

# UTERINE BLEEDINGS AND QUALITY OF WOMAN'S LIFE

## RESOLUTION OF ADVISORY BOARD

### INTRODUCTION

On March 12, 2019, an Advisory Board on impact of uterine bleedings on the quality of life of a woman was held in Kyiv, with participation of leading Ukrainian and European experts, which have an experience in researching of this problem. During the meeting special attention was paid on a role and place of prolonged and/or heavy menses in the formation of premenstrual symptoms and, respectively, the development of premenstrual syndrome (PMS) and premenstrual dysphoric disorder.

Taking into consideration modern regulatory documents, which define abnormal uterine bleedings (AUB) diagnostics and treatment in Ukraine, it is stated that the use of the recommendations which is listed in the Unified clinical protocol "Abnormal uterine bleedings" approved by the MoH of Ukraine №353 of April 13, 2016 [42], currently allows to adequately detect and treat this pathology and meets the modern international standards, first of all, the Guideline of International Federation of Gynecology and Obstetrics (FIGO) of 2011. However, this document does not set out an assessment of monthly bleedings impact on women's quality of life and today quite often both women and physicians underestimate the duration and menstrual bleeding loss and do not take into consideration a number of symptoms caused by heavy and prolonged menstruation. This causes a lack of appropriate management of this pathology.

The complexity of the problem of AUB in non-pregnant women is largely relates to the fact that they can be a manifestation of different by their nature disorders. In 2011, the international expert group under the auspices of FIGO has developed uterine bleedings classification system PALM-COEIN, which has been adopted in Ukraine, in the most other European countries, USA and Canada. The FIGO classification system includes 9 categories of AUB, 4 of which are caused by uterine pathology (PALM: polyp, adenomyosis, leiomyoma and malignancy/hyperplasia), and 5 are not related to organic changes (COEIN: coagulopathy, ovulatory dysfunction, endometrial dysfunction, iatrogenic causes, as well as a category that includes yet unclassified disorders) [40].

In 2018, changes were made to the PALM-COEIN classification, in particular: the diagnostic cri-

teria for adenomyosis were specified; AUB related to the use of anticoagulants and medicines, that suppress ovulation were categorized as AUB related to iatrogenic processes; a new potential cause of AUB, so-called "niche" of the uterus or an isthmocele after a caesarean section of the lower segment of the uterus, is attributed to the category "not otherwise unclassified" [40].

The updated in 2018 international recommendations (guideline of the UK National Institute for Health and Care Excellence (NICE) and FIGO) also offered a modern characteristics of parameters of normal menstrual cycle (Table) and the management of its possible disorders, which must be given special attention in clinical practice.

Such parameters of menstrual cycle as regularity, frequency and duration are relatively easy to establish based on menstrual calendar data, whereas menstrual blood loss is a rather subjective indicator.

Usually the threshold for diagnostics of heavy menstrual bleeding is considered to be menstrual blood loss >80 ml, but it should be noted that iron deficiency is already observed in case of monthly blood loss of more than 60 ml. Therefore, according to the opinion of international experts (NICE and FIGO recommendations, 2018), the choice of patient management tactics is determined not by blood loss measurement, but the patient's sense of well-being (distress, decrease of work ability, sexual activity and quality of life in general) [40, 41]. In women with acute or chronic AUB, a laboratory assessment of serum ferritin level should be conducted to detect iron deficiency and hemoglobin and/or hematocrit (it is advisable to conduct a general blood test) to diagnose anemia [40].

### SYSTEMIC BIOLOGICAL EFFECTS OF MENSTRUATION

Historically, in all cultures, monthly bleedings in women were considered as the norm and even as a "purification" process. Why in recent decades so much attention has been paid to studying the problem of menstrual bleeding? That is why for millennia, and until the beginning of the 20th century, women experienced from 140 to 160 menstrual periods throughout their lives. Today a woman has an average of 450–480 menstruations, which means that their number has tripled [1, 2] in only 100 years, that

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**Table. System of normal menstrual cycle parameters identification (FIGO, 2018) [40]**

Parameter	Normal	Abnormal	
Frequency (interval between menstruations, days)	amenorrhea		
	infrequent (>38 days)		
	normal (≥24 – ≤38 days)		
	frequent (<24 days)		
Duration of menstruation (days)	normal (≤8 days)		
	prolonged (>8 days)		
Regularity	regular (cycle variation ≤7–9 days): 18–25 years of age ≤9 days; 26–41 years of age ≤7 days; 42–45 years of age ≤9 days		
	irregular (cycle variation ≥8–10 days)		
Menstrual flow (patient determined)	light		
	normal		
	heavy		
Intermenstrual bleeding	none		
	rarely		
	cyclic (predictable)	early cycle	
		mid cycle	
		late cycle	
Unscheduled bleeding on hormonal contraceptives (progestines, combined hormonal contraceptives, contraceptive vaginal ring, contraceptive patch)	not applicable (woman does not use gonadal steroid medication)		
	none (woman uses gonadal steroid medication)		
	present		

is a “blinking time”, in comparison to the evolution time of the Homo sapiens, estimated around 200 000 years. This huge change is related to an earlier age of menarche, fewer pregnancies, a decrease in the duration of breastfeeding and later menopause.

The physiology of the menstrual cycle is regulated by the fluctuations of 5 key hormones: luteinizing hormone (LH) and follicle stimulating hormone (FSH), which are produced by cells of the anterior pituitary gland; estradiol, progesterone and testosterone, which are produced by the ovaries [1]. The molecular mechanisms by which estradiol and progesterone control the menstrual cycle include the interaction between the endocrine and immune systems [1, 2–8]. In the premenstrual phase of the cycle, the reduction and fall of estradiol and progesterone levels triggers a cascade of events that includes the release of inflammatory molecules by mast cells and other immune cells.

This causes a local and systemic increase of key inflammatory mediators' concentration (chemokines, interleukin-8, matrix metalloproteinase-1, cyclooxygenase-2, an enzyme responsible for the synthesis of prostaglandins, as well as for inhibition of prostaglandin dehydrogenase expression). This, in turn,

leads to an increase in the concentration of prostaglandins PGE<sub>2</sub> and PGF<sub>2a</sub> [1, 8, 9]. In addition, a corresponding perimenstrual migration of leukocytes and macrophages occurs with a local increase of mast cells number [1, 2–8]. These cells produce and release cytokines that stimulate further leukocyte migration in endometrium. Together with the endometrial stromal cells they release matrix metalloproteinase, which results in destruction of the extracellular matrix, endometrial shedding and menstruation begin.

Mast cells play a key role in development of inflammation, they are present in the endometrium and myometrium, and are mainly localized in the basal layer of the endometrium itself [1, 3–7]. These cells are activated in response to a wide range of stimuli, including neurogenic factors, estrogen level fluctuations, and presence of menstrual blood in tissue [10]. Mast cells mediators in myometrium are histamine, serotonin, heparin, bradykinin, prostaglandins, tumor necrosis factor α and interleukins (IL-4, IL-6) [3].

Taking into consideration the aforementioned data, today a new view is forming on the pathophysiological processes, which lead to menstrual symptoms onset. In particular, the cyclic

premenstrual fall of estradiol and progesterone levels triggers degranulation of the mast cells and other immune cells in different organs, where local inflammation occurs in response to genetic and/or acquired vulnerabilities. This scenario may happen:

- 🔴 in the bowel's wall – menstrual worsening of bowel symptoms such as in the woman suffers from irritable bowel syndrome (IBS);
- 🔴 in the bladder wall – menstrual flares of bladder pain if she is vulnerable to recurrent cystitis and/or if she complains of symptoms of bladder pain syndrome;
- 🔴 in the vestibulum of the vagina – vestibulodynia or dyspareunia in women affected by vulvar vestibulitis or coital pain;
- 🔴 in the myometrium – adenomyosis development, and also progression of endometriosis in other organs (peritoneum, ovaries, bladder wall, bowel wall, upper third of the vagina, recto-vaginal septum and/or utero-sacral ligaments) if woman suffers from endometriosis;
- 🔴 in the meningeal dura mater and brain – headache worsening during menstruation if woman suffers from menstrual headache;
- 🔴 in the bronchi and lungs – progression of asthma if woman suffers from it (27% of asthmatic women suffers from menstrual attacks – up to 13 acute respiratory crisis per year) [38].

The local cyclic worsening of the inflammatory process causes abdominal and pelvic symptoms (with changes in the state of gut microbiota, inflammation of gut walls and pain, pelvic floor changes, and activation of gut-brain axis). At the same time, the cyclic fall of sex hormones levels causes brain related symptoms (dysregulation of serotonergic and dopaminergic receptors) with neuroinflammation and activation of the brain-gut axis (neurogenic bowel inflammation and pain, intestinal symptoms).

However it should be noted, that **menstrual inflammation is a physiological process that is necessary for the monthly endometrial restoration in non-pregnant women. Menstrual inflammation is physiological and menstrual symptoms are usually mild/minor or absent when three criteria are fulfilled:**

1. “resolving” (normal cytoarchitecture of the tissue is reconstructed, endometrium first);

2. limited in time;

3. adequate and sufficient by intensity to finalize the reconstruction to the histological and functional characteristics of the different tissues involved.

At the same time, if local and systemic inflammation associated with menstruation is excessive by intensity and duration, it can cause both different pathological symptoms with increasing severity, which associated with formation of such pathological conditions as PMS and premenstrual dysphoric disorder.

### **MENSTRUAL SYMPTOMS**

Vaginal bleeding is a primary genital sign of menstruation start. Menstruation may be accompanied by such symptoms as abdominal bloating and cramping, fatigue, food cravings, headache, mood swings, irritability and mastodynia [1]. Usually they are so frequent that they are considered as a part of "normal" menstruation, and respectively considered as ones, that not required a high quality management.

Heavy menstrual bleedings are associated with dysmenorrhea increase, iron deficiency anemia and concomitant conditions (weakness, fatigue, depression, concentration and memory difficulties, poor work productivity and loss of sexual drive). As mentioned above other menstrual symptoms may include perimenstrual worsening of asthma, allergy, joint pain and myalgia.

### ***Dysmenorrhea and heavy menstrual bleedings***

Primary dysmenorrhea is the most common the menstrual symptoms which occurs in about 90% of adolescents and more than 50% of menstruating women [11]. This pain is caused by uterine contractions associated with endometrial ischemia and with inflammatory molecules level increase (prostaglandins, vasopressin, leukotrienes, and numerous mediators of mast cells) [1, 5, 6, 11]. According to the systematic review, in case of heavy menstrual bleeding, the likelihood of dysmenorrhea occurrence increases by more than 4 times (OR (odds ratio) = 4.73 (95% CI (confidence interval) 2.95–7.58)), and in case of prolonged bleedings – in more than 2 times (OR = 2.38 (95% CI 1.69–3.37)) [12]. This in turn may increase the risk of endometriosis, which is the main cause of secondary dysmenorrhea and chronic pelvic pain [1, 13].

### ***Chronic pelvic pain***

Fluctuations of ovarian hormones during the menstrual cycle are associated with pain increase, which may be associated with concomitant diseases (painful bladder syndrome/interstitial cystitis, vulvar vestibulitis/provoked vestibulodynia/vulvodynia, IBS) [10, 14]. Pelvic and systemic inflammation is a prerequisite of chronic pelvic pain, concomitant diseases, neuroinflammation and depression [1, 10, 14]. Premenstrual reduction of estrogen level causes and potentiates mast cells degranulation in organs with already existing inflammation, and thus leads to a significant pelvic pain increase during the natural menstrual cycle and during the 7-day hormone free interval (HFI) in women using combined oral contraceptives (COCs) [15].

Menstrual symptoms can also be associated with neuroinflammation (menstrual migraine, mood changes, sleep disturbances, irritability).

### ***Menstrual migraine***

In women suffering from menstrual migraines a decrease in circulating estrogen levels occurring 2–3 days before menstruation is considered to be partially responsible for increase in migraine risk. Likely migraine occurrence is mediated by the degranulation of mast cells in dura mater and in the brain in synergy with up regulation of microglial cells with local release of inflammatory molecules [16–17].

### ***Mood disorders***

Inflammatory reactions also play an important role in the pathophysiology of mood disorders; in patients with depression, a higher level of proinflammatory cytokines, acute phase proteins, chemokines and cellular adhesion molecules is observed [10, 14]. Mood disorders can also be influenced by reducing fluctuations in estradiol levels and duration of HFI to 2–4 days in women using COCs [1].

### ***Gastrointestinal symptoms***

The gastrointestinal tract is the largest immune organ of the organism; it is intensively innervated and contains mast cells, receptors for immune mediators and neuropeptides. In women with IBS [19], the severity of symptoms varies during the menstrual cycle and tends to increase in the perimenstrual period. Compared to healthy women, women with IBS have more severe gastrointestinal symptoms associated with menstrual cycles (cramps, abdominal bloating, diarrhea and/or constipation).

### ***Bronchial asthma***

It is shown that the intensity of bronchial asthma manifestation varies during the menstrual cycle. Bronchial hyperactivity is more likely in the perimenstrual period than in other days of the cycle [20]. One third of the cases of acute respiratory distress in symptomatic women prevail during menstruation, leading to so-called perimenstrual asthma, which is related to increase in emergency department visits. Taking into account that reduction of estradiol and progesterone levels during menstrual cycle causes asthmatic crises in vulnerable women, new preventive strategies that are pathophysiologically oriented such as hormones levels stabilizing and reducing of COCs HFI interval can be proposed [1]. However, prospective, controlled trials are needed to prove it.

**Menstrual bleeding is a genital sign of systemic endocrine and inflammatory events. Severe menstrual symptoms are clinically correlated with local and systemic inflammation, which is not resolving (menstruation is excessive in duration and intensity, i.e. is not physiological). Therefore, reducing menstrual inflammation is important to reduce the frequency and intensity of menstrual symptoms and improve the quality of life of women of reproductive age.**

**Women need appropriate stable levels of estrogen and progesterone to optimize their physical and mental health.**

### **BIOLOGICAL EFFECTS OF COCs USE**

Today COCs are the most widely used contraceptives with more than 100 million users worldwide [21]. COCs not only effectively prevent pregnancy, but also have additional non-con-

traceptive benefits. Since the development of the first contraceptive pill (in the sixties of the previous century), COCs have undergone significant changes, which were most focused on reducing the dose of the estrogen component and the development of innovative progestogens with different pleiotropic effects. Historically traditional regimen of COCs (21+7) imitated the menstrual cycle for psychological reasons: also in the fifties women were "afraid" of amenorrhea as it was the first sign of a new (often unwanted) pregnancy, particularly when the family already had many children. The monthly "reassurance" of the cyclic bleeding was therefore considered essential for the pill to be accepted. However, the presence of a monthly withdrawal bleeding is not biologically necessary, from the strictly physiological point of view. Before express pregnancy tests were available, withdrawal bleeding served indeed as a signal for a woman taking COCs that she was not pregnant. However, there are currently not enough arguments regarding the need for menstruation during COCs use, and taking into consideration the abovementioned biological effects of menstruation, women using COCs need stable levels of estrogen and progesterone, the strongest indication being for women with different menstrual symptoms. [1].

According to the updated guidelines on COC use of the Faculty of Sexual and Reproductive Health of the UK Royal College of Obstetricians and Gynecologists (2019) [22], the presence of monthly bleeding during COCs use is not beneficial for women health, since a 7-day HFI may be associated with such symptoms as headache and mood changes, dysmenorrhea and/or pelvic pain, although on reduced intensity in comparison to the intensity of symptoms during the natural cycle.

The persistence of symptoms during the 7 day HFI between one pill box and the following is well reported in women's pain diary, focused on menstrual cycle.

Inhibition of ovarian activity during HFI decreases and follicle growth may occur. Mistakes in pills administration in the period which follows the HFI may increase the risk of ovulation and pregnancy that peaks if the pill is forgotten at the beginning of a new box of pills.

Taking of the first 7 tablets of a new box of COCs is the most important biological step to inhibit ovulation, while taking of following 8–21 maintains anovulation. At 3–4 day of a 7-day HFI, the FSH level increases, and stimulates the growth of the follicles in the ovary with endogenous estradiol synthesis [23], which leads to an increase in the incidence of estrogen-related symptoms, including nausea, mastodynia, fluid retention, mood changes, and headache pain. After start of COCs use from the next packaging, the FSH production is suppressed and the subsequent growth of the follicle stops, which resulting in follicular atresia and decrease in the concentration of estradiol. Similar to women who do not use hormonal contraceptives menstrual symptoms prevail during a 7-day HFI in women who use it [15]. In a study involving 262 women, pelvic pain, headache, mastalgia, abdominal bloating, and the need for analgesics use appeared much more frequently during the 7-day HFI compared to the 21 days of active pills taking [15].

In case, if after a 7-day HFI the woman will forget to start taking the pills from the next packaging on time, ovulation may occur [24]. In a randomized cohort study involving 3030 wom-

en, it was shown that 23% of women who had been taking COC in 21+7 regimen missed at least 1 tablet in the previous cycle (n = 737). 42% of these women made a mistake in drug administration during the first week after the 7-day HFI [25]. A study on 1438 women indicates that anxious women are the most vulnerable to forget fullness causing an inadequate intake of a daily contraceptive pill [39].

According to the updated guidelines on COC use of the Faculty of Sexual and Reproductive Health of the UK Royal College of Obstetricians and Gynecologists (2019) [22], women can take COCs continuously or can shorten HFI to avoid menstrual bleeding and associated symptoms. However, despite the fact that continuous use of COCs can reduce the frequency of withdrawal bleeding and hormone-withdrawal associated symptoms women may complain about irregular bleedings, which in turn reduces women's adherence to this regimen. It should be noted, the use of COC in continuous regimen is out of labeling. At the same time, the shortening of HFI to 4 or 2 days may reduce the risk of unintended pregnancy, also in case of mistakes in pills use [1, 25].

British clinical guidelines [22] also indicate, that most women may be prescribed COCs for 1 year during their first visit to a doctor, when a rigorous clinical history indicates adequate health, no contraindications and that a yearly follow-up is sufficient. This may prevent the premature COC withdrawal and reduce the risk of unintended pregnancy.

### THE RATIONAL OF COCs HORMONE-FREE INTERVAL SHORTENING

The use of COCs with shortened HFI (24+4, 26+2 regimen) may have several benefits:

1. More effective suppression of ovulation [1, 24, 26, 27]. Studies have shown that during COCs use with 21+7 regimen follicular growth may occur during a 7-day HFI; so, the probability of an ovulation may increase when woman forgot to take pills from the next packaging in time [25].
2. Good control of the cycle (less endometrial stimulation by endogenous estrogen, no increase in the number of irregular bleedings, when using a lower dose of estrogen) [26, 28].
3. Reduction of genital and systemic inflammation, which is associated with menstruation and symptoms, associated with fall of estrogen and progesterin that may negatively affect the quality of life of a woman [1].
4. Menstrual flow reduction, including women with heavy menstrual bleedings [29, 30].
5. Better compliance (packaging of the most COCs with shortened HFI contain 28 tablets (compared to COCs with 21+7 regimen), which may help to minimize mistakes in COCs use from the next packaging).

### Data supporting the necessity of COCs HFI shortening

In a study involving women, who used a combination of 20 µg ethynilestradiol (EE) and 3 mg drospirenone (DRSP), it was shown that a shortening of HFI to 3–4 days provides a more stable suppression of LH and FSH synthesis, and prevents the growth of follicles during HFI [27].

Shortening of HFI reduces the risk of accidental ovulation in case of pill miss in clinical practice and increases the con-

traceptive efficacy compare to the traditional 21+7 regimen. According to results of the study involving more than 50,000 patients, in a group of women who use a combination of estradiol valerate ( $E_2V$ )/dienogest (DNG) with 26+2 regimen, the contraceptive failure rate was lower (0.9%) compared to combination of EE/levonorgestrel (LNG) (2.8%) and other COCs (2.1%) [31].

During COC use with 24+4 regimen, there is more pronounced suppression of the follicle growth compared with COCs with 21+7 regimen, since in 22% of women significant growth of follicles (up to 13 mm) was observed during HFI [24, 27]. It can be suggested that 24+4 regimen will be an optimal choice for women with a tendency to develop functional ovarian cysts, since more pronounced inhibition of ovulation leads to a lower probability of these formations occurrence.

For women who suffer from symptoms associated with an increase in the production of endogenous sex hormones during the HFI, reducing the number of days without the use of hormones can minimize estrogen-dependent effects (including premenstrual dysphoric disorder [1, 32, 33]). During the use of combination of 20  $\mu$ g EE/DRSP with 24+4 regimen the frequency of physical and behavioral symptoms, including those associated with fluid retention (breast tenderness and body weight gain), was reduced. According to the clinical study data during the use of COC with 26+2 regimen ( $E_2V$ /DNG) the level of estradiol remains stable throughout the cycle, which contributes to a reduction of the intensity and frequency of hormone-withdrawal associated symptoms (headache and pelvic pain), as well as the reduction of the need in analgesics use during 22–28 days of the cycle [34].

Moreover, the use of the combination of  $E_2V$ /DNG with 26+2 regimen can reduce the menstrual bleedings in women with heavy menstrual bleedings (by 88% after 6 months of use) [26], improve the iron metabolism parameters (hemoglobin, hematocrit, ferritin) and increase the subjective sense of energy, and well-being [30]. In healthy women who use combination

of  $E_2V$ /DNG with 26+2 regimen the duration and intensity of withdrawal bleedings was lower compared with the use of a combination of 30  $\mu$ g EE/LNG with 21+7 regimen [36].

## CONCLUSIONS

1. Estrogen and progesterone levels fall in the premenstrual phase of the cycle are associated with a number of genital (for example, heavy menstrual bleedings, dysmenorrhea, pelvic pain) and systemic (depression, fatigue, headache, symptoms of irritable bowel syndrome, flares of bladder pain and/or of vestibulodynia, cyclic asthma attacks) symptoms, which are caused by local and systemic increase in the number of inflammatory molecules released by mast cells.

2. To maintain better physical and mental health women need stable levels of estrogen and progesterone. A stable level of estradiol is associated with a woman's better state of health as compared with the situation when its fluctuations occur.

3. During COCs selection for healthy women it is reasonable to give preference to COCs with short HFI (24+4, 26+2) compared to the traditional regimen (21+7), since the reduction of HFI provides a more stable level of estradiol, reduces the risk of casual ovulation in case of missed pill and increases contraceptive efficacy in comparison with the traditional regimen. In addition, it allows reducing the incidence of hormone-withdrawal associated symptoms that affect the quality of life of women, couples and families.

4. Women, who have symptoms during COCs use with 21+7 regimen (mastodynia, headache, bloating), which are associated with increase of endogenous hormone production should be recommended to switch to COC with shortened HFI (24+4, 26+2).

5. Selection of COC with a short HFI (24+4, 26+2) is especially important for women with PMS, heavy menstrual bleedings, primary dysmenorrhea, with a tendency to formation of functional ovarian cysts, bronchial asthma, menstrual migraine, arthritis, chronic pelvic pain associated with vulvodina, painful bladder syndrome/interstitial cystitis and irritable bowel syndrome.

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## МАТКОВІ КРОВОТЕЧІ ТА ЯКІСТЬ ЖИТТЯ ЖІНКИ

### Резолюція Експертної ради

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12 березня 2019 р. у Києві відбулося засідання Експертної ради з питань впливу маткових кровотеч на якість життя жінки, до роботи якої були залучені провідні вітчизняні та європейські фахівці.

Згідно з думкою міжнародних експертів (клінічні рекомендації Національного інституту здоров'я і якості медичної допомоги Великобританії та Міжнародної федерації гінекології та акушерства від 2018 р.), вибір тактики ведення пацієнтки визначається не результатом вимірювання кровотрати, а самопочуттям жінки (дистрес, зниження працездатності, сексуальної активності та якості життя).

Менструальні симптоми зазвичай є легкими і незначними або взагалі відсутні за умови, якщо менструальне запалення відповідає наступним трьом критеріям: «завершується» (відновлюється нормальна цитоархітектура тканини, перш за все ендометрія); обмежене в часі; адекватне і достатнє за інтенсивністю для завершення відновлення гістологічних та функціональних характеристик залучених тканин. Однак якщо локальне і системне запалення, асоційоване з менструацією, є надмірною та тривалистою, воно викликає різні патологічні симптоми. Тяжкі менструальні симптоми клінічно корелюють з місцевим та системним запаленням, яке не завершується (менструація є надмірною за тривалістю та інтенсивністю). Тому пригнічення менструального запалення є важливим для зменшення частоти проявів та інтенсивності менструальних симптомів і покращення якості життя жінок репродуктивного віку.

Для оптимізації фізичного та психічного здоров'я жінкам необхідні належні стабільні рівні естрогенів та прогестерону. При виборі комбінованих оральних контрацептивів для здорових жінок доцільно віддавати перевагу препаратом із коротким безгормональним інтервалом (24+4, 26+2) у порівнянні з традиційним режимом (21+7). Скорочення цього інтервалу забезпечує більш стабільний рівень естрадіолу, знижує ризик випадкової овуляції в разі пропуску таблеток, підвищує резерв контрацептивної надійності в порівнянні з традиційним режимом, а також дозволяє зменшити частоту появи симптомів, асоційованих з відміною гормонів.

**Ключові слова:** резолюція Експертної ради, аномальні маткові кровотечі, менструальні симптоми, комбіновані оральні контрацептиви, безгормональний інтервал.

## МАТОЧНЫЕ КРОВОТЕЧЕНИЯ И КАЧЕСТВО ЖИЗНИ ЖЕНЩИНЫ

### Резолюция Экспертного совета

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**и другие авторы**

12 марта 2019 г. в Киеве состоялось заседание Экспертного совета по вопросам влияния маточных кровотечений на качество жизни женщины, к работе которого были привлечены ведущие отечественные и европейские специалисты. Согласно мнению международных экспертов (клинические рекомендации Национального института здоровья и качества медицинской помощи Великобритании и Международной федерации гинекологии и акушерства от 2018 г.), выбор тактики ведения пациентки определяется не результатом измерения кровопотери, а самочувствием женщины (дистресс, снижение работоспособности, сексуальной активности и качества жизни).

Менструальные симптомы, как правило, являются легкими и незначительными или вообще отсутствуют при условии, если менструальное воспаление соответствует следующим трем критериям: «завершается» (восстанавливается нормальная цитоархитектура ткани, прежде всего эндометрия); ограничено во времени; адекватно и достаточно по интенсивности для завершения восстановления гистологических и функциональных характеристик привлеченных тканей. Однако если локальное и системное воспаление, ассоциированное с менструацией, является чрезмерным по интенсивности и продолжительности, оно вызывает различные патологические симптомы. Тяжелые менструальные симптомы коррелируют с местным и системным воспалением, которое не заканчивается (менструация избыточна по продолжительности и интенсивности). Поэтому подавление менструального воспаления является важным для уменьшения частоты проявлений и интенсивности менструальных симптомов и улучшения качества жизни женщин репродуктивного возраста.

Для оптимизации физического и психического здоровья женщинам необходимы надлежащие стабильные уровни эстрогенов и прогестерона. При выборе комбинированных оральных контрацептивов для здоровых женщин целесообразно отдавать предпочтение препаратам с коротким безгормональным интервалом (24+4, 26+2) по сравнению с традиционным режимом (21+7). Сокращение этого интервала обеспечивает более стабильный уровень эстрадиола, снижает риск случайной овуляции при пропуске таблеток, повышает резерв контрацептивной надежности по сравнению с традиционным режимом, а также позволяет уменьшить частоту появления симптомов, ассоциированных с отменой гормонов.

**Ключевые слова:** резолюция Экспертного совета, аномальные маточные кровотечения, менструальные симптомы, комбинированные оральные контрацептивы, безгормональный интервал.

## UTERINE BLEEDINGS AND QUALITY OF WOMAN'S LIFE

### Resolution of Advisory Board

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**and other authors**

On March 12, 2019, an Advisory Board on impact of uterine bleedings on the quality of life of a woman was held in Kyiv, with participation of leading Ukrainian and European experts.

According to opinion of international experts (guidelines of the UK National Institute for Health and Care Excellence and the International Federation of Gynecology and Obstetrics from 2018), the choice of patient management tactics is not determined by measuring blood loss, but by the patient's well-being (distress, decrease of work ability, sexual activity and quality of life).

Menstrual inflammation is physiological and menstrual symptoms are usually mild/minor or absent when three criteria are fulfilled: resolving (normal cytoarchitecture of the tissue is reconstructed, endometrium first); limited in time; adequate and sufficient by intensity to finalize the reconstruction to the histological and functional characteristics of the different tissues involved. At the same time, if local and systemic inflammation associated with menstruation is excessive by intensity and duration, it can cause different pathological symptoms. Severe menstrual symptoms are clinically correlated with local and systemic inflammation, which is not resolving (menstruation is excessive in duration and intensity). Therefore, reducing menstrual inflammation is important to reduce the frequency and intensity of menstrual symptoms and improve the quality of life of women of reproductive age.

Women need appropriate stable levels of estrogen and progesterone to optimize their physical and mental health. During combined oral contraceptives selection for healthy women it is reasonable to give preference to contraceptives with short hormonal free interval (24+4, 26+2) compared to the traditional regimen (21+7), since the reduction of this interval provides a more stable level of estradiol, reduces the risk of casual ovulation in case of missed pill, increases contraceptive efficacy in comparison with the traditional regimen and reduce the incidence of hormone-withdrawal associated symptoms.

**Keywords:** resolution of Advisory Board, abnormal uterine bleeding, menstrual symptoms, combined oral contraceptives, hormonal free interval.