.1% [13, 14].

The aim of the literature review is to teach practitioners to improve the quality of life with awareness of the minimal risks of MHT against the background of a modification of the way of life in compliance with international and Ukrainian recommendations.

### AGE CHANGES

We judge it expedient to consider age-related changes as a prerequisite for the pathophysiological strategy of the need for the MHT use according to academician G.M. Butenko [15].

I. Age-associated polymorbidity: heart disease, brain disease (myocardial infarction, stroke); malignant neoplasms; diseases of the musculoskeletal system (osteoporosis, osteoarthritis); diseases of the central nervous system (parkinsonism, Alzheimer's disease); type 2 diabetes mellitus; infections with a chronic course;

II. Changes in the neuroendocrine system are manifested in the rhythm, disturbance, duration and level of steroid hormone secretion, their binding and transfer by blood transport systems, interaction with receptors and post-receptor systems. In this case, the release of releasing hormones by the neurosecretory nuclei of the hypothalamus, which act through the tropic pituitary hormones on the target glands that secrete peripheral hormones, is disturbed.

III. Production of secondary mediators in the liver is disturbed – insulin-like growth factors I and II, in the cells of the immune system – cytokines, with reducing estradiol levels and enhancing spontaneous baseline and induced production of anti-inflammatory cytokines (interleukin (IL) 1, IL-6, tumor necrosis factor  $\alpha$ ) by phagocytic cells.

The production of cytokines is increasing, which causes a special tendency to development of sluggish chronic inflammatory diseases in the aging organism, with unexpected consequences in the form of damage to blood vessels, brain cells, disturbances in bone remodeling and development of inflammatory joint diseases. There are changes in the function of the pineal gland (pineal gland) – atrophy, calcification, a distortion in the frequency of release of melatonin, which is accompanied by desynchronization of the work of many organs and systems of the body during the day (circadian rhythms), as well as when changing seasons (circannual rhythms). There is mononuclear infiltration of the islets of the pancreas, adrenal cortex, ovaries, which may be evidence of involutive changes in the immune system. This is accompanied by an age-related decrease in the hormonal activity of the thymus gland, a decrease in the level of the cytokine IL-7, key for the multiplication and differentiation of thymocytes. At the same time, there is a decrease in the number of sex hormones, thyroid hormones, which is accompanied not only by increased levels of adrenocorticotrophic hormone, luteinizing hormone, FSH, glucocorticoids, but also a break in succession and rhythmicity of the release of somatotrophic hormone, releasing hormones of the hypothalamus [12, 15, 16].

There exists a connection between immunity and morbidity and mortality, there has been established the prognostic value of reducing the anamnestic response to widespread microbial antigens in the form of a reaction to skin tests or lymphocyte reactions *in vitro*, an increase in the level of autoantibodies to a number of organ antigens, circulating substances and hormones prolactin, insulin. The elderly are at risk for the COVID-19 pandemic.

A change in immune homeostasis is considered an unfavorable prognosis: a decrease in blood CD4+ T-cells, CD19+ B-cells, an increase in the number of CD8+ T-cells with a reduced reaction to mitogens and an increase in the level of circulating immune complexes.

The above explains the fact that age-related changes not only lead to pathology, a deterioration in the quality of life, but also require the use of the “gold standard” of treatment is MHT because: the elderly are 4–5 times more likely to suffer from tuberculosis, 6–7 times more often die from pneumonia, 90% of those who die from influenza are people over 65 years old, every second cancer develops after the age of 60 years [15, 17].

### ENDOTHELIAL DYSFUNCTION AND AGING PROCESSES

There is practically no exaggeration in the thesis that the beauty and health of a person directly depend on the state of his/her vessels. In the body of an average patient weighing 70 kg, the total length of the vessels is 60 thousand miles, or 96.6 thousand km. Therefore, the endothelium lining all this vascular space, in a logical way is considered to be an independent organ of the endocrine system [18]. The area of “endothelial responsibility” includes many critical functions: hemostasis, angiogenesis, transmission of hormonal signals, attraction of neutrophils to the focus of inflammation, filtration of liquids, etc. In the context of events in the cardiovascular system (and, consequently, the risk of premature death), the most significant are regulatory effects of endothelium on vascular tone and blood flow characteristics [18].

Arterial wall aging is the main cause of arterial hypertension and other diseases of the circulatory system. Reducing the synthesis of nitric oxide and the impairment of its bioavailability under the influence of well-known risk factors (smoking, dyslipidemia, hypertension, diabetes mellitus and others) form the very foundation of endothelial dysfunction. Its formation is the total indicator of the action of atherogenic factors of aging, including reproductive, in each particular woman, taking into account the genetic "heritage" and lifestyle [19, 20].

One of the first manifestations of endothelial aging is an imbalance between vasodilation and vasoconstriction, which forms non-localized chest pains and/or shortness of breath, mainly on tension, and this cannot be called classical angina of effort. In women with such symptoms, the risk of developing CHD (frequent manifestation of which is just angina pectoris and myocardial infarction) doubles in the next 5–7 years, and therefore they urgently need correction of existing risk factors and lifestyle changes.

A special place in the aging process should be given to CVD in women. CHD, deep vein thromboembolism and stroke are called "silent epidemics". Although CHD was considered a "male disease", it is the most widespread cause of morbidity and mortality among both men and women. At a young age, men have the highest risk of developing coronary heart disease, but with increasing age, this indicator in women approaches that of men. So, if at the age from 45 to 64 years the incidence of the disease in women in relation to men is 1:7, then at the age over 65 years – only 1:3. Atherosclerotic changes in blood vessels in the absence of clinical manifestations of CHD are revealed in a significant number of women [21, 22].

## INTERGENDER CHARACTERISTICS OF CVD

Mortality increases with increasing age among both men and women. However, if the ratio of the indicator men/women aged 35–44 is 5:1, then over the age of 75 it is only 1.5:1. One of four women aged 60 and over is expected to die from coronary heart disease. Every 50-year-old woman has a 46% risk of developing CHD and a 36% risk of dying from it. Despite the fact that the incidence of CHD in women increases with the onset of menopause, these changes do not occur sharply, but gradually. Mortality from CHD and cancer in young women is approximately equal, but after 65 years, mortality from CHD begins to prevail. Although cardiovascular diseases are the main cause of morbidity and mortality, cancer is the most worrisome for women, even those with higher education who are more informed about these issues [11, 23].

Clinical manifestations of CHD in women are different from those in men. Undoubtedly, unstable angina is more characteristic for women, while men are more likely to experience acute angina attacks. Women recover more difficult after a heart attack, firstly, because they often receive medical care late, and secondly, the processes of thrombolysis in them are less pronounced and develop more slowly. In addition, women, as a rule, have more risk factors and a higher incidence of complications, apparently, due to the difference in the pathophysiological mechanisms of the course of the disease. The development of atherosclerosis in women begins later than in men, and normal production of ovarian hormones coun-

teracts these changes, while estrogen deficiency contributes to atherosclerotic transformations and the development of CHD [24, 25].

Despite some trends emerging in recent decades, there are clear differences in mortality from CVD and cerebrovascular disease, which differs significantly in different countries of the world. Thus, the highest mortality rate from coronary heart disease is registered in the USA (166 per 100,000 women) and in Canada (133 per 100,000 women), as well as in northern European countries. The countries of Central and Eastern Europe are intermediate in this indicator. Due to the fact that the risk of developing these diseases differs in different countries and parts of the world among different ethnic groups due to the peculiarities of their nutrition and lifestyle, this should be taken into account when discussing the benefits and risks of using MHT and hormone replacement therapy (HRT) and during surgical menopause [22, 26]. Risk factors for CVD development are common for men and women, namely: heredity, diet, obesity, smoking, and disorders of lipid profile, high levels of homocysteine and fibrinogen, low physical activity, diabetes mellitus, arterial hypertension.

However, women have a unique risk factor – menopause. Women have a higher relative risk of developing these diseases if they are diagnosed with diabetes mellitus, elevated triglycerides level, low levels of high density lipoproteins (HDL) or if they are smokers. The incidence of CHD is higher in countries where people traditionally consume foods high in saturated fatty acids and cholesterol. People with high cholesterol are characterized by an early onset of coronary heart disease, and lowering cholesterol reduces the risk of developing this disease. As for women, such risk factors for coronary heart disease as a decrease in the level of HDL and an increase in the concentration of triglycerides are more important than the level of low density lipoproteins (LDL) cholesterol.

It has not yet been established which risk factor is more important for women – the level of HDL or triglycerides. Nevertheless, a decrease in the risk of developing coronary heart disease when using statins suggests that lowering LDL levels has a beneficial effect in women. Recent studies have shown that lifestyle changes, a balanced diet, weight loss, smoking cessation, and exercise can reduce the risk and incidence of CHD. In addition, in the presence of CVD, the administration of acetylsalicylic acid,  $\beta$ -blockers and cholesterol lowering agents (statins) is indicated for women. Presumably, it is due to the protective effect of estrogen that CVD in women begins to develop 10 years later [26].

## STRATEGY FOR MAINTAINING WOMEN'S HEALTH DURING PERI- AND POST-MENOPAUSE

Particular attention is drawn to the state of this problem precisely in Ukraine, where the proportion of women who have entered perimenopause is a great social and professional responsibility of obstetrician-gynecologists, who today have to be guided by a new paradigm: the onset of a period of perimenopausal transition in itself should be considered as a direct indication for drug therapy and with the obligatory modification of the way of life for the "school of exquisite aging" according to the figurative expression of professor V.E. Radzinsky [27].

The difference in average-expectancy life in different regions is believed to be due not only to the influence of genes, but also to environmental conditions, including dietary habits. Improper nutrition is one of the most dangerous factors accelerating the aging process. Another important aspect of accelerated aging is the accumulated burden of disease: most people actually die from age-related diseases (consequences of untreated atherosclerosis), undetected oncological problems, not prevented Alzheimer's disease, and other ones than aging.

The natural process of ovarian failure with the development of estrogen deficiency results in many risks for complications for every woman, for example: recompense for anaerobic metabolism. The first documented evidence of aging research of the year 1532 belongs to the Persian physician Muhammad ibn Yusuf al-Harawi [28]. Almost 6 centuries have passed since the writing of his book ("Ainul Hayat"), and the mechanisms and causes of aging are still not clear. There are several hypotheses explaining the stages of fading of the body. One of them, the theory of free radicals, was proposed in the middle of the last century by the American scientist David Harman [29]. In his opinion, the aging of the human body is the price that people pay for anaerobic metabolism.

In cells the formation of energy-rich adenosine triphosphoric acid occurs in the mitochondria, where oxygen with the release of energy is converted into water through several biochemical processes with the associated release of highly reactive oxygen molecules. Usually, the active forms of oxygen remain within the mitochondria; however, some of them can penetrate the cell cytoplasm. As a result, vital biomolecules (lipids, proteins, DNA) are damaged.

Since mitochondria are involved in the utilization of active oxygen, their quantity is also of paramount importance. With age, cell division decreases, which leads to a reduction in the number of mitochondria. Proponents of the mitochondrial hypothesis of aging argue: it is the respiratory capacity of the mitochondria that determines the person's longevity [30], so the lack of these essential organelles leads to the biological death of the individual.

The earliest manifestations of climacteric syndrome are autonomic disorders, which are diagnosed in almost 90% of women with this pathology. The severity of this syndrome is affected by the presence and nature of concomitant extragenital pathology. The prevalence of vascular diseases of the brain in women during the menopause is 43%. In women with severe course of climacteric syndrome, an earlier formation of severe forms of cerebrovascular pathology is observed; and MHT is an effective way to correct it [31]. However, the use of hormonal drugs is contraindicated in women with cerebral ischemia, since this increases the risk of developing ischemic stroke [17]. In recent years, an in-depth analysis of clinical trials and international recommendations has been carried out [11, 26]. This provided the basis for the creation of a group of leading endocrinologist-gynecologists – foreign (Tobie de Villiers) and Ukrainian (T.F. Tatarчук et al.) – the National Consensus on the Management of Patients During the Menopause (2016), in which, based on the principles of evidence-based medicine, they were updated international guidelines for management of menopause and MHT [32]. Particular attention is drawn to

the state of this problem in Ukraine, where the proportion of women who use MHT in different regions is 2–3% of those who need it, although the census and demographic studies will clarify the true numbers.

Every year, the number of women entering menopause with pre-existing endocrinological diseases is increasing, of which the most common are metabolic syndrome, type 2 diabetes mellitus and thyroid pathology. The modern experience of the use of MHT for half a century has made it possible to formulate its main principles:

- timely start during the perimenopause taking into account the "therapeutic window";
- no more than 10 years of use in the postmenopausal period;
- use of drugs in a minimally effective dose, taking into account a history of reproductive system disorders, the presence of extragenital pathology and preventive correction of possible disorders;
- use of sex steroids similar to natural ones [33, 34].

In postmenopausal women, the most increased incidence of urogenital disorders and osteoporosis is observed, which correlates positively with age [12]. However, recent studies have established that urogenital atrophy is already noted in perimenopause, which is what practitioners should pay attention to [22, 35]. Much attention should be paid not only to the justification of indications for MHT, but also to the initial state of a woman's health and the assessment of risk factors for concomitant extragenital diseases. In this regard, before starting MHT, each patient should be referred to one of the following categories, which were clearly outlined in the works of Y.Z. Zaydieva:

- healthy woman;
- healthy woman with risk factors for CVD and osteoporosis;
- healthy woman with latent manifestations of these diseases;
- patient who has already been diagnosed with somatic diseases [33].

The literature discusses the feasibility and features of the use of statins for primary and secondary prevention of cardiovascular events, their effects on the woman's body as a whole and on MHT background. In this regard, "yentl syndrome" is discussed, the essence of which is that this social phenomenon is associated with the fact that general practitioners, cardiologists are less likely to prescribe statins, acetylsalicylic acid, angiotensin converting enzyme inhibitors and invasive procedures to women. The term was coined by Dr. B. Healy in 2001. It is associated with the name of the play, in which a woman had to disguise in a man's dress in order to gain access to various social achievements. The use of standardized recommendations from foreign guidelines when prescribing therapy (MHT, HRT, statins) will allow doctors to "recover" from this syndrome [36]. The age of natural menopause is considered a marker of biological aging and is increasingly recognized as a period of increased risk of chronic diseases, clinically manifested in a later period of life [33].

Most women experience vasomotor symptoms during the menopausal transition, which is reported by up to 85% of women [37, 38]. Moreover, in 55% of women their onset is at the beginning of menstrual disorder which is determined upon entry into the menopausal transition. A meta-analysis of 10 studies with a total of 35,445 women confirmed the average 4–5-year duration of hot flashes, and they started about a year

before the last menstruation [39, 40]. Vasomotor symptoms, hot flashes can last longer than previously thought - from 10 to 15 years or more, sometimes until the end of life [41, 42].

The reduced quality of life is far from the only negative result of the flashes. Modern methods of neuro-imaging have established that at the time of influx, blood circulation in certain areas of the brain decreases sharply, including the one responsible for the memory mechanisms in the hippocampus. Short-term episodes of ischemia can become the basis for the development of degenerative processes in the brain with a result in vascular dementia and Alzheimer's disease. Flashes are also considered to be an indicator of CVD with latent course [43] and directly correlating with their subclinical signs - impaired vascular endothelial function, aortic calcification, increased thickness of the media of the carotid artery, increased levels of procoagulant factors, development of dyslipoproteinemia [44, 45, 46]. Women with hot flashes have a higher level of systolic blood pressure, which is an independent risk factor for the development of CVD and their complications [10, 47].

During menopause, more than 50% of women report on sleep disorders [48]. Objectively confirmed fragmentation of sleep (frequent awakenings), correlated with a high incidence of moderate/severe flashes, which in turn is associated with an increase in blood pressure. There is a significant correlation of the level of nocturnal blood pressure with cerebrovascular and cardiac complications and an increase in total mortality in women [48, 49]. It is noted that the correlation between the level of nocturnal blood pressure and total mortality from cardiovascular events is significantly higher for women than for men ( $p = 0.023$ ) [48]. Several large cohort studies have shown an increased risk of mood swings and anxiety during the menopausal transition and about a three-fold increase in the risk of developing depression during postmenopause, with approximately 20% of women prone to depression [50]. It has been proven that depression is the result of dysregulation of monoaminergic pathways in the central nervous system (in the serotonergic and noradrenergic regions), which are influenced by changes in estrogen levels [51]. In a review by N. Santoro et al. it is noted that low estrogen levels in perimenopause are an important factor in the development of depression in some women, but do not fully explain the increased risk of depression in this population. In addition, these data indicate the possibility of the antidepressant effect of estradiol in women in the perimenopausal period, but in the postmenopausal period, depression does not respond to estrogen therapy [52]. The same work emphasizes that MHT should be used with caution in women with depression and concomitant vasomotor symptoms, since they are less likely to respond to estrogen therapy. Drugs with estrogens should also be avoided in the treatment of depressive symptoms in postmenopausal women due to a lack of proven efficacy and an increased risk of side effects.

Many women complain of changes in cognitive function during perimenopause, with 62–82% of them reporting memory and concentration impairment. In general, cognitive symptoms are more common in postmenopausal women than in the early stages of transition to menopause [53]. This is confirmed by an observational study of 2124 participants with an average age of 54 years and a follow-up of 6.5 years. It was shown

that cognitive functions decreased on average by 4.9% within 10 years, and the average indicators of verbal episodic memory – by 2% over the same period [54]. Difficulties with concentration are closely correlated with hot flashes, anxiety, depressive mood, sleep disorders and negative perception of one's health [55], which was proved in a study by L. Drogos et al. (2013) [52].

So, convincing data have already been accumulated in favor of the administration of exogenous estrogens (under progestogen add-back) at the stage of transition in order to reduce the harm to endothelial dysfunction and reduce the threat of cardiovascular diseases, including fatal ones. This tactic allows a practicing obstetrician-gynecologist (and no other specialist!) to reverse vascular remodeling and correct the initial stages of the development of atherosclerosis.

Foreign experts recommend that, when deciding on the form of administrations, consider the possible need for contraception. Protection from unwanted pregnancy is indicated for women younger than 50 years of age at least for 2 years after menopause, which forms a very specific selection algorithm. The domestic recommendations on this issue say the following: if a woman is older than 50 years, then, whereas approximately 90% of respondents stop menstruating by the age of 55, experts consider it possible until this age to continue using combined oral contraceptives for women (with annual FSH control since the age of 50 years, if necessary with transition to MHT), not having corresponding contraindications, and then turn to the possibilities of MHT [56]. Prevention and treatment of osteoporosis, osteoarthritis requires a separate discussion.

The advantages of MHT over its absence are undeniable [6]. And yet, despite the proven benefits, hormone phobia is the reality of modern society. Moreover, not only patients, but also doctors themselves voluntarily refuse MHT both in Ukraine and abroad [57]. Without going into the reasons for such a categorical attitude to hormonal drugs, it is worth recognizing the following fact. Like any other treatment, MHT has a number of contraindications [32, 58]:

- blood-tinged discharge of unknown origin;
- breast and endometrial cancer; acute hepatitis;
- acute deep vein thrombosis;
- acute thromboembolism;
- allergy to MHT ingredients;
- cutaneous porphyria.

Contraindications to certain sex hormones should be highlighted separately:

- estrogens: breast cancer, endometrial cancer (in case history), severe liver dysfunction, porphyria;
- gestagens: meningioma.

Relative contraindications for MHT: uterine fibroids; migraine; venous thrombosis and embolism (including in a case history); familial hypertriglyceridemia; cholelithiasis; epilepsy; ovarian cancer (including in a case history).

## CONCLUSION

MHT in age related perimenopause and postmenopause should be the prerogative of the transitional rather than senile period of a woman's life, being a multidisciplinary problem, since the further development of MHT or HRT requires using besides medical and philosophical approaches as well.

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## CONCEPT OF COMPLICATIONS OF REPRODUCTIVE AGING IN WOMEN FOR ANTI-AGING THERAPY

### Literature review

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Modern mankind, through the development of medicine and using its scientifically grounded innovations has learned to prolong human life. In Ukraine as in the whole world there is a tendency to increase in life expectancy. Since aging is a natural physiological process, a person from time immemorial has been preoccupied with the search for the so-called "Philosophy Stone" is a substance that prevents aging.

This article analyzes data from scientific publications on modern aspects of the problems associated with aging of the female body. It has been proven that aging and anti-aging processes substantiate the individualization of modern approaches to the correction of pre- and perimenopause complications. The general strategy for maintaining of women's health in peri- and postmenopause according to the International Menopause Society includes menopausal hormone therapy, taking into accounts the therapy goals and individual risk factors. Despite all the desire to give a modern definition of aging, it is currently not possible, therefore in this literature review an attempt is made to analyze the known strategies of premature aging to develop the potential for prolonging active life.

In any case, the doctor needs to correlate the benefits and risks of menopausal hormone therapy, taking into account individual risk factors and select appropriate rehabilitation methods aimed at "improving the female face" of the classic image of old age. Since the role of estrogen deficiency in the formation of perimenopausal complications and especially premature aging, is not questioned, anti-aging strategies should be considered a pathogenetically justified method of treating vasomotor, psychosomatic symptoms and sleep disorders, as well as a method of preventing metabolic syndrome. It should be remembered that hormone therapy has a number of limitations and contraindications, which is an incentive for every doctor to contribute to prolongation of the active and healthy life of women 40+ and 50+ years old. Creation of a conceptual model for overcoming the complications of reproductive aging and especially cardiovascular events, osteoporosis, cerebrovascular pathology based on the identification of risk factors will allow to develop the protective anti-aging therapy not only to prolong a woman's life, but also to improve its quality.

**Keywords:** quality of life, reproductive aging, menopausal hormone therapy.

## КОНЦЕПЦІЯ УСКЛАДНЕНЬ РЕПРОДУКТИВНОГО СТАРІННЯ ЖІНОК ДЛЯ ПРОВЕДЕННЯ АНТИВІКОВОЇ ТЕРАПІЇ

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Сучасне людство за рахунок розвитку медицини і застосування її науково обґрунтованих інновацій навчилася продовжувати своє життя. В Україні, як і в усьому світі, спостерігається тенденція до збільшення тривалості життя. Оскільки старіння – закономірний фізіологічний процес, людина споконвіку стурбована пошуком так званого «філософського каменя» – субстанції, що запобігає старінню.

У статті проаналізовані дані зарубіжних наукових публікацій про сучасні аспекти проблем, пов'язаних зі старінням жіночого організму. Доведено, що процеси старіння та анти-старіння обґрунтовують індивідуалізацію сучасних підходів до корекції ускладнень пре- і перименопаузи. Загальна стратегія підтримки здоров'я жінок в пери- та постменопаузі, за даними Міжнародного товариства з менопаузи, включає менопаузальну гормональну терапію з урахуванням цілей лікування та розрахунку індивідуальних чинників ризику. При всьому бажанні надати сучасне визначення старіння в даний час неможливо, тому в даному огляді зроблено спробу проаналізувати відомі стратегії передчасного старіння для розробки потенціалу продовження активного життя.

У будь-якому випадку лікарю необхідно співвіднести переваги і ризики менопаузальної гормональної терапії з урахуванням індивідуальних факторів ризику і вибрати відповідні методи реабілітації, спрямовані на «поліпшення жіночого обличчя» класичного образу старості. Оскільки роль естрогенної недостатності у формуванні ускладнень перименопаузи, а особливо передчасного старіння, не піддається сумніву, застосування стратегій антивікової терапії слід вважати патогенетично обґрунтованим методом лікування вазомоторних, психосоматичних симптомів і розладів сну, а також методом профілактики метаболічного синдрому. Слід пам'ятати про ряд обмежень і протипоказань до гормональної терапії, що є для кожного лікаря стимулом зробити свій внесок у справу продовження активного та здорового життя жінки у віці 40+ та 50+.

Створення концептуальної моделі подолання ускладнень репродуктивного старіння, особливо серцево-судинних подій, остеопорозу, цереброваскулярної патології на основі визначення факторів ризику дозволить розробити захисну антивікову терапію не тільки для продовження життя жінки, але й для поліпшення його якості.

**Ключові слова:** якість життя, репродуктивне старіння, менопаузальна гормональна терапія.

## КОНЦЕПЦІЯ ОСЛОЖНЕНИЙ РЕПРОДУКТИВНОГО СТАРЕНИЯ ЖЕНЩИН ДЛЯ ПРОВЕДЕНИЯ АНТИВОЗРАСТНОЙ ТЕРАПИИ

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Современное человечество за счет развития медицины и применения ее научно обоснованных инноваций научилось продлевать свою жизнь. В Украине, как и во всем мире, наблюдается тенденция к увеличению продолжительности жизни. Поскольку старение – закономерный физиологический процесс, человек испокон веков озабочен поиском так называемого «философского камня» – субстанции, предотвращающей старение.

В статье проанализированы данные зарубежных научных публикаций о современных аспектах проблем, связанных со старением женского организма. Доказано, что процессы старения и анти-старения обосновывают индивидуализацию современных подходов к коррекции осложнений пре- и перименопаузы. Общая стратегия поддержания здоровья женщин в пери- и постменопаузе, по данным Международного общества по менопаузе, включает менопаузальную гормональную терапию с учетом целей лечения и расчета индивидуальных факторов риска. При всем желании дать современное определение старению в настоящее время не представляется возможным, поэтому в данном обзоре сделана попытка проанализировать известные стратегии преждевременного старения для разработки потенциала продления активной жизни.

В любом случае, врачу необходимо соотнести преимущества и риски менопаузальной гормональной терапии с учетом индивидуальных факторов риска и выбрать соответствующие методы реабилитации, направленные на «улучшение женского лица» классического образа старости. Поскольку роль эстрогенной недостаточности в формировании осложнений перименопаузы, а особенно преждевременного старения, не подвергается сомнению, применение стратегий антивозрастной терапии следует считать патогенетически обоснованным методом лечения вазомоторных, психосоматических симптомов и расстройств сна, а также методом профилактики метаболіческого синдрома. Следует помнить о ряде ограничений и противопоказаний к гормональной терапии, что является для каждого врача стимулом внести свой вклад в дело продления активной и здоровой жизни женщины в возрасте 40+ и 50+.

Создание концептуальной модели преодоления осложнений репродуктивного старения, особенно сердечно-сосудистых событий, остеопороза, цереброваскулярной патологии на основе выделения факторов риска позволит разработать защитную антивозрастную терапию не только для продления жизни женщины, но и для улучшения ее качества.

**Ключевые слова:** качество жизни, репродуктивное старение, менопаузальная гормональная терапия.